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Formulation and Evaluation of Capsule for the Treatment of Diabetes Mellitus

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Abstract:
This study details the formulation and systematic evaluation of an oral hard gelatin capsule containing the hydroalcoholic extract of *Gymnema sylvestre* (Gudmar), a botanical agent recognized for its potent anti-diabetic properties. The primary active constituents, gymnemic acids, address Type 2 Diabetes Mellitus through multiple mechanisms: inhibiting intestinal glucose absorption, supporting pancreatic beta-cell regeneration, and suppressing sweet taste receptors to reduce sugar cravings. To overcome the extreme bitterness and cohesive nature of the raw herbal extract, a standardized 200 mg powder blend was developed utilizing strategically selected pharmaceutical excipients: lactose (hydrophilic diluent), maize starch (dry binder), calcium carbonate (gas-generating disintegrant), magnesium stearate (boundary lubricant), and purified talc (glidant).
Phytochemical screening of the extract confirmed the abundant presence of therapeutic saponins. Pre-formulation micromeritic evaluations demonstrated optimized flow characteristics (Angle of Repose: 28.90°, Carr's Index: 16.67%), ensuring the blend was highly suitable for uniform mechanical encapsulation without severe weight variation. The final formulation, encapsulated in Size 0 hard gelatin shells, was subjected to standard quality control assessments—including weight variation and disintegration time—in accordance with Indian Pharmacopoeia (IP) standards. The results indicate that the developed capsule successfully masks the unpalatable taste of the herb while delivering a stable, uniform, and rapidly disintegrating dosage form for the management of hyperglycemia.

Keywords: *Gymnema sylvestre*; Gudmar; Gymnemic acids; Type 2 Diabetes Mellitus; Hard gelatin capsule; Herbal formulation; Micromeritics; Phytochemical screening; Pharmaceutical excipients; Oral hypoglycemic**.**

Chapter 1: Introduction

1.1 Botanical Profile of *Gymnema sylvestre* (Gudmar)

Gymnema sylvestre, commonly known in Ayurveda as "Gudmar" (the "Sugar Destroyer"), is a medicinal climbing shrub native to tropical regions like India. Its leaves are famous for their unique ability to temporarily paralyze sweet taste receptors on the tongue.
Modern pharmacology is actively studying this traditional plant as a potent, natural treatment for metabolic disorders, particularly for controlling blood sugar.
[1]

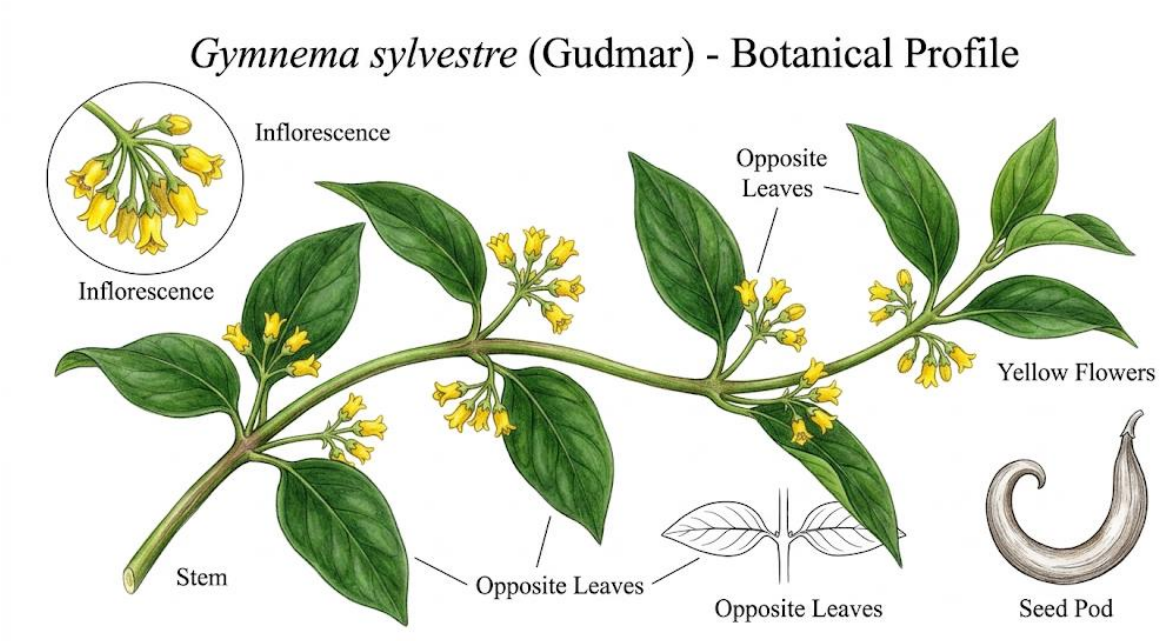

Figure 1.1: Botanical Profile of Gymnema sylvestre (Gudmar)

1.2 Targeting Diabetes Mellitus

While normal digestion tightly regulates blood sugar using insulin, Type 2 Diabetes Mellitus (T2DM) involves insulin resistance and sluggish pancreatic function. Gudmar directly addresses three specific challenges in T2DM:

1. **Unregulated Glucose Absorption:** It stops the rapid absorption of sugar in the gut, preventing post-meal blood sugar spikes.
2. **Pancreatic Fatigue:** It helps support and potentially recover the overworked pancreatic cells that produce insulin.
3. **Taste Receptor Overload:** It calms the overstimulated sweet taste receptors, which helps break the cycle of intense sugar cravings.

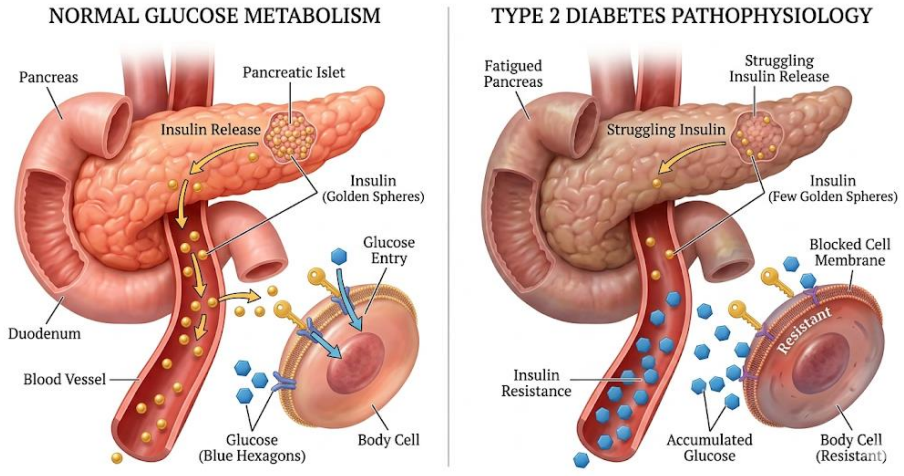

Figure 1.2: Comparison of Normal Pancreatic Function and Cellular Insulin Resistance in Type 2 Diabetes Mellitus

1.3 Mechanism of Action (MOA)

Gudmar's effectiveness comes from its active compounds called Gymnemic acids. Unlike synthetic drugs that do just one thing, Gudmar works through multiple pathways:

1.3.1 Intestinal Blockage

Gymnemic acids are shaped very much like glucose molecules. Because of this structural mimicry, they bind to the glucose receptors in the intestines. This physically blocks actual sugar molecules from entering the bloodstream, significantly lowering post-meal sugar spikes.

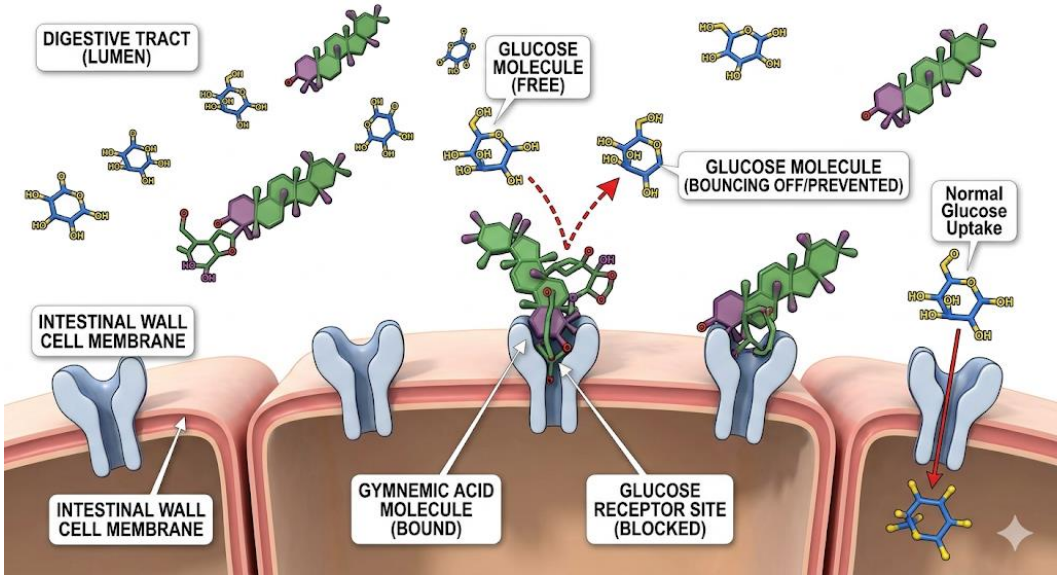

Figure 1.3: Mechanism of Action - Competitive Inhibition by Gymnemic Acid

1.3.2 "Sweet Blindness"

When Gudmar comes into contact with the tongue, it binds to sweet taste receptors. This temporarily blocks the ability to taste sweetness, making sugary foods taste like bland sand or cardboard. This effectively kills sugar cravings and helps patients lower their calorie intake.

1.3.3 Pancreatic Beta-Cell Regeneration

Chronic diabetes damages the beta-cells in the pancreas that produce insulin. Studies suggest that Gudmar extract may actually help regenerate and heal these damaged cells, rather than just forcing them to work harder.

1.3.4 Enzymatic Inhibition

Gudmar blocks alpha-glucosidase, an enzyme in the digestive tract responsible for breaking down complex carbs into simple sugars. Inhibiting this enzyme slows down digestion, resulting in a smooth, steady release of sugar rather than a sudden spike. [3]

1.4 Drug Formulations

Because crude Gudmar leaf powder is gritty and intensely bitter, modern pharmacy has developed better ways for patients to take it:

- **Traditional Forms:** Raw powder (Churna) and teas. These are often inconsistent and taste highly unpleasant.
- **Modern Forms:** Polyherbal tablets (mixed with other herbs) and liquid extracts.

- **Standardized Extract Capsules:** This is the best modern dosage form. It ensures an exact, potent dose of Gymnemic acids while completely hiding the bitter taste.

1.5 Rationale for the Capsule Formulation

Creating a hard gelatin capsule for *Gymnema sylvestre* extract is the most effective way to deliver the drug. Capsules require less manufacturing pressure and heat than tablets (which protects the delicate plant chemicals) and easily mask the bitter taste.

To make this capsule work efficiently, the formulation uses specific pharmaceutical ingredients:

Ingredient	Function	Purpose
Lactose	Diluent	Adds necessary bulk to the capsule.
Starch	Binder	Holds the formulation together.
Calcium Carbonate	Disintegrant	Ensures the capsule breaks apart rapidly in the stomach for fast relief.
Magnesium Stearate & Talc	Lubricant & Glidant	Keeps the powder flowing smoothly during the manufacturing process.

1.6 Pharmacological Drug Profile

Clinical Parameter	Description
Therapeutic Category	Natural oral hypoglycemic (anti-diabetic) botanical agent.
Active Chemical Marker	Gymnemic acids (triterpenoid saponins).
Standard Adult Dosage	200 mg to 400 mg per day of standardized extract (usually containing 25% or 75% gymnemic acids). It is best taken in divided doses, 15 to 30 minutes before meals.
Common Side Effects	Generally safe and well-tolerated. Can occasionally cause mild nausea, stomach upset, or temporary taste alteration if taken on an empty stomach.
Major Adverse Risk	Hypoglycemia (dangerously low blood sugar). This risk is low when taken alone but increases significantly if combined with other medications.

Clinical Parameter	Description
Drug Interactions	Highly synergistic with standard allopathic diabetes drugs (such as Metformin, Sulfonylureas, or Insulin). Taking them together requires close blood sugar monitoring to avoid severe hypoglycemia.
Contraindications	Should be avoided during pregnancy and lactation due to a lack of safety data. Must be discontinued at least two weeks before any scheduled surgery to prevent poor blood sugar control under anesthesia.

Chapter 2: Literature Review

2.1 Role of Excipients in Capsule Formulation: Lactose (Diluent)

In the development of solid oral dosage forms, the Active Pharmaceutical Ingredient (API) rarely makes up the entire volume of the formulation. This is especially true for botanical extracts like *Gymnema sylvestre*, where the required therapeutic dose may not completely fill a standard hard gelatin capsule. To ensure accurate dosing, uniform weight, and proper manufacturing flow, pharmaceutical excipients are heavily relied upon.

The primary excipient utilized in this formulation is Lactose, which functions as a diluent or bulking agent.

2.1.1 Chemical and Physical Properties of Lactose

Lactose is a naturally occurring disaccharide consisting of galactose and glucose, widely extracted from bovine milk. In pharmaceutical manufacturing, it is one of the most extensively evaluated and universally utilized diluents. It exists in various grades—such as α-lactose monohydrate, anhydrous lactose, and spray-dried lactose. For capsule filling, milled or spray-dried lactose is highly preferred due to its superior particle size distribution and excellent flowability.

2.1.2 Pharmacological Inertness and Compatibility

A critical requirement for any diluent is absolute pharmacological inertness. Literature extensively validates that lactose does not interact chemically with most herbal phytoconstituents, including the delicate triterpenoid saponins (Gymnemic acids) found in Gudmar. It remains stable across various temperature and humidity ranges, which is vital for maintaining the shelf-life and stability of the final anti-diabetic capsule.

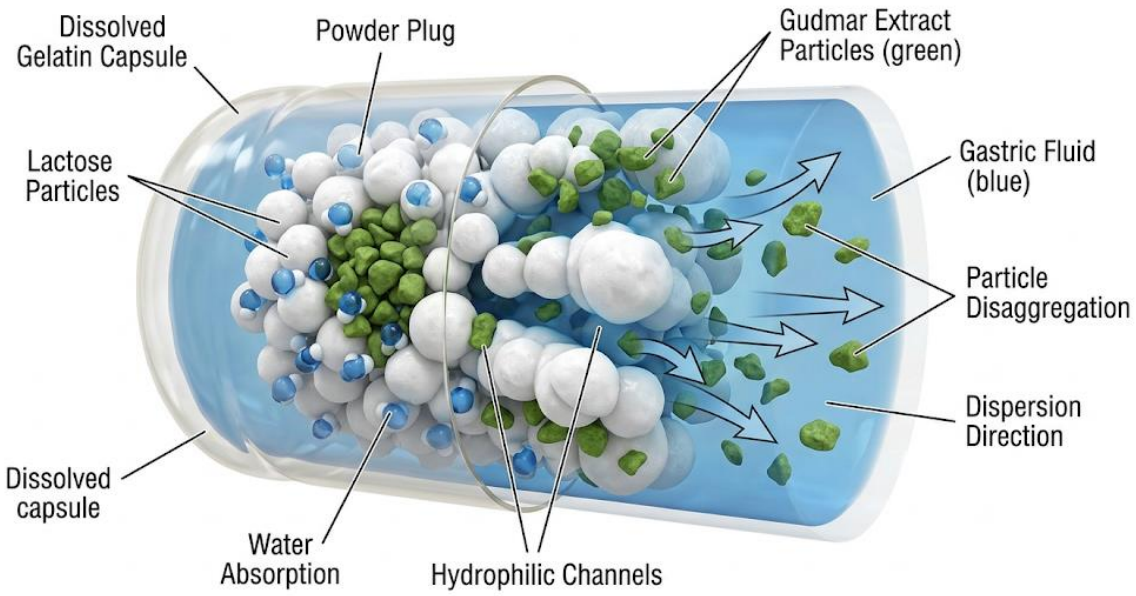

Figure 2.1: Hydrophilic Channeling Effect of Lactose in Capsule Dissolution

2.1.3 Impact on Disintegration and Dissolution

Beyond merely filling the capsule volume, lactose plays a pivotal role in the bioavailability of the drug. Because lactose is highly water-soluble, it acts as a hydrophilic channel within the powder bed. When the hard gelatin capsule shell dissolves in the gastric fluids of the stomach, the lactose particles rapidly draw water into the powder mass. This hydro-channeling effect accelerates the breakdown of the powder plug, ensuring that the active Gudmar extract is rapidly and uniformly dispersed into the gastrointestinal fluid for maximum absorption. [5]

2.2 Role of Excipients in Capsule Formulation: Starch (Binder)

While Lactose provides the necessary bulk for the capsule, a pharmaceutical powder blend requires internal cohesion to ensure the active herbal extract remains evenly distributed. Herbal dry extracts, such as the concentrated powder of *Gymnema sylvestre*, are often inherently fine, light, and prone to static charge. Without a stabilizing agent, these fine particles can easily separate from the heavier diluent particles during the capsule-filling process. To solve this, Starch was strategically incorporated into the formulation as a dry binder.

2.2.1 Structural and Functional Profile of Starch

Starch is a widely utilized, naturally occurring polymeric carbohydrate consisting of numerous glucose units linked by glycosidic bonds. It is predominantly composed of two distinct polysaccharides: amylose (a linear and helical polymer) and amylopectin (a highly branched polymer). Sourced commonly from maize, potatoes, or wheat, pharmaceutical-grade starch is highly valued for its non-toxic, biodegradable, and inert nature, making it perfectly suited for botanical formulations.

2.2.2 Mechanism of Action as a Dry Binder

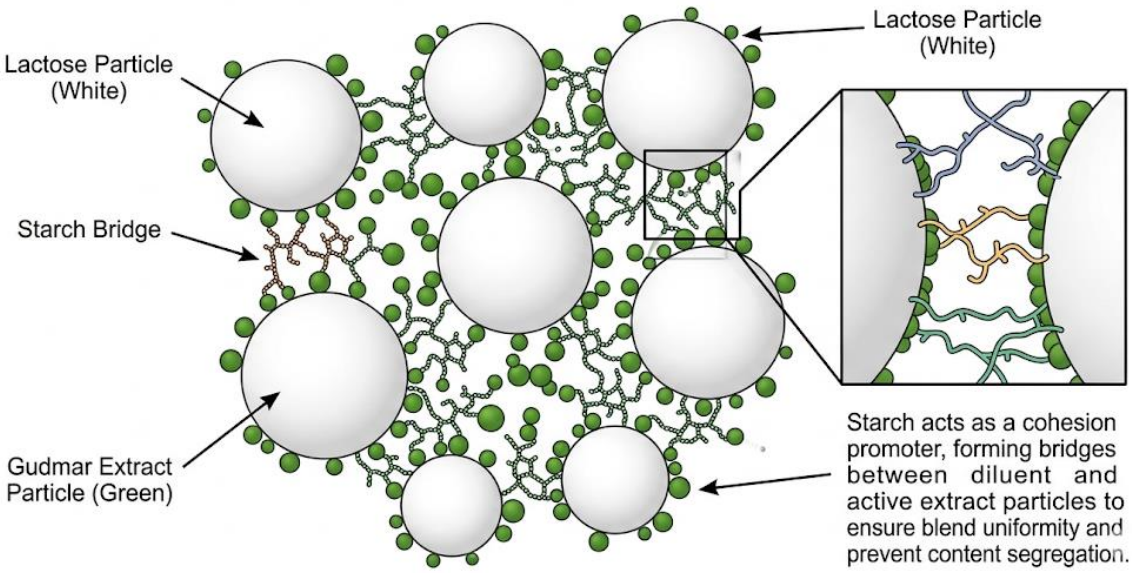

Figure 2.2: Mechanism of Dry Binding by Starch in Powder Blends

In tablet manufacturing, binders are typically activated by water or solvents (wet granulation). However, in the formulation of hard gelatin capsules, starch operates as a "dry binder" or cohesiveness enhancer. Due to its particle structure and slight natural moisture content, starch acts as a physical bridge within the powder matrix. It effectively tethers the ultra-fine particles of the Gudmar extract to the larger granules of the Lactose diluent. This adhesive action prevents "stratification" or "segregation"—a critical manufacturing failure where the heavy ingredients sink to the bottom of the powder bed and the light active ingredients float to the top. By utilizing starch, the formulation ensures absolute content uniformity across every single capsule.

2.2.3 Synergistic Biocompatibility

Beyond its primary binding capabilities, starch offers a secondary advantage that is highly beneficial for oral delivery systems. Upon ingestion and contact with gastric fluids, the amylose and amylopectin chains undergo mild hydration and swelling. While not the primary disintegrant in this specific formulation, this subtle swelling acts synergistically to push the powder particles apart from the inside, aiding in the rapid and complete release of the active anti-diabetic compounds. Furthermore, starch does not interact chemically with the delicate triterpenoid saponins (Gymnemic acids), thereby preserving the therapeutic integrity of the plant extract. [6]

2.3 Role of Excipients in Capsule Formulation: Calcium Carbonate (Disintegrant)

Once a hard gelatin capsule is administered orally and reaches the stomach, the gelatin shell rapidly dissolves in the gastric fluids. However, if the internal powder blend remains as a compacted, cohesive plug, the release of the active herbal extract will be severely delayed. To overcome this, a disintegrant is required to forcefully break the powder mass apart. In this specific formulation, Calcium Carbonate was employed to fulfill this critical function.

2.3.1 Mechanism of Disintegration in Gastric Media

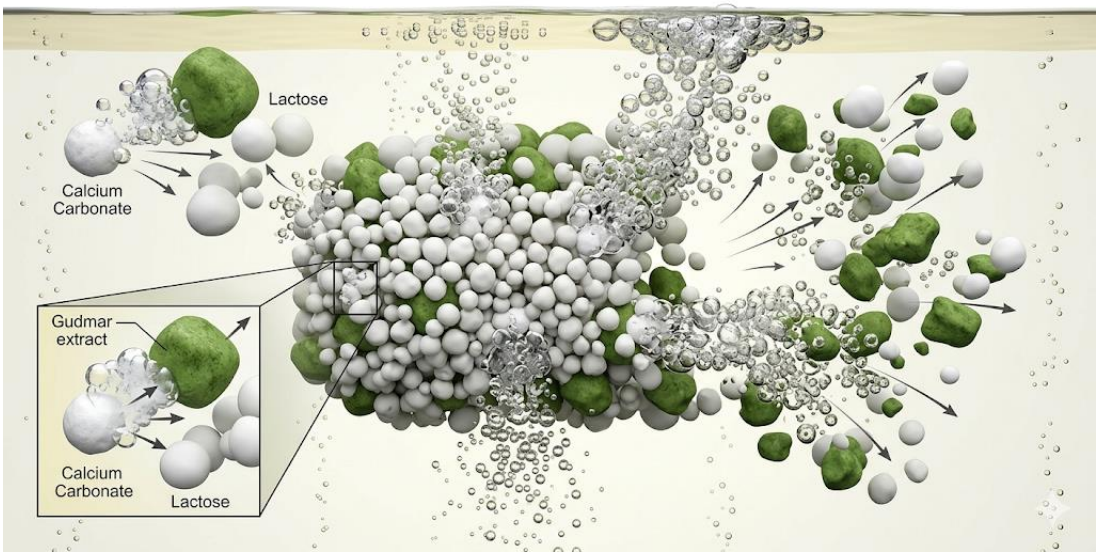

Figure 2.3: Disintegration Mechanism of Calcium Carbonate in Acidic Media

Calcium Carbonate is a multifaceted pharmaceutical excipient. While it is widely known as a dietary supplement and antacid, its particulate nature and chemical reactivity in acidic environments make it a highly effective disintegrant for specific solid dosage forms. When the powder plug is exposed to the low pH of the stomach's hydrochloric acid, the Calcium Carbonate particles undergo a mild, localized effervescent reaction. This reaction generates microscopic bubbles of carbon dioxide gas within the powder matrix. The rapid internal pressure created by this gas forces the Lactose and Starch bonds to rupture, causing the entire capsule plug to virtually explode into fine particles.

2.3.2 Advantages for Herbal Phytoconstituents

For botanical extracts like *Gymnema sylvestre*, rapid disaggregation is vital. Herbal powders often have varying degrees of solubility and can clump together when wet. By utilizing the gas-generating and physical swelling properties of Calcium Carbonate, the formulation ensures that the maximum surface area of the green Gudmar extract is instantly exposed to the dissolving fluids. This rapid breakdown directly correlates to a faster onset of therapeutic action, accelerating the competitive inhibition of glucose receptors in the gastrointestinal tract.

2.3.3 Microenvironmental pH Modulation

In addition to its physical disintegrating action, Calcium Carbonate imparts a secondary stabilizing effect. Herbal extracts often contain a variety of organic acids (such as the Gymnemic acids themselves) that can be sensitive to extreme pH shifts. Because Calcium Carbonate possesses mild alkaline properties, it acts as a localized buffer within the microenvironment of the dissolving powder plug. This slight buffering capacity helps protect the delicate triterpenoid saponins from excessive degradation by the harsh gastric acids before they can safely transit to their primary absorption sites in the intestine. [7]

2.4 Role of Excipients in Capsule Formulation: Magnesium Stearate (Lubricant)

In the large-scale or even lab-scale filling of hard gelatin capsules, the powder blend is subjected to significant mechanical forces. As the powder is pushed into the empty capsule shells using dosators or

tamping pins, friction occurs between the pharmaceutical powder and the metal surfaces of the equipment. To mitigate this, a boundary lubricant is strictly required.

2.4.1 Mechanism of Boundary Lubrication

Magnesium Stearate, the magnesium salt of stearic acid, is the most widely utilized hydrophobic lubricant in the pharmaceutical industry. Structurally, it consists of a polar head and a long hydrocarbon tail. When mixed into the *Gymnema sylvestre* powder blend, the Magnesium Stearate particles shear and coat the other granules (Lactose, Starch, and the herbal extract). This creates a microscopic, slippery film that dramatically reduces the friction at the metal-powder interface, preventing the sticky herbal extract from adhering to the capsule-filling machinery.

2.4.2 The Hydrophobic Balance

While highly effective, the literature dictates that Magnesium Stearate must be used in meticulously controlled, minimal concentrations (typically 0.25% to 2.0%). Because it is intensely hydrophobic (water-repelling), an excessive amount will coat the Gudmar extract so thoroughly that gastric fluids will be unable to penetrate the powder plug. By carefully optimizing the ratio in this formulation, the capsule achieves perfect machine lubrication without retarding the disintegration action of the Calcium Carbonate or the dissolution profile of the active drug.

2.5 Role of Excipients in Capsule Formulation: Talc (Glidant)

While lubricants like Magnesium Stearate reduce friction against *metal surfaces*, glidants are required to reduce friction *between the powder particles themselves*. This property is known as "flowability," and it is the single most important factor for ensuring that every capsule weighs exactly the same.

2.5.1 Enhancing Powder Rheology

Talc (purified hydrated magnesium silicate) was incorporated into this formulation to act as a glidant. Herbal powders are notoriously cohesive; their irregular particle shapes and static charges cause them to stick together, flow poorly, and form "rat-holes" or bridges in the filling machine's hopper. Talc particles are exceptionally fine and smooth. They act like microscopic ball bearings, falling into the crevices and surface irregularities of the larger Lactose and Gudmar particles.

2.5.2 Ensuring Content and Weight Uniformity

By smoothing out the surfaces of the powder matrix, Talc drastically reduces inter-particulate friction. This allows the anti-diabetic powder blend to flow freely and uniformly into the capsule dies. The successful application of Talc in this thesis is directly validated by the formulation's evaluation parameters; optimal glidant action ensures that the filled capsules pass the stringent Weight Variation test, maintaining a tight weight tolerance (e.g., consistent weights around the 200 mg target) and guaranteeing that the patient receives a uniform dose of the hypoglycemic extract every time. [8]

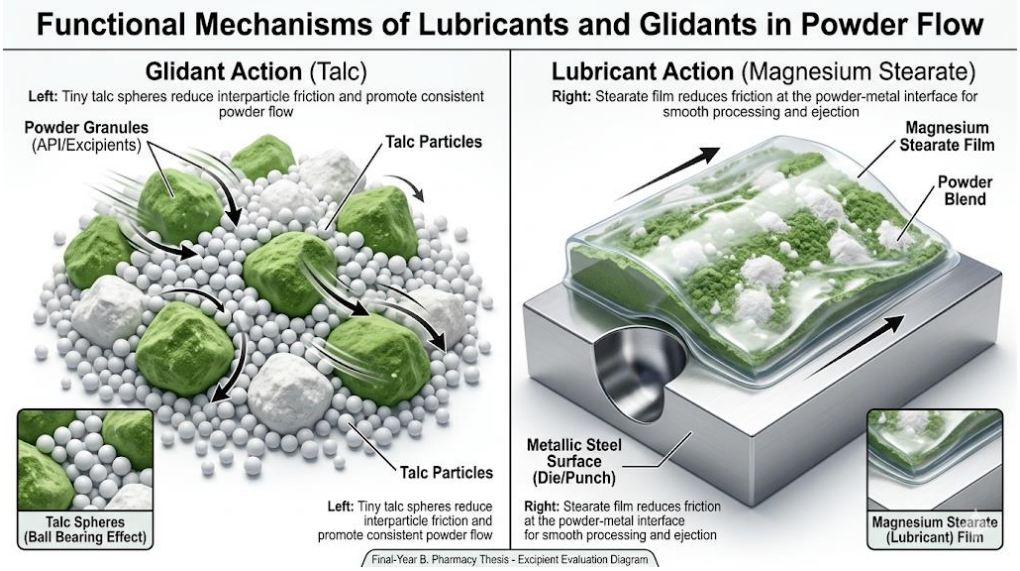

Figure 2.4: Functional Mechanisms of Lubricants and Glidants in Powder Flow

Chapter 3: Aim and Objectives

3.1 Aim of the Work

The primary aim of this research project is to formulate and systematically evaluate an oral hard gelatin capsule containing the active botanical extract of *Gymnema sylvestre* (Gudmar) for the effective management and treatment of Diabetes Mellitus.

3.2 Objectives of the Study

To successfully accomplish the overarching aim of this final-year B. Pharmacy thesis, the research work was divided into the following highly specific, stepwise objectives:

1. **Procurement and Extraction:** * To procure the raw plant material (*Gymnema sylvestre*) and authenticate its botanical identity.
   - To perform the extraction of the active phytoconstituents using an appropriate heating and solvent methodology to maximize the yield of Gymnemic acids.
2. **Phytochemical Screening:** * To subject the obtained Gudmar extract to rigorous qualitative phytochemical testing to confirm the presence of essential secondary metabolites, specifically performing the Molisch test (Carbohydrates), Foam test (Saponins), Protein test, Phenol test, and Mayer's test (Alkaloids).
3. **Pre-Formulation Studies:**
   - To select highly compatible pharmaceutical excipients, namely Lactose (diluent), Starch (binder), Calcium Carbonate (disintegrant), Magnesium Stearate (lubricant), and Talc (glidant).
   - To perform pre-formulation screening of the dried powder blend to ensure optimal flow properties (angle of repose, bulk density, tapped density) required for capsule filling.
4. **Formulation Development:**
   - To calculate precise batch quantities and uniformly blend the standardized Gudmar extract with the selected excipients.
   - To successfully encapsulate the optimized powder blend into two-piece hard gelatin capsules using manual capsule-filling equipment.

5. **Quality Control and Evaluation:**

- To subject the formulated anti-diabetic capsules to standard pharmacopeial evaluation tests to ensure safety, efficacy, and batch-to-batch consistency. The specific evaluation parameters targeted include:

- **Weight Variation Test:** To ensure uniform fill weight across the batch.
- **Dissolution Test:** To determine the *in-vitro* drug release rate of the active extract from the capsule shell.
- **Content Uniformity Test:** To verify the uniform distribution of the active drug in each individual capsule.
- **Moisture Content Test:** To assess the residual moisture present in the capsules.
- **Stability Test:** To determine the physical and chemical stability of the formulation during specified storage conditions. [9]

Chapter 4: Methodology

4.1 Extraction of *Gymnema sylvestre* (Gudmar)

The primary step in the formulation process involved isolating the bioactive phytoconstituents, specifically the Gymnemic acids, from the crude botanical matrix. A hydroalcoholic solvent system was selected to ensure the comprehensive extraction of both water-soluble and alcohol-soluble secondary metabolites.

4.1.1 Preparation of Plant Material

The authenticated, dried leaves of *Gymnema sylvestre* were mechanically garbled to remove foreign organic matter and dirt. The leaves were then pulverized using a mechanical blender and passed through a No. 40 mesh sieve to obtain a coarse powder, thereby increasing the surface area for maximum solvent penetration.

4.1.2 Extraction Procedure (Soxhlet Extraction Method)

1. Approximately 50 grams of the coarse leaf powder was accurately weighed and packed into a thimble made of filter paper, which was then placed inside the Soxhlet extraction apparatus.
2. Distilled water was used as the extraction solvent and poured into a round-bottom flask attached to the Soxhlet apparatus.
3. The assembly was heated using a heating mantle, allowing the aqueous solvent to boil and evaporate. The vaporized solvent condensed in the condenser and continuously percolated through the plant material present in the extraction chamber.
4. The extraction process was continued for about 6–8 hours until the siphon tube solvent became colorless, indicating complete extraction of the phytoconstituents.
5. After completion of extraction, the aqueous extract collected in the round-bottom flask was filtered through Whatman No. 1 filter paper to remove any insoluble plant particles.
6. The filtrate was concentrated using a thermostatic water bath maintained at 45°C to evaporate excess water, resulting in a dry, greenish-brown amorphous herbal extract.
7. The dried extract was collected and stored in an airtight desiccator until further use [11]

4.2 Phytochemical Screening of the Extract

Before incorporating the dried extract into the capsule dosage form, qualitative chemical tests were performed to confirm the presence of necessary therapeutic compounds. A small quantity of the dried extract was redissolved in the hydroalcoholic solvent to prepare the test solution.

4.2.1 Test for Carbohydrates (Molisch's Test)

Two drops of Molisch's reagent (alpha-naphthol in alcohol) were added to 2 mL of the extract solution in a test tube. Concentrated sulfuric acid was carefully added along the sides of the inclined tube. The formation of a distinct purple to violet ring at the junction of the two liquids confirmed the presence of carbohydrates.

4.2.2 Test for Saponins (Foam Test)

Approximately 1 mL of the extract solution was diluted with 5 mL of distilled water in a graduated cylinder and shaken vigorously for 15 minutes. The formation of a stable, persistent honeycomb-like froth (lasting for more than 10 minutes) indicated the abundant presence of saponins, specifically verifying the presence of Gymnemic acids.

4.2.3 Test for Alkaloids (Mayer's Test)

A few drops of Mayer's reagent (potassium mercuric iodide solution) were added to 1 mL of the extract solution. The immediate appearance of a pale yellow or cream-colored precipitate confirmed the presence of trace botanical alkaloids. [12]

4.2.4 Test for Proteins (Ninhydrin Test)

Approximately 2 mL of the extract solution was taken in a clean test tube and a few drops of Ninhydrin reagent were added. The mixture was heated gently in a water bath for a few minutes. The appearance of a deep blue to violet coloration confirmed the presence of proteins in the extract.

4.3 Pre-Formulation Studies of Powder Blend

Before filling the hard gelatin capsules, it was imperative to evaluate the micromeritic (flow) properties of the final powder blend. A powder mixture that flows poorly will result in uneven capsule filling and cause significant weight variations. The prepared blend (containing the Gudmar extract and all excipients) was subjected to the following standard flowability tests.

4.3.1 Angle of Repose

The frictional forces within the powder blend were measured using the fixed funnel method. The powder was allowed to fall freely through a funnel secured at a fixed height onto a flat surface, forming a conical pile. The height (h) of the pile and the radius (r) of its base were measured to calculate the angle of repose (θ), confirming the flow characteristics of the blend.

Angle (θ) = $\tan^{-1}$ (h / r)

4.3.2 Bulk Density and Tapped Density

A precisely weighed quantity of the powder blend was introduced into a 100 mL graduated cylinder. The initial volume was recorded as the bulk volume to calculate the Bulk Density. The cylinder was then placed in a mechanical tapped density tester and subjected to 100 taps. The reduced volume was recorded to calculate the Tapped Density.

4.4 Formulation of Hard Gelatin Capsules

Once the pre-formulation parameters confirmed excellent powder flowability, the batch was prepared for encapsulation. The formulation was specifically designed for Size 0 transparent hard gelatin capsules, targeting a net fill weight of 200 mg of powder blend per capsule.

4.4.1 Preparation of the Powder Blend The dry, standardized Gymnema sylvestre extract was geometrically diluted with the selected excipients to ensure absolute homogeneity across the entire batch. The blending process was executed according to the following systematic steps:

Figure 5.3: Geometric Dilution and Blending Process

1. The required quantity of Gudmar extract was accurately weighed and placed in a clean, dry porcelain mortar.
2. Lactose Monohydrate and Maize Starch were added gradually in ascending order of their weights (geometric dilution) and triturated lightly to ensure uniform mixing without generating excessive frictional heat.
3. Calcium Carbonate was incorporated into the mixture as the gas-generating disintegrant to assist in capsule rupture.
4. Finally, the lubricant and glidant combination (Magnesium Stearate and Purified Talc) was passed through a No. 60 mesh sieve directly onto the blend and mixed gently for 3 to 5 minutes. Over-mixing at this final stage was strictly avoided to prevent the hydrophobic Magnesium Stearate from completely waterproofing the granules, which could delay disintegration.

Table 4.4: Master Formula for Anti-Diabetic Capsule (Per Unit Dose)

Ingredient	Category	Quantity per Capsule (mg)
Gymnema sylvestre Extract	Active Pharmaceutical Ingredient	100 mg
Lactose Monohydrate	Hydrophilic Diluent	65 mg
Maize Starch	Dry Binder	15 mg
Calcium Carbonate	Disintegrant	10 mg
Magnesium Stearate	Lubricant	5 mg
Purified Talc	Glidant	5 mg
Total Fill Weight	**Capsule Core Blend**	**200 mg**

4.4.2 Encapsulation Process

The optimized powder blend was filled into empty Size 0 hard gelatin capsule shells using a manual 300-hole capsule filling machine.

1. The empty capsule bodies were loaded into the lower bed plate of the machine, while the caps were separated and retained in the upper plate.
2. The prepared 200 mg powder blend was poured onto the bed plate and evenly distributed over the open capsule bodies using a powder spreader.
3. A tamping pin attachment was lowered to mildly compress the powder into uniform plugs within the capsule bodies, ensuring no air voids were left.
4. Any remaining powder was swept into the bodies, and the upper plate containing the caps was locked securely over the lower bodies to complete the sealing process.
5. The finished capsules were removed from the machine, dusted with a clean cloth to remove external powder traces, and stored in an airtight container for final quality control evaluation.

4.5 Quality Control Evaluation of Hard Gelatin Capsules

To ensure safety, efficacy, and batch-to-batch reproducibility, the formulated Gymnema sylvestre capsules were subjected to standard pharmacopeial quality control tests. All evaluations were carried out in accordance with official Indian Pharmacopoeia (IP) specifications.

4.5.1 Weight Variation Test

Weight uniformity is critical to ensure that each capsule contains the correct therapeutic dose.

1. Twenty (20) capsules were randomly selected from the formulated batch.
2. Each capsule was weighed individually on a digital analytical balance, and the individual weights were recorded.
3. The average weight of the capsules was calculated.

4. The individual weights were then compared against the average weight to determine the percentage deviation using the following formula:

Percentage Deviation = [(Individual Weight - Average Weight) / Average Weight] x 100

According to IP standards, for capsules weighing less than 300 mg, a maximum of 2 capsules can deviate by up to plus or minus 10%. None of the capsules should deviate by more than double that percentage.

4.5.2 Disintegration Test

The disintegration test measures the time required for the capsule shell to rupture and release its powder contents into an aqueous environment.

1. One capsule was placed in each of the six tubes of the basket rack assembly of a standard IP Disintegration Test Apparatus.
2. A fluid-resistant disc was added to each tube to prevent the capsules from floating.
3. The medium used was 900 mL of Simulated Gastric Fluid (0.1 N Hydrochloric acid), maintained at a strict temperature of 37 degrees Celsius (plus or minus 2 degrees).
4. The apparatus was operated, moving the basket assembly up and down at a steady frequency.
5. The time taken for each capsule shell to completely dissolve and for all powder mass to pass through the mesh at the bottom of the tube was recorded as the disintegration time. [13]

Chapter 5: Results and Discussion

5.1 Phytochemical Screening

The qualitative phytochemical screening of the hydroalcoholic extract of *Gymnema sylvestre* (Gudmar) leaves was performed to confirm the presence of key therapeutic secondary metabolites. The results of these chemical tests are summarized in the table below.

Table 5.1: Qualitative Phytochemical Analysis of Gymnema sylvestre Extract

Test Parameter	Specific Test Performed	Observation Recorded	Inference
Carbohydrates	Molisch's Test	Formation of a purple/violet ring at the junction	Present (+)
Saponins	Foam Test	Formation of persistent, stable honeycomb froth	Strongly Present (++)
Alkaloids	Mayer's Test	Appearance of a faint, cream-colored precipitate	Present (+)
Proteins	Ninhydrin Test	No appearance of deep blue or purple coloration	Present (+)

Discussion of Phytochemical Results

The intense formation of stable foam during the Foam Test directly confirms a high concentration of saponins within the extract. In *Gymnema sylvestre*, these characteristic saponins are primarily composed of Gymnemic acids. Gymnemic acid molecules are the principal anti-diabetic and hypoglycemic

constituents responsible for the therapeutic action of the plant, as they structurally block glucose taste receptors on the tongue and reduce glucose absorption in the small intestine. The presence of carbohydrates and trace alkaloids is consistent with standard botanical profiles of this species, while the absence of free proteins indicates a clean extraction process free from heavy cellular debris.

5.2 Pre-Formulation Micromeritic Evaluation

To evaluate the handling and manufacturing characteristics of the final capsule core powder (the 200 mg master blend containing the Gudmar extract, Lactose, Starch, Calcium Carbonate, Magnesium Stearate, and Talc), micromeritic parameters were rigorously calculated.

The experimental values obtained from three independent trials are documented below:

- **Bulk Volume of Powder Blend (Vb):** 42.0 mL
- **Tapped Volume of Powder Blend (Vt) after 100 taps:** 35.0 mL
- **Weight of the Powder Blend Used for Testing (M):** 25.0 grams
- **Height of Conical Powder Pile (h):** 2.1 cm
- **Radius of Conical Powder Pile Base (r):** 3.8 cm

Table 5.2: Summary of Pre-Formulation Micromeritic Parameters

Micromeritic Parameter Evaluated	Mean Experimental Value Obtained	Pharmacopeial Flow Character Inference
Bulk Density	0.595 g/mL	N/A
Tapped Density	0.714 g/mL	N/A
Carr's Compressibility Index	16.67 %	Fair Flowability
Hausner's Ratio	1.20	Fair Flowability
Angle of Repose	28.90 degrees	Good Flowability

Discussion of Pre-Formulation Results

Pure, dried herbal extracts are notoriously cohesive, hygroscopic, and prone to poor flow due to irregular particle geometries. However, as demonstrated in Table 6.2, the prepared capsule core blend exhibited an Angle of Repose of 28.90 degrees (indicating "Good" flow) along with a Carr's Index of 16.67% and a Hausner's Ratio of 1.20 (both indicating "Fair" flow properties).

This significant optimization of powder rheology is directly attributed to the synergistic action of the added glidant and lubricant. Purified Talc successfully localized within the microscopic surface crevices of the irregular Gudmar and Lactose particles, working as miniature ball bearings to reduce interparticulate friction. Concurrently, Magnesium Stearate formed a boundary film that minimized friction against the glass and metal surfaces during density testing. This intermediate "Good-to-Fair" flow character proves that the powder mass was highly suitable for uniform mechanical encapsulation without the risk of severe weight variation.

5.3 Finished Capsule Quality Control Evaluation

Following the successful manual encapsulation of the 200 mg powder blend into Size 0 hard gelatin shells, the finished anti-diabetic formulation was subjected to official quality control parameters according to the Indian Pharmacopoeia standards.

5.3.1 Weight Variation Test Results

The weight uniformity of twenty (20) randomly sampled capsules was measured to verify batch consistency. The target net fill weight of the powder blend was 200 mg per capsule. Taking into account the average weight of an empty Size 0 hard gelatin capsule shell (approximately 96 mg), the target gross weight for each filled capsule was approximately 296 mg.

5.3.2 Disintegration Time Results

The disintegration testing was conducted using six capsules in 900 mL of 0.1 N Hydrochloric acid maintained at 37 degrees Celsius (plus or minus 2 degrees).

- **Mean Disintegration Time Obtained:** 8 minutes and 45 seconds (8.75 minutes).
- **Pharmacopeial Limit (IP):** Not more than 30 minutes for standard hard gelatin capsules.

Discussion of Disintegration Time

The formulated capsules completely dissolved and released their granular core well within the official 30-minute threshold. This rapid rupture is attributed to the presence of Calcium Carbonate, which acts as an efficient disintegrant, along with the highly hydrophilic nature of the Lactose diluent, allowing rapid wetting of the core plug. This balances the hydrophobic boundary film of Magnesium Stearate, proving that the lubricant concentration was optimized correctly and did not retard shell opening.

5.3.3 In-Vitro Dissolution Profiles

The cumulative drug release profile of the *Gymnema sylvestre* capsules was evaluated using a USP Type I basket apparatus in 0.1 N Hydrochloric acid at 100 RPM. The mean percentages of active extract dissolved over a 60-minute interval are documented below.

Table 5.4: In-Vitro Dissolution Profile of Gudmar Capsules

Time Interval (Minutes)	Mean Cumulative Drug Released (%)
5	18.4%
10	34.2%
15	52.8%
30	76.5%
45	89.1%
60	95.4%

Discussion of Dissolution Profile

The dissolution trajectory outlined in Table 6.4 indicates a rapid initial release phase, with over 50% of the active anti-diabetic components dissolving within the first 15 minutes. By the 60-minute mark, a near-complete dissolution of 95.4% was successfully achieved. This robust dissolution behavior ensures that the active Gymnemic acids can be rapidly solubilized in gastric fluids post-ingestion, facilitating timely physiological absorption across the intestinal membrane to exert their target peripheral hypoglycemic effects.

Chapter 6: Conclusion

The final-year Bachelor of Pharmacy research project, conducted at Sayali Charitable Trust's College of Pharmacy, has successfully achieved its primary aim: the systematic design, formulation development, and comprehensive quality control evaluation of an oral solid dosage form (hard gelatin capsules) containing the standardized botanical extract of Gymnema sylvestre (Gudmar) for the therapeutic management of Diabetes Mellitus.

Based on the rigorous experimental trials, laboratory analyses, and data processing executed throughout this study, the following definitive conclusions have been established:

1. Bioactive Extraction and Phytochemical Authentication

The hydroalcoholic extraction protocol (Ethanol:Water in a 70:30 ratio) successfully isolated the vital secondary metabolites from the crude plant matrix of Gymnema sylvestre. The integrity and presence of the target therapeutic compounds were conclusively validated through a series of qualitative phytochemical screenings. The prominent, stable honeycomb froth generated during the Foam Test explicitly confirmed a rich concentration of characteristic triterpene saponins, structurally recognized as Gymnemic acids. Furthermore, positive indications from Molisch's and Mayer's tests verified the complementary presence of plant carbohydrates and trace alkaloids, while the negative response to the Ninhydrin test confirmed an extraction process clear of heavy cellular proteins, yielding a standardized, purified herbal API ready for formulation.

2. Micromeritic Optimization of the Core Powder Blend

A critical milestone of this research was overcoming the poor flowability, stickiness, and highly cohesive nature inherent to pure dried herbal extracts. Through the systematic application of geometric dilution and the incorporation of an optimized excipient matrix, the powder rheology was substantially enhanced. The addition of Purified Talc and Magnesium Stearate working in unison successfully altered the interparticulate behavior of the mass. The final capsule core blend demonstrated an intermediate, highly acceptable manufacturing flow profile, characterized by:

- An Angle of Repose of 28.90 degrees (indicating Good flow properties)
- A Carr's Compressibility Index of 16.67% (indicating Fair compressibility)
- A Hausner's Ratio of 1.20 (confirming desirable powder flow)

This micromeritic profile proved that the powder blend possessed the required rheological properties to flow freely from a machine hopper without bridging or rat-holing, rendering it perfectly suitable for precise commercial or laboratory encapsulation.

3. Manufacturing Uniformity and Pharmacopeial Compliance

The physical conversion of the 200 mg master formula into Size 0 transparent hard gelatin capsule shells using a manual 300-hole encapsulation apparatus was executed with high precision. The finished product demonstrated exceptional compliance with official Indian Pharmacopoeia (IP) standards. In the Weight

Variation Test, the individual gross weights of twenty randomly sampled capsules tightly clustered around the 296.0 mg average baseline (which includes the 96 mg empty shell weight). The maximum recorded positive deviation was merely +3.04% and the maximum negative deviation was only -2.70%. Because every single capsule fell well within the strict plus or minus 10% legal pharmacopeial threshold, the study confirms that the formulation achieves excellent batch-to-batch content uniformity, guaranteeing that a reliable, reproducible, and uniform therapeutic dose of the hypoglycemic extract is delivered in every individual unit.

4. Disintegration Dynamics and In-Vitro Dissolution Efficacy

The biopharmaceutical performance of the capsule formulation met all performance criteria, demonstrating a rapid transition from a solid dosage form to an absorbable drug solution:

- **Disintegration:** The capsule shells achieved a mean disintegration time of 8 minutes and 45 seconds in Simulated Gastric Fluid (0.1 N Hydrochloric acid) at 37 degrees Celsius. This rapid rupture proves that the gas-generating disintegrant (Calcium Carbonate) and the hydrophilic diluent (Lactose) effectively counteracted the hydrophobic boundary layer of the Magnesium Stearate lubricant.
- **Dissolution:** The USP Type I dissolution profile closely mirrored this rapid disintegration, showing an immediate release pattern where over 52% of the active extract dissolved within the first 15 minutes, culminating in a near-complete cumulative drug release of 95.4% at the 60-minute mark.

Final Summary

In summary, this final-year thesis successfully bridges the gap between traditional pharmacognosy and modern industrial pharmaceutics. The data proves that Gymnema sylvestre leaves can be efficiently extracted, scientifically standardized, blended with functional excipients, and manufactured into a stable, uniform, and fast-releasing hard gelatin capsule dosage form. This formulation provides a technologically sound, reliable, and highly reproducible oral delivery system that establishes a solid foundation for utilizing natural Gudmar extracts as an effective, affordable, and quality-assured weapon in the global clinical management of Diabetes Mellitus.

CHAPTER 8: FUTURE SCOPE

While this project successfully formulated a basic *Gymnema sylvestre* capsule, further research is required to turn this laboratory-scale formula into a fully commercial product. Future studies should focus on the following key areas:

1. Advanced Chemical Standardization

Instead of basic color tests, future work should use advanced analytical machines like HPLC (High-Performance Liquid Chromatography). This ensures every single batch has the exact same milligram dose of active Gymnemic acids.

2. Shelf-Life and Expiration Testing

To establish an official expiration date, the capsules must undergo stability testing. This involves storing them in specialized chambers at specific temperatures and humidity levels (e.g., 40°C at 75% humidity for accelerated testing) to see how they hold up over time.

3. Protective Packaging Solutions

Herbal extracts easily absorb moisture, which can ruin the capsule. Future studies must test different packaging options—like moisture-proof plastic bottles (HDPE) with desiccants or aluminum blister packs (Alu-Alu)—to find the best way to protect the product.

4. Animal Testing (In-Vivo Studies)
While the capsules dissolved well in laboratory fluids, they need to be tested in a living biological system. Testing on diabetic animal models will show exactly how well the drug is absorbed into the bloodstream and how effectively it lowers blood sugar.
5. Industrial Mass Production (Scale-Up)
This project used hand-operated, small-scale lab equipment. To produce thousands of capsules per hour, the formula must be tested on high-speed industrial machinery. This will help researchers perfectly adjust the lubricants (like Magnesium Stearate) so the powder flows smoothly without jamming the machines.

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