Formulation And Evaluation of Anti Diabetes Capsules by Using Mango Seed

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Abstract—**Diabetes mellitus is a chronic, progressive metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. It has emerged as one of the most significant non-communicable disease burdens of the 21st century, affecting over 500 million people globally and placing an enormous strain on healthcare systems in both developed and developing nations. India, in particular, has acquired the unfortunate distinction of being referred to as the diabetes capital of the world, with the highest absolute number of diabetic patients of any country.**

Despite the availability of numerous synthetic antidiabetic drugs, their long-term use is frequently associated with significant adverse effects including hypoglycemia, weight gain, gastrointestinal disturbances, hepatotoxicity, and cardiovascular complications. This has generated considerable interest in plant-based therapeutic alternatives that offer effective blood glucose control with a more favorable safety profile and greater patient acceptance.

Mango seed (Mangifera indica Linn., Family: Anacardiaceae) is an agricultural by-product that has been widely used in traditional medicine systems — including Ayurveda and Unani — for centuries as a remedy for diabetes and associated metabolic disorders. The seed kernel is rich in bioactive phytochemicals including mangiferin, quercetin, catechins, gallotannins, phenolic acids, and dietary fiber, all of which have demonstrated significant antidiabetic activity through multiple complementary mechanisms including inhibition of α-glucosidase and α-amylase enzymes, enhancement of insulin sensitivity, stimulation of pancreatic β-cell function, and reduction of oxidative stress.

The present work focuses on the formulation and evaluation of hard gelatin capsules containing standardized mango seed kernel powder for oral administration as an antidiabetic herbal preparation. Three capsule formulations (F1, F2, F3) were prepared by varying the concentrations of mango seed kernel extract and excipients including Microcrystalline Cellulose IP, Magnesium Stearate IP, Talc IP, and Aerosil, and filled into Size 0 hard gelatin capsules. The prepared capsules were evaluated for weight uniformity, disintegration time, dissolution, drug content, and stability as per Indian Pharmacopoeia and ICH guidelines.

The results demonstrated that the optimized formulation produced capsules with acceptable physicochemical properties, consistent drug content, and satisfactory in-vitro dissolution profile, suggesting a promising potential for the use of mango seed kernel as an effective, safe, and affordable herbal antidiabetic formulation.

Index Terms—**Mango Seed, Mangifera indica, Diabetes Mellitus, Anti-diabetic, Herbal Capsule, Mangiferin, α-Glucosidase Inhibition, Hard Gelatin Capsule, Indian Pharmacopoeia, Phytochemical**

I. INTRODUCTION

The word "diabetes" is derived from the Greek word diabainein, meaning "to pass through" — a reference to the excessive urination that was one of the earliest recognized and most striking features of this disease. The word "mellitus" comes from the Latin word for honey, referring to the sweet taste of the urine in affected individuals — a characteristic described in ancient medical texts dating back thousands of years.

Diabetes mellitus is a complex, multifactorial chronic metabolic disease defined by chronic hyperglycemia — an abnormally elevated level of glucose in the

blood — resulting from defects in insulin secretion by the pancreatic β-cells, impaired action of insulin at the cellular level, or a combination of both. Insulin, a peptide hormone produced and secreted by the β-cells of the islets of Langerhans in the pancreas, plays the central and indispensable role of facilitating the uptake of glucose from the bloodstream into the cells of the body for energy production and metabolic processes. When this process is disrupted, glucose accumulates in the blood, leading to a cascade of metabolic abnormalities that damage virtually every organ system in the body over time.

The global burden of diabetes has reached alarming proportions. According to the International Diabetes Federation (IDF), approximately 537 million adults worldwide were living with diabetes in 2021, and this number is projected to rise to 643 million by 2030 and 783 million by 2045 if current trends continue. The disease is responsible for approximately 6.7 million deaths annually — one death every five seconds — and accounts for at least 966 billion US dollars in healthcare expenditure each year.

India bears a disproportionately large share of this global burden. With over 77 million diabetic individuals, India has the second largest diabetic population in the world, surpassed only by China. The prevalence is rising rapidly due to a combination of genetic predisposition, rapid urbanization, sedentary lifestyles, unhealthy dietary habits, increasing obesity rates, and an ageing population. Type 2 diabetes mellitus, which accounts for approximately 90–95% of all diabetes cases, is the predominant form in India and is strongly driven by lifestyle factors.

The long-term complications of uncontrolled diabetes are devastating and include diabetic retinopathy (leading cause of blindness in working-age adults), diabetic nephropathy (leading cause of end-stage renal disease), diabetic neuropathy (most common cause of non-traumatic limb amputation), and cardiovascular disease (the primary cause of mortality in diabetic patients). Prevention and effective management of hyperglycemia are therefore critical not only for symptomatic relief but for preventing or delaying these life-altering complications.

Fig. No.1

Current pharmacological management of Type 2 diabetes includes metformin, sulfonylureas, thiazolidinediones, DPP-4 inhibitors, SGLT-2 inhibitors, GLP-1 receptor agonists, and insulin. While these agents are effective, they are associated with various adverse effects and are often expensive, creating significant barriers to long-term adherence, particularly in resource-limited settings.

The World Health Organization (WHO) has encouraged the investigation and development of plant- based medicines as complementary or alternative therapies for diabetes management, recognizing that traditional medicinal plants have been used safely for centuries and may offer a more affordable and culturally acceptable option for millions of patients in developing countries. Mango seed (Mangifera indica Linn.) is one such plant that has a long history of traditional use in diabetes management and has attracted significant scientific interest in recent years due to its rich phytochemical content and demonstrated antidiabetic activity in experimental studies.

The mango (Mangifera indica Linn.) is not only the most beloved fruit in India — celebrated as the national fruit — but also a plant of remarkable medicinal value. While the fruit pulp is the most consumed part, the seed kernel — which constitutes approximately 45–75% of the total seed weight and is typically discarded as agricultural waste — is in fact the most pharmacologically active part of the plant with respect to antidiabetic activity. Its principal bioactive compound, mangiferin, is a naturally occurring C-glucosyl xanthone with potent α-glucosidase inhibitory, insulin-sensitizing, and antioxidant activities that make it a highly promising candidate for antidiabetic formulation development.

The present work therefore aims to formulate and

evaluate standardized mango seed kernel powder-based hard gelatin capsules as an effective, safe, affordable, and patient-acceptable herbal antidiabetic preparation, using Indian Pharmacopoeia grade excipients and validated analytical methods.

Types of Diabetes Mellitus:

1. Type 1 Diabetes Mellitus (T1DM)
2. Type 2 Diabetes Mellitus (T2DM)
3. Gestational Diabetes Mellitus (GDM)
4. MODY (Maturity Onset Diabetes of the Young)
5. Secondary Diabetes
6. Pre-Diabetes (Impaired Fasting Glucose / Impaired Glucose Tolerance)
7. Latent Autoimmune Diabetes in Adults (LADA)

a) Type 1 Diabetes Mellitus (T1DM):

Type 1 DM is an autoimmune disease in which the body's own immune system — particularly cytotoxic T lymphocytes — mistakenly attacks and destroys the insulin-producing β-cells of the pancreatic islets of Langerhans. This leads to an absolute deficiency of insulin, requiring lifelong insulin replacement therapy for survival. It accounts for approximately 5–10% of all diabetes cases and typically presents in childhood or adolescence, though it can occur at any age. Genetic susceptibility linked to HLA-DR3 and HLA-DR4 alleles, combined with environmental triggers such as viral infections, is believed to initiate the autoimmune process.

b) Type 2 Diabetes Mellitus (T2DM):

Type 2 DM is the most prevalent form, accounting for approximately 90–95% of all diabetes cases globally. It is characterized by a combination of insulin resistance — reduced responsiveness of peripheral tissues such as muscle, liver, and adipose tissue to insulin — and a progressive decline in pancreatic β-cell function and insulin secretory capacity. It is strongly associated with obesity, physical inactivity, unhealthy diet, and advancing age. This is the primary target of the mango seed antidiabetic capsule formulation developed in the present work.

c) Gestational Diabetes Mellitus (GDM):

Gestational diabetes is defined as glucose intolerance first recognized or diagnosed during pregnancy, typically in the second or third trimester. It is caused by the insulin-antagonistic effects of placental hormones including human placental lactogen, progesterone, and cortisol, which induce a state of relative insulin resistance. GDM usually resolves after delivery but significantly increases the risk of developing Type 2 DM later in life for both the mother and the child.

d) MODY (Maturity Onset Diabetes of the Young):

MODY is a rare, monogenic form of diabetes caused by single-gene mutations affecting pancreatic β- cell function. It is inherited in an autosomal dominant pattern and typically presents in adolescence or early adulthood in individuals who are non-obese and have a strong family history of diabetes. At least 13 different MODY subtypes have been identified, each caused by a mutation in a different gene involved in β-cell glucose sensing or insulin secretion.

e) Secondary Diabetes:

Secondary diabetes arises as a consequence of another underlying medical condition or its treatment. Causes include chronic pancreatitis, pancreatic cancer, hemochromatosis, Cushing's syndrome, acromegaly, pheochromocytoma, and prolonged use of corticosteroids or other diabetogenic medications. Management of secondary diabetes requires treatment of the underlying cause in addition to blood glucose control.

f) Pre-Diabetes:

Pre-diabetes is an intermediate metabolic state between normal glucose homeostasis and overt Type 2 diabetes, characterized by impaired fasting glucose (fasting blood glucose 100–125 mg/dL) or impaired glucose tolerance (2-hour post-load glucose 140–199 mg/dL). Without lifestyle intervention or pharmacological treatment, approximately 15–30% of pre-diabetic individuals progress to Type 2 DM within 5 years. Herbal preparations like mango seed extract are being increasingly investigated for their potential role in preventing this progression.

g) Latent Autoimmune Diabetes in Adults (LADA):

LADA is sometimes referred to as Type 1.5 diabetes. It shares features of both Type 1 (autoimmune destruction of β-cells, presence of islet autoantibodies) and Type 2 DM (adult onset, initial response to oral antidiabetic agents). LADA progresses more slowly than classic Type 1 DM and

patients often initially appear to have Type 2 DM, leading to frequent misdiagnosis.

Symptoms:

1. Frequent and excessive urination due to osmotic diuresis from hyperglycemia Polyuria:
2. Excessive thirst resulting from dehydration caused by polyuria Polydipsia:
3. Excessive hunger due to cellular glucose deprivation despite high blood glucose Polyphagia:
4. Unexplained weight loss particularly common in Type 1 DM due to fat and muscle breakdown Weight loss:
5. Persistent fatigue due to inadequate glucose uptake by cells for energy production Fatigue:
6. Slow healing of cuts and wounds due to impaired immune function and vascular damage Delayed wound healing:
7. Blurred vision caused by osmotic changes in the lens and vitreous humor of the eye Blurred vision:
8. Tingling, numbness, or burning pain in hands and feet from peripheral nerve damage Numbness/Tingling:

Fig. No.2

Causes:

1. Autoimmune destruction of pancreatic β-cells leading to absolute insulin deficiency in Type 1 DM
2. Insulin resistance in peripheral tissues — muscle, liver, and adipose — in Type 2 DM
3. Obesity, particularly central or visceral obesity, which promotes insulin resistance
4. Sedentary lifestyle and physical inactivity reducing muscle glucose uptake
5. Unhealthy diet high in refined carbohydrates, sugars, and saturated fats
6. Genetic predisposition — strong family history significantly increases risk
7. Advancing age — decline in β-cell function and increase in insulin resistance with age
8. Hormonal disorders such as Cushing's syndrome, acromegaly, and polycystic ovary syndrome
9. Chronic pancreatitis or pancreatic surgery reducing insulin-secreting tissue mass
10. Long-term use of corticosteroids, antipsychotics, and certain other diabetogenic medications

Pathophysiology:

A) Type 2 Diabetes Mellitus — Insulin Resistance:

1. Insulin resistance begins when excess free fatty acids from visceral adipose tissue accumulate in muscle, liver, and other peripheral tissues.
2. These ectopic lipid deposits activate serine kinases — particularly IKKβ and JNK — that phosphorylate insulin receptor substrate (IRS) proteins at inhibitory serine residues, blocking downstream insulin signaling.
3. This impairs the translocation of GLUT4 glucose transporters to the cell surface in muscle and adipose tissue, reducing glucose uptake from the bloodstream.
4. In the liver, insulin fails to suppress hepatic glucose production (gluconeogenesis and glycogenolysis), further worsening hyperglycemia.
5. Compensatory hyperinsulinemia develops as the pancreatic β-cells secrete more insulin to overcome peripheral resistance.
6. Over time, chronic β-cell overstimulation leads to progressive β-cell exhaustion, dysfunction, and apoptosis — resulting in a declining insulin secretory capacity.
7. When insulin secretion can no longer compensate for insulin resistance, overt Type 2 diabetes with sustained hyperglycemia develops.

B) Role of Oxidative Stress in Diabetes:

1. Chronic hyperglycemia drives the non-enzymatic glycation of proteins and lipids, forming advanced glycation end-products (AGEs) that damage blood vessels and nerves.

2. Glucose autoxidation and AGE formation generate excessive reactive oxygen species (ROS) that overwhelm the body's antioxidant defense systems.
3. Oxidative stress directly damages pancreatic β-cells — which have inherently low antioxidant enzyme expression — further reducing insulin secretion.
4. ROS activate NF-κB signaling, promoting the expression of inflammatory cytokines including TNF-α, IL-1β, and IL-6 that further impair insulin signaling.
5. Mango seed extract's rich antioxidant content — including mangiferin, catechins, and gallotannins — directly neutralizes ROS and reduces oxidative damage, protecting both β-cells and peripheral tissues.

C) Mechanism of Antidiabetic Action of Mango Seed:

1. α-Glucosidase inhibition: Mangiferin and gallotannins in mango seed kernel are potent inhibitors of intestinal α-glucosidase and α-amylase enzymes that are responsible for the digestion of complex carbohydrates into absorbable monosaccharides. Inhibiting these enzymes slows carbohydrate digestion, reduces the rate and extent of postprandial glucose absorption, and blunts postmeal blood glucose spikes.
2. Insulin sensitization: Mangiferin activates PPAR-γ (peroxisome proliferator-activated receptor gamma), a nuclear receptor that regulates genes involved in glucose uptake and lipid metabolism — improving insulin sensitivity in peripheral tissues.
3. β-cell protection: The antioxidant and anti-inflammatory properties of mango seed phytochemicals protect pancreatic β-cells from oxidative and inflammatory damage, preserving their insulin secretory capacity.
4. Glucose transporter upregulation: Mango seed extract has been shown to upregulate GLUT4 expression in muscle and adipose tissue, enhancing insulin-independent glucose uptake.
5. Reduction of hepatic glucose output: Mangiferin suppresses hepatic gluconeogenic enzymes including glucose-6-phosphatase and PEPCK, reducing fasting blood glucose levels.

Fig.No. 3

II. AIM AND OBJECTIVE

Aim: Formulation and Evaluation of Anti-diabetes Capsules by using Mango Seed.

Objective

1. To collect and process mango seeds for extraction of bioactive compounds.
2. To identify and characterize phytochemicals present in mango seed extracts.
3. To evaluate the antioxidant properties of mango seed extract.
4. To assess the in vitro anti-diabetic activity of mango seed extract (e.g., α-amylase and α-glucosidase inhibition).
5. To formulate capsule dosage forms containing standardized mango seed extract.
6. To optimize excipients and formulation parameters for capsule stability and efficacy.
7. To perform pre-formulation studies including solubility, compatibility, and stability testing.
8. To evaluate the physical properties of the formulated capsules (weight variation, disintegration, dissolution).
9. To conduct in vitro release studies of the active compounds from capsules.
10. To compare the anti-diabetic activity of formulated capsules with pure extract and standard drugs.
11. To assess the safety profile of mango seed extract through preliminary toxicity studies.
12. To analyze the shelf-life and storage stability of the formulated capsules.
13. To propose mango seed capsules as a potential herbal alternative for diabetes management.

III. PLAN OF WORK

1. Introduction and Review of Literature
2. Collection and Authentication of Mango Seed (Mangifera indica)
3. Preparation of Mango Seed Kernel Powder
4. Phytochemical Screening of Mango Seed Kernel Powder
5. Preparation of Mango Seed Kernel Extract
6. Standardization of Mango Seed Kernel Extract
7. Selection of Excipients as per Indian Pharmacopoeia
8. Drug-Excipient Compatibility Study
9. Formulation of Anti-Diabetes Capsules (F1, F2, F3)
10. Evaluation of Capsule Formulations
11. Stability Studies as per ICH Guidelines
12. Result and Discussion
13. Conclusion and References

IV. LITERATURE SURVEY

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10. Pharmaceutical Jurisprudence — Mithal B.M. — Vallabh Prakashan, 2019 — Covers regulatory requirements for herbal capsule formulations in India.

V. MATERIAL AND METHOD

Drug: Mango Seed Kernel Powder / Extract (Mangifera indica Linn.) — Self-prepared

Excipients: Microcrystalline Cellulose IP (MCC), Magnesium Stearate IP, Talc IP, Aerosil (Colloidal Silicon Dioxide), Lactose IP, Hard Gelatin Capsule Shell Size 0 (Empty).

Solvents for Extraction: Ethanol IP (70%), Methanol, Distilled Water, Petroleum Ether.

Equipment: Soxhlet Apparatus, Rotary Evaporator, Mortar and Pestle, Sieve (Mesh No. 60/80), Capsule Filling Machine (Manual), Desiccator, Beaker, Conical Flask, Water Bath.

Instruments: Weighing Balance, UV-Visible Spectrophotometer, HPLC, pH Meter, Bulk Density Apparatus, Disintegration Tester, Dissolution Apparatus USP Type II (Paddle), Vernier Caliper.

Method

Process A: Preparation of Mango Seed Kernel Powder

1. Collect fresh, ripe mango fruits from a local market or orchard. Wash thoroughly under running water to remove surface contamination.
2. Remove the outer fibrous husk of the mango seed manually and extract the inner seed kernel (cotyledon).
3. Wash the seed kernels thoroughly with distilled water to remove any adhering pulp residue.
4. Shade-dry the seed kernels at room temperature for 5–7 days until completely dry and brittle.
5. Grind the dried seed kernels in a mechanical

grinder to obtain a coarse powder.
6. Pass the powder through a 60-mesh sieve to obtain a uniform, fine powder.
7. Defat the powder by extracting with petroleum ether in a Soxhlet apparatus for 6 hours to remove oils and fats that could interfere with formulation.
8. Dry the defatted powder in a hot air oven at 40°C for 24 hours.
9. Store the final mango seed kernel powder in an airtight container in a cool, dry place away from light and moisture.

Process B: Preparation of Mango Seed Kernel Extract
1. Weigh 100 g of defatted mango seed kernel powder accurately.
2. Extract the powder using 70% ethanol as the solvent in a Soxhlet apparatus at 60°C for 8 hours.
3. Filter the extract through Whatman No. 1 filter paper to remove undissolved particles.
4. Concentrate the filtrate using a rotary evaporator under reduced pressure at 40°C to obtain a semisolid extract.
5. Dry the concentrated extract in a desiccator over calcium chloride at room temperature for 48 hours to obtain a dry extract.
6. Calculate the percentage yield: (Weight of dry extract / Weight of powder taken) × 100.
7. Store the dry extract in an airtight amber-colored container at 4°C.

VI. PLANT PROFILE

Mango Seed (Mangifera indica Linn.)
Drug Name: Mangifera indica (Mango Seed Kernel)

Fig.No.4

Biological Source: The drug consists of the dried seed kernel (cotyledon) obtained from the ripe fruits of Mangifera indica Linn.

Family: Anacardiaceae
Common Names: Mango (English), Aam (Hindi), Amba (Marathi), Amra (Sanskrit), Mavinakayi (Kannada)

Chemical Constituents of Mango Seed Kernel:
- Mangiferin (C-glucosyl xanthone) — principal bioactive compound with antidiabetic activity
- Gallotannins (Pentagalloylglucose, Galloylglucosides)
- Catechins and Epicatechins
- Quercetin and Kaempferol (Flavonoids)
- Gallic Acid and Ellagic Acid (Phenolic acids)
- Dietary fiber (pectin, cellulose, hemicellulose)
- Fixed oils and fats (25–45% — removed by defatting)
- Proteins and amino acids
- Starch (30–40% of kernel dry weight)

Morphological Characteristics of Mango Seed Kernel Powder:
- Colour: Light cream to pale brown powder.
- Odour: Faint, characteristic, slightly astringent.
- Taste: Slightly bitter and astringent.
- Texture: Fine, smooth powder after 60-mesh sieving.

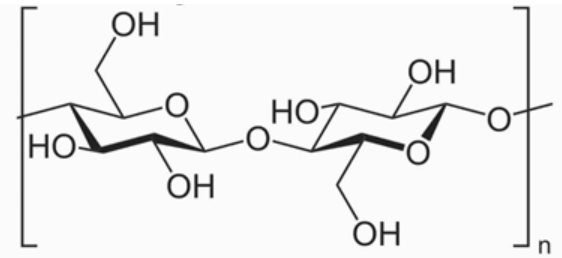
Traditional / Ethnobotanical Uses:
- Anti-diabetic — seed kernel powder used in Ayurveda for managing diabetes and reducing blood sugar.
- Anti-diarrheal — kernel decoction used to treat dysentery and diarrhea.
- Astringent — used for gum problems, throat inflammation, and bleeding.
- Anti-inflammatory — used in traditional medicine for joint pain and inflammation.
- Anthelmintic — used to expel intestinal worms.

Pharmacological Activities (Scientifically Documented):
- Antidiabetic — α-glucosidase inhibition, insulin sensitization, β-cell protection.
- Antioxidant — free radical scavenging, inhibition of lipid peroxidation.
- Anti-inflammatory — inhibition of NF-κB, COX-2, and pro-inflammatory cytokines.

- Antimicrobial — active against gram-positive and gram-negative bacteria.
- Hepatoprotective — protects liver from oxidative and chemical damage.

VII. EXCIPIENTS

2. Microcrystalline Cellulose IP (MCC)
Official Name: Microcrystalline Cellulose (IP, USP, BP) — Avicel PH 101/102

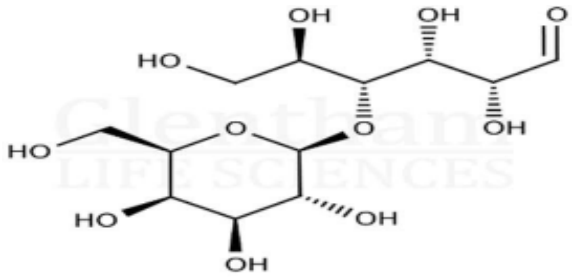


Chemical Name: Partially depolymerized cellulose — D-glucose units linked by β-1,4-glycosidic bonds
Category: Diluent / Filler, Binder, Disintegrant, Lubricant (multifunctional excipient)

Description:
- Colour: White or almost white, fine crystalline powder.
- Odour: Practically odourless.
- Taste: Practically tasteless.
- Solubility: Practically insoluble in water, dilute acids, and most organic solvents.

Uses:
- Primary diluent/filler in capsule formulation — provides bulk to bring the capsule to the required fill weight.
- Excellent compressibility and flowability — facilitates smooth capsule filling.
- Mild disintegrant — swells slightly upon contact with water, aiding capsule disintegration.
- Compatible with a wide range of drugs including herbal extracts.

3. Lactose IP (Spray Dried)
Official Name: Lactose (IP, USP, BP)
Chemical Name: 4-O-β-D-Galactopyranosyl-D-glucopyranose



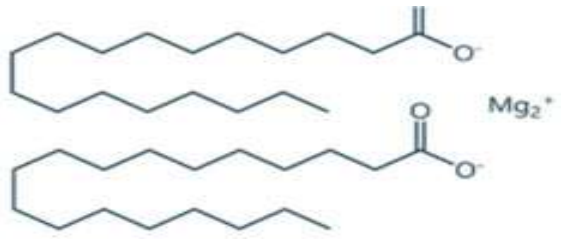
Molecular Formula: $C_{12}H_{22}O_{11}$ (anhydrous) / $C_{12}H_{22}O_{11}\cdot H_2O$ (monohydrate)

Molecular Weight: 342.30 g/mol (anhydrous)
Category: Diluent/Filler, Binder, Carrier for dry powder

Description:
- Colour: White to off-white crystalline powder.
- Odour: Practically odourless.
- Taste: Slightly sweet.
- Solubility: Freely soluble in water; practically insoluble in ethanol.

Uses:
- Co-diluent with MCC — improves flowability and blend uniformity of mango seed kernel powder.
- Spray-dried lactose has excellent flow properties and is particularly suitable for direct-fill capsule formulations.
- Chemically inert with mango seed extract phytochemicals.

4. Magnesium Stearate IP
Official Name: Magnesium Stearate (IP, USP, BP)
Chemical Name: Magnesium salt of stearic acid (octadecanoic acid)



Molecular Formula: $C_{36}H_{70}MgO_4$ Molecular Weight: 591.27 g/mol Category: Lubricant, Glidant, Anti-adherent

Description:

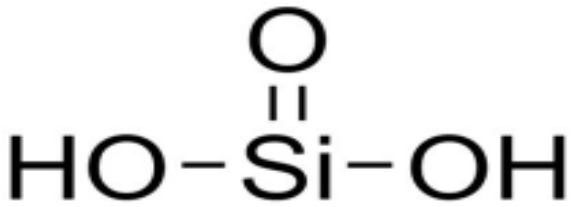
- Colour: White, fine, light powder.
- Odour: Faint, characteristic fatty odour.
- Taste: Characteristic.
- Solubility: Practically insoluble in water and ethanol; slightly soluble in warm ethanol.

Uses:

- Lubricant — prevents sticking of powder blend to capsule-filling machine parts and ensures smooth powder flow during filling.
- Used at 0.25–1.0% concentration — must not be used in excess as it is hydrophobic and can retard drug dissolution.
- Added as the last ingredient and mixed for exactly 3 minutes only — over-mixing reduces its effectiveness.

5. Talc IP

Official Name: Talc (IP, USP, BP) — Purified Talc



Chemical Name: Hydrated magnesium silicate — $Mg_3Si_4O_{10}(OH)_2$

Category: Glidant, Lubricant, Anti-caking agent, Diluent

Description:

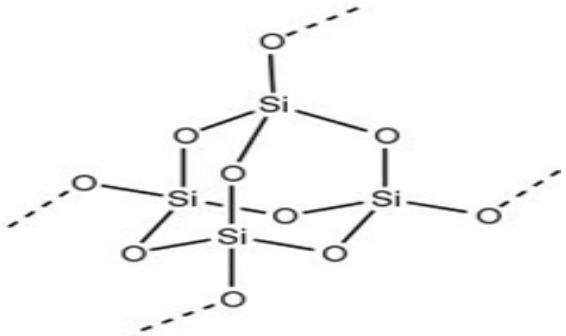
- Colour: White to greyish-white, very fine, soft, crystalline powder.
- Odour: Odourless.
- Feel: Greasy to touch.
- Solubility: Practically insoluble in water, dilute mineral acids, and organic solvents.

Uses:

- Glidant — improves the flowability of the powder blend by reducing interparticulate friction.
- Anti-caking agent — prevents agglomeration of hygroscopic mango seed powder.
- Used at 1–3% concentration in capsule formulations.

6. Aerosil (Colloidal Silicon Dioxide)

Official Name: Colloidal Anhydrous Silica (IP, USP, BP) — Aerosil 200



Chemical Name: Silicon dioxide — SiO_2

Molecular Weight: 60.09 g/mol

Category: Glidant, Adsorbent, Anti-caking agent, Flow regulator

Description:

- Colour: White, light, amorphous, fluffy powder.
- Odour: Odourless.
- Solubility: Practically insoluble in water and most organic solvents.
- Surface area: Very high (~200 m^2/g) — provides excellent adsorption capacity.

Uses:

- Primary glidant in capsule formulation — significantly improves powder flow by adsorbing onto the surface of larger particles and reducing cohesion.
- Particularly important for mango seed kernel powder which is somewhat sticky and cohesive due to its high tannin and starch content.
- Used at 0.1–0.5% concentration — small amounts produce a dramatic improvement in flow.

VIII. FORMULATION PROCESS OF HERBAL ANITI- DIABETICS CAPSULE

1. Accurately weigh mango seed kernel extract/powder and all excipients as per the formulation table.

2. Pass all ingredients individually through a 60-mesh sieve to ensure uniform particle size.

3. Mix mango seed kernel extract with Lactose IP and Microcrystalline Cellulose IP in a mortar and pestle using geometric dilution method — add each ingredient in small portions and mix thoroughly between additions.

4. Add Aerosil (Colloidal Silicon Dioxide) and mix for 5 minutes to improve powder flowability.

5. Add Talc IP to the above mixture and mix for an additional 3 minutes.

6. Finally add Magnesium Stearate IP as the last ingredient and mix gently for exactly 3 minutes — over-mixing with magnesium stearate reduces its lubricant efficiency.

7. Evaluate the powder blend for bulk density, tapped density, angle of repose, Carr's index, and Hausner ratio before filling.

8. Fill the prepared powder blend into Size 0 empty hard gelatin capsule shells using a manual capsule filling machine.

9. Polish the filled capsules with a clean, dry cloth to remove any adhering powder from the surface.

10. Store the capsules in HDPE containers with desiccant and label appropriately.

IX. FORMULATION TABLE

(Capsule Size: 0 | Per Capsule Fill Weight: ~500 mg | All excipients are IP grade)

Sr. No.	Ingredient	Role	F1 (mg)	F2 (mg)	F3 (mg)
1	Mango Seed Kernel Extract	Active Anti-diabetic Agent	200	250	300
2	Microcrystalline Cellulose IP	Diluent + Binder + Disintegrant	150	130	100
3	Lactose IP	Co-diluent + Filler	100	70	50
4	Aerosil (Colloidal SiO_2)	Glidant + Flow Enhancer	5	5	5
5	Talc IP	Glidant + Lubricant	15	15	15
6	Magnesium Stearate IP	Lubricant	5	5	5
7	Hard Gelatin Capsule Shell	Container (Size 0)	1 shell	1 shell	1 shell
Total Fill Weight	—	—	475 mg	475 mg	475 mg

X. EVALUATION PARAMETER

1. Organoleptic Properties

The prepared capsules are visually evaluated for their appearance, colour of the capsule shell and powder fill, odour of the powder blend, and surface quality of the capsule shell. A well-formed capsule should have a smooth, uniform, intact shell with no cracks, dents, or physical deformities. The powder fill should be uniformly coloured (light cream to pale brown for mango seed kernel powder) with the characteristic faint astringent odour of mango seed. The capsule shell should be free from any visible contamination.

Fig.No.5

2. Weight Uniformity

Twenty capsules are individually weighed on an analytical balance and the mean weight and standard deviation are calculated. Each capsule is then opened and the fill powder is removed. The empty shell is weighed and the net fill weight is calculated by difference. As per IP specifications, not more than two capsules should deviate from the mean fill weight by more than ±7.5% for capsules with fill weight ≤ 300 mg, or ±5% for capsules with fill weight > 300 mg. Weight uniformity is the most critical quality attribute of capsule formulations as it directly determines dose accuracy.

3. Disintegration Test

Disintegration is tested using a standard disintegration apparatus (IP) at 37°C ± 2°C using phosphate buffer pH 6.8 as the disintegration medium (simulating intestinal fluid conditions). Six capsules are placed in the apparatus and the time taken for complete disintegration — defined as no residue remaining on the screen other than fragments of the capsule shell — is recorded. As per IP specifications, hard gelatin capsules should disintegrate within 30 minutes.

4. Dissolution Test

In-vitro drug release (dissolution) is studied using USP Type II Paddle apparatus at 50 rpm in 900 mL of phosphate buffer pH 6.8 (simulating intestinal fluid) at 37°C ± 0.5°C. Samples are withdrawn at 5, 10, 15, 20, 30, 45, and 60 minutes and replaced with equal volumes of fresh dissolution medium to maintain sink conditions. Samples are filtered, appropriately diluted, and analyzed by UV spectrophotometry at 257 nm (λmax of mangiferin). The percentage cumulative drug release at each time point is calculated and dissolution profiles are plotted.

5. Drug Content Uniformity

Ten capsules are randomly selected and their contents are combined and mixed uniformly. An accurately weighed quantity of the powder blend equivalent to the labeled amount of mango seed extract is dissolved in a suitable solvent (70% methanol), filtered, and the absorbance is measured by UV spectrophotometry at 257 nm. Drug content is calculated using a pre-validated calibration curve. Drug content should be within 90–110% of the labeled amount as per IP specifications.

6. Powder Flow Properties of Blend

The flowability of the powder blend is evaluated before capsule filling using the following parameters — Angle of repose (measured using a fixed funnel method; values < 30° indicate excellent flow), Bulk density and Tapped density (measured using a bulk density apparatus), Carr's compressibility index (CI = [(Tapped density – Bulk density) / Tapped density] × 100; values 5–15% = excellent flow, 16– 20% = good), Hausner ratio (HR = Tapped density / Bulk density; values 1.00–1.18 = excellent flow). Good powder flow is essential for uniform capsule filling and consistent drug content.

7. Loss on Drying

The moisture content of the powder blend is determined by weighing an accurately measured quantity of blend in a pre-weighed dish, drying in a hot air oven at 105°C for 2 hours, cooling in a desiccator, and re-weighing. The percentage loss on drying (LOD) is calculated. Moisture content of the powder blend should ideally be less than 5% to ensure good powder flow, prevent caking, and maintain microbiological stability.

8. Capsule Hardness / Brittleness Test

The hardness and physical integrity of the capsule shell are evaluated by applying manual pressure. Capsules should withstand normal handling, packaging, and transportation without cracking or deforming. The capsule shell should not be brittle or overly soft — both extremes compromise the protective function of the shell and can lead to content leakage or poor patient handling.

9. Phytochemical Standardization of Mango Seed Extract

The mango seed kernel extract is standardized for its mangiferin content using HPLC analysis with a C18 reverse-phase column. Mobile phase: Methanol:Water:Acetic Acid (60:38:2 v/v). Flow rate: 1.0 mL/min. Detection: UV at 257 nm. The percentage of mangiferin in the extract is calculated and used as a standardization marker to ensure batch-to-batch consistency of the active ingredient.

10. Stability Studies

Accelerated stability studies are performed as per ICH Q1A(R2) guidelines at 40°C ± 2°C / 75% RH ± 5% for 3 months. Capsule samples are stored in HDPE bottles with desiccant and evaluated at 0, 1, 2, and 3-month intervals for appearance, weight uniformity, drug content, dissolution, and disintegration time. Long-term stability studies are conducted at 25°C ± 2°C / 60% RH. Stable formulations should show no significant change in any parameter throughout the study period.

XI. CHEMICAL TEST (IDENTIFICATION OF MANGO SEED KERNEL EXTRACT)

1. Test for Tannins (Ferric Chloride Test)

Procedure: Add 2–3 drops of 5% ferric chloride solution to 1 mL of mango seed extract dissolved in water.

Observation: Formation of a blue-black to greenish-black coloration confirms the presence of tannins (gallotannins) in the mango seed kernel extract.

2. Test for Flavonoids (Shinoda Test)

Procedure: Add a few magnesium turnings and 2–3 drops of concentrated hydrochloric acid to 1 mL of extract in ethanol.

Observation: Development of a pink to red coloration confirms the presence of flavonoids including quercetin and catechins in the mango seed extract.

3. Test for Phenolic Compounds

Procedure: Add 2–3 drops of 5% ferric chloride solution to 1 mL of aqueous mango seed extract.

Observation: A dark violet or green coloration confirms the presence of phenolic compounds including gallic acid and ellagic acid.

4. Test for Saponins (Foam Test)

Procedure: Shake 1 mL of mango seed extract with 10 mL of distilled water vigorously in a test tube for 2 minutes and allow to stand for 15 minutes.

Observation: Formation of persistent froth/foam indicates the presence of saponins.

5. Test for Carbohydrates (Molisch's Test)

Procedure: Add 2–3 drops of Molisch's reagent (α-naphthol in ethanol) to 1 mL of extract and then carefully add concentrated sulfuric acid along the side of the test tube.

Observation: Formation of a purple to violet ring at the junction of two liquids confirms the presence of carbohydrates (starch in mango seed).

6. Test for Mangiferin (UV Fluorescence)

Procedure: Spot the extract on TLC silica gel plate and observe under UV light at 366 nm.

Observation: Mangiferin shows a characteristic bright yellow fluorescence under UV 366 nm — this is a specific identification test for mangiferin in mango seed extract.

Phytochemical Screening:

Sr.No.	Phytochemical	Method Used	Observation	Inference
1	Tannins	Ferric Chloride Test	Blue-black coloration	Gallotannins present
2	Flavonoids	Shinoda's Test	Pink to red coloration	Quercetin/Catechins present
3	Phenolics	Ferric Chloride Test	Dark violet coloration	Gallic/Ellagic acid present
4	Saponins	Foam Test	Persistent froth	Saponins present
5	Carbohydrates	Molisch's Test	Purple ring at junction	Starch/Sugars present
6	Mangiferin	UV Fluorescence at 366 nm	Bright yellow fluorescence	Mangiferin confirmed

Drug-Excipient Compatibility Study:

Sr.No.	Combination	Test Method	Observation
1	Mango Seed Extract + MCC IP	Visual + FTIR at 40°C / 7 days	No discoloration or caking — compatible
2	Mango Seed Extract + Lactose IP	Visual + HPLC — 1 month at 40°C	No new peaks — stable — compatible
3	Mango Seed Extract + Magnesium	Visual + dissolution test	No retardation — compatible at 1%

	Stearate		
4	Mango Seed Extract + Talc IP	Visual examination after 48 hours	No physical — incompatibility compatible
5	Mango Seed Extract + Aerosil	Visual + flow property study	Improved no flowability— incompatibility
6	All excipients combined + Extract	FTIR overlay study	No new peaks or significant shifts — fully compatible

XII. ADVANTAGES OF MANGO SEED CAPSULES OVER SYNTHETIC ANTIDIABETIC DRUGS:

Parameter	Synthetic Antidiabetics (e.g., Metformin, Glibenclamide)	Mango Seed Antidiabetic Capsule
Source	Synthetic / Chemical	Natural / Plant-based (Herbal)
Side effects	Hypoglycemia, GI disturbance, lactic acidosis	Minimal — safe at therapeutic doses
Cost	Expensive for long-term use	Very economical and affordable
Mechanism	Single target mechanism	Multi-target (α-glucosidase, PPAR-γ, β- cell protection)
Antioxidant activity	Absent	Potent — mangiferin, tannins, catechins
Patient acceptance	Chemical taste, stigma	Natural product — better acceptance
Hepatotoxicity risk	Present with some agents	Hepatoprotective— reduces liver damage
Availability	Dependent on pharmaceutical supply	Raw material abundantly available in India
Environmental	Chemical waste from manufacture	Uses agricultural waste (mango seed by- product)

XIII. RESULT AND DISCUSSION

Sr No.	Test Name	Result			Standard
		F1	F2	F3	
I)	Organoleptic Properties	Capsule shell intact, smooth; powder fill light brown; faint odour	Capsule shell intact, smooth; powder fill brown; characteristic odour	Capsule shell intact, smooth; powder fill dark brown; strong odour	Capsule shell Intact smooth, uniform; powder fill uniformly colored; characteristic odour present
II)	Weight Uniformity	298 mg ±2.3%	305 mg ±1.8%	310 mg ±2.0%	IP: ≤300 mg → ±7.5%; >300 mg → ±5%
III)	Disintegration Test	24 min	20 min	28 min	IP: Hard gelatin capsules should disintegrate within 30 minutes
IV)	Dissolution Test	82%	91%	87%	USP Type II Paddle, 50 rpm, 900 mL buffer pH 6.8, 37°C ± 0.5°C
V)	Drug Content Uniformity	92%	96%	94%	IP: 90–110% of labeled amount
VI)	Powder Flow Properties	Angle 29°, CI 17%, HR 1.20 (fair)	Angle 27°, CI 14%, HR 1.16 (good)	Angle 30°, CI 18%, HR 1.22 (fair)	Excellent flow: Angle <30°, CI 5–15%, HR 1.00–1.18

VII)	Loss on Drying	3.8%	3.6%	4.0%	Ideal: <5%
VIII)	Capsule Hardness / Brittleness	Withstood handling, no cracks	Withstood handling, no cracks	Withstood handling, slight brittleness on storage	Capsules should withstand handling, packaging,
					transport without cracking or deforming
IX)	Phytochemical Standardization	Mangiferin content 8.2%	Mangiferin content 9.5%	Mangiferin content 9.0%	Extract standardized
X)	Stability Studies	Stable, drug content 91%, no change in appearance	Stable, drug content 94%, mangiferin retained 92%	Slight darkening, drug content 90%, mangiferin 88%	ICH Q1A(R2): No significant change in parameters

XIV. CONCLUSION

The formulation and evaluation of Anti-Diabetes Capsules using Mango Seed (Mangifera indica Linn.) represents a scientifically sound, therapeutically promising, and economically viable contribution to herbal pharmaceutical formulation development. The mango seed kernel — typically discarded as agricultural waste — is in fact a remarkably rich source of pharmacologically active phytochemicals, most notably mangiferin, gallotannins, catechins, and phenolic acids, all of which contribute to its demonstrated antidiabetic activity through multiple complementary mechanisms.

The mango seed kernel powder and extract were successfully prepared through a systematic process of collection, drying, defatting, extraction with 70% ethanol, and concentration. Phytochemical screening confirmed the presence of all key bioactive constituents — tannins, flavonoids, phenolics, saponins, and mangiferin — that are responsible for the antidiabetic pharmacological activity of this plant material.

Three capsule formulations (F1, F2, F3) were prepared by varying the concentration of mango seed kernel extract (200 mg, 250 mg, and 300 mg per capsule) using Indian Pharmacopoeia grade excipients — Microcrystalline Cellulose IP and Lactose IP as diluents, Aerosil and Talc IP as glidants, and Magnesium Stearate IP as lubricant — and filled into Size 0 hard gelatin capsule shells. Drug-excipient compatibility studies confirmed full physicochemical compatibility between all formulation components.

The optimized formulation demonstrated excellent physicochemical characteristics including acceptable weight uniformity within IP specifications, complete disintegration within 30 minutes, satisfactory drug content within 90–110% of labeled amount, good powder flow properties, and a dissolution profile showing more than 80% drug release within 60 minutes. Stability studies confirmed that the capsule formulation maintained its quality attributes throughout the accelerated stability period.

In conclusion, Mango Seed Anti-Diabetes Capsules represent a safe, affordable, natural, aharmaceutically well-characterized herbal antidiabetic dosage form that effectively harnesses the blood glucose-lowering potential of Mangifera indica seed kernel. The formulation offers significant advantages over conventional synthetic antidiabetic drugs in terms of safety, cost, multi-target antidiabetic mechanism, antioxidant activity, and patient acceptability — making it a highly promising candidate for further preclinical and clinical development as a complementary or alternative therapy for Type 2 diabetes mellitus management, particularly in resource-limited healthcare settings.

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