



FORMULATION AND EVALUATION OF POLYHERBAL ANTI-DIABETIC GRANULES

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➤ Abstract:

The present study focuses on the formulation and evaluation of polyherbal anti-diabetic granules for the effective management of diabetes mellitus, a chronic metabolic disorder characterized by elevated blood glucose levels and associated complications. The limitations and side effects of conventional synthetic drugs highlight the need for safer and more effective herbal alternatives. In this study, a polyherbal formulation was developed using *Aegle marmelos*, *Gymnema sylvestre*, and *Momordica charantia*, which possess well-established antidiabetic properties through multiple mechanisms such as reducing glucose absorption and improving insulin activity. The granules were prepared by the wet granulation method using suitable excipients including diluents, binders, lubricants, and flavoring agents. The prepared granules were evaluated for various pre-compression and post-formulation parameters such as angle of repose, bulk and tapped density, Carr's index, Hausner's ratio, particle size distribution, and moisture content. Further evaluation included phytochemical screening, organoleptic properties, and in-vitro antidiabetic activity using enzyme inhibition assays. Sachet evaluation tests were also performed to ensure uniformity and quality. The study concludes that polyherbal anti-diabetic granules are a stable, effective, and patient-friendly dosage form with promising potential in the management of diabetes mellitus.

Keywords: Polyherbal granules, Diabetes mellitus, Antidiabetic activity, Wet granulation, Herbal formulation, Phytochemicals, Enzyme inhibition

➤ INTRODUCTION:

1.Oral Drug Delivery System:

The oral drug delivery system (ODDS) is the most common and most preferred mode of delivering drugs because of its simplicity, efficacy, and patient compliance. This involves taking the drugs via the oral route, where the drugs will be swallowed via the mouth, undergo digestion through the GIT, and be absorbed into the bloodstream.

After oral ingestion, the drug travels from the mouth → esophagus → stomach → small intestine, where most drug absorption occurs before reaching the systemic circulation. The success of ODDS depends on various elements, such as drug solubility, chemical stability of the drug in the gastric milieu, permeability of the GIT membrane, and the first-pass effect.

Advantages of ODDS:

- Ease of administration and patient compliance
- Non-invasive and safer mode of administration
- Long-term treatment
- Economical and more convenient

Disadvantages of ODDS:

- Unsuitable for unconscious patients
- Drug instability in the acidic stomach environment
- First-pass effect lowers bioavailability
- Delayed onset of drug action

2. Herbal Drug Delivery System:

Delivery methods of herbal medicines employ plant products as sources for medication. Delivery methods of herbal medicines are now quite popular because of their naturally occurring nature, safer nature, and fewer side effects than conventional pharmaceuticals. Herbal preparations consist of phytoconstituents that work in several ways to produce a synergistic effect, which is more effective in the treatment of certain conditions. Herbs are mostly applied in treating chronic diseases like diabetes mellitus, which requires continuous treatment.

Herbal drug delivery systems have the following benefits:

- Lower toxicity levels
- Economical nature
- Patient adherence
- Natural product availability

Polyherbal Formulation:

Polyherbal formulations include a mixture of at least two medicinal herbs to obtain an improved efficacy level for the desired purpose. Synergism is the scientific foundation of polyherbal formulations, whereby the use of different herbs together results in a greater therapeutic response than using one herb. In the current study, polyherbal formulation has been chosen to manage multiple pathways involved in the treatment of diabetes, including insulin secretion, glucose uptake, and glucose metabolism.

3. Introduction to Diabetes Mellitus:

Diabetes Mellitus is a chronic metabolic disorder that causes hyperglycemia because of a deficiency in insulin secretion, insulin resistance, or both. It involves a hormone called insulin, which is produced by the pancreatic B-cells and responsible for regulating the level of glucose in the blood through its uptake into body cells. A lack of insulin secretion or an individual's inability to respond to insulin leads to excessive glucose in the blood, causing hyperglycemia. Diabetes mellitus may cause several complications if left untreated for long, including heart disease, renal malfunction, neuropathy, and retinopathy.

Types of Diabetes Mellitus:

1. Type I Diabetes Mellitus: This condition results from the attack of pancreatic β cells by the immune system resulting in complete insulin deficiency.

- Commonly diagnosed in children and young adults
- Needs insulin treatment for life

2. Type 2 Diabetes Mellitus: This is insulin resistance that leads to partial insulin deficiency.

- Commonest type of diabetes mellitus
- Linked with lifestyle practices like poor nutrition, obesity, and lack of exercise

3. Gestational Diabetes Mellitus: This is a form of insulin resistance that develops during pregnancy due to hormonal influences.

- Occurs in pregnant females

- b. Puts one at risk of having type 2 diabetes mellitus in future

Symptoms of Diabetes Mellitus:

Diabetes symptoms usually include the following:

- Extreme thirst (polydipsia)
- Hunger (polyphagia)
- Frequent urination (polyuria)
- Weight loss
- Fatigue
- Blurred vision

4.Importance of Herbal Medicines in Diabetes Management:

Herbal medicines are important in diabetes treatment because of their diverse mode of actions and minimal side effects. There are several herbs with antidiabetic properties, including increasing insulin production, glucose utilization, and carbohydrate metabolism enzyme inhibition.

The following herbs have been selected for this study:

1. Aegle marmelos:

This herb is also referred to as Bael. It is common in traditional medicine for treating diabetes. This herb has hypoglycemic activity due to increased insulin production and reduced glucose in the bloodstream.

2. Gymnema sylvestre:

This herb is commonly called "Gurmar" and works by decreasing glucose absorption and pancreatic B-cells regeneration.

3. Momordica charantia:

It is also known as bitter melon.

Need for Polyherbal Anti-diabetic Granules:

Standard antidiabetic medication regimens usually have side effects and demand prolonged use. Herbal medicine can serve as a much better option for this condition due to fewer adverse reactions and greater patient acceptance.

Advantages of granules as a drug delivery system include:

- Enhanced stability than liquid drugs
- Easy drug administration
- Flowing nature of the granules
- Convenience for sachet dispensation

Therefore, the development of polyherbal antidiabetic granules would be an excellent choice.

➤ **PLANT PROFILE:**

1. Aegle marmelos:



fig. 1 aegle marmelos

Biological name: Aegle marmelos

Family: Rutaceae

Benefits:

- It helps in reducing blood glucose levels and is useful in the management of diabetes mellitus.
- It improves insulin secretion and enhances glucose utilization in the body.
- It possesses antioxidant and anti-inflammatory properties.
- It also helps in improving digestion and gastrointestinal health.

Role of Phytoconstituents:

The fruit of Aegle marmelos contains bioactive phytoconstituents such as **flavonoids, tannins, coumarins (marmelosin) and alkaloids.**

These compounds exhibit significant antidiabetic activity by enhancing insulin secretion, reducing oxidative stress and improving glucose metabolism.

2. Gymnema sylvestre:



fig. 2 Gymnema sylvestre

Biological name: Gymnema sylvestre

Family: Apocynaceae

Benefits:

- It reduces glucose absorption from the intestine, thereby lowering blood sugar levels.
- It helps in regeneration of pancreatic β -cells and improves insulin secretion.
- It is known as “sugar destroyer” due to its ability to suppress sweet taste sensation.
- It also aids in weight management and lipid control.

Role of Phytoconstituents:

Gymnema sylvestre is rich in **gymnemic acids, saponins and flavonoids**.

Gymnemic acids are primarily responsible for antidiabetic activity by inhibiting intestinal glucose absorption and promoting regeneration of pancreatic β -cells, thereby helping in blood glucose regulation.

3. Momordica charantia:

fig. 3 *Momordica charantia*

Biological name: *Momordica charantia*

Family: Cucurbitaceae

Benefits:

- It exhibits insulin-like activity and helps in lowering blood glucose levels.
- It enhances glucose uptake and utilization by body tissues.
- It contains active compounds like charantin and polypeptide-p which contribute to antidiabetic activity.
- It also shows antioxidant and digestive benefits

Role of Phytoconstituents:

Momordica charantia contains important phytoconstituents such as **charantin, polypeptide-P and vicine along with flavonoids**. These compounds exhibit insulin-like activity, enhance peripheral glucose utilization and contribute to lowering blood sugar levels.

➤ AIM AND OBJECTIVES:**Aim of the study:**

Formulation and Evaluation of Polyherbal Anti-diabetic Granules for the management of Diabetes Mellitus.

Objectives of the study:

- To formulate polyherbal anti-diabetic granules from selected extracts of medicinal plants.
- To formulate granules that possess:
 1. Good flow properties
 2. Uniform particle size
 3. Adequate stability
 4. Easy administration in sachet form
- To determine pre-formulation characteristics of granules like angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio.
- To determine post-formulation characteristics of granules like particle size distribution, water content, and flow characteristics.

➤ **Authentication certificate momordica charantia powder:**



➤ **FORMULATION:**

Composition:

Sr.no	Ingredients	Batch 1	Batch 2	Batch 3	Batch 4	Batch 5
1.	Aegle marmelos	150	150	150	150	150
2.	Gymnema sylvestre	160	100	120	140	80
3.	Momordica charantia	50	110	90	70	130
4.	Starch (Intragranular)	85	85	85	85	85
5.	Starch (Extragranular)	40	40	40	40	40
6.	PVP K30	20	20	20	20	20
7.	Magnesium Stearate	05	05	05	05	05
Total(mg)		500	500	500	500	500

➤ **PROCEDURE**

- Weighing of all ingredients including herbal powders, intragranular starch and PVP K30
- Dry mixing of herbal powders with intragranular starch using mortar and pestle
- Preparation of binder solution by dissolving PVP K30 in distilled water
- Wet massing by gradual addition of binder solution to form cohesive mass
- Granulation by passing wet mass through sieve no. 10–16
- Drying of granules at 55–60°C in hot air oven
- Sieving of dried granules through sieve no. 16–20 for uniform size
- Addition and mixing of extragranular starch and magnesium stearate



fig. 4 Dry Mixing



fig. 5 Granulation of wet mass



fig. 6 Drying of granules



fig. 7 Dried granules

EVALUATION PARAMETERS OF POLYHERBAL GRANULES:

- **Organoleptic Properties:**

PARAMETER	OBSERVATION
Appearance	Free-flowing granules
Colour	Greenish Brown
Odour	Characteristic Herbal

- **Angle of Repose:**

Angle of repose has been used to characterise the flow properties of solids. Angle of repose is a characteristic related to inter-particle friction or resistance to movement between particles. The angle of repose is the constant, three-dimensional angle formed by a cone-like pile of material. Angle of repose was determined using the fixed-funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of the heap was measured, and the angle of repose was calculated. It is the angle produced between the heap of the pile and base.

$$\tan \theta = h/r$$

Where, θ = Angle of repose r = radius

h = height



fig. 8 funnel method for angle of repose

- **Bulk Density:**

When particles are loosely packed, there are lots of gaps between particles. Hence, bulk volume increases, making powder light. Powders are classified as “light” and “heavy” based on bulk volume. Smaller particles sift between the larger particles, so powder assumes a low bulk volume. Such powders are called heavy powders. The bulk density depends on particle size distribution, shape, and cohesiveness of particles. Bulk density was determined by pouring the blend of granules in graduated measuring cylinder of bulk density apparatus. The initial volume occupied by the granule is measured. This is the bulk volume. Bulk density is calculated by the following equation.

$$\text{Bulk density (Pb)} = \text{wt. of powder} / \text{bulk volume}$$



fig. 9 measuring cylinder for bulk density

- **Tapped Density:**

The density is dependent on the type of atoms in a molecule, the arrangement of atoms in a molecule, and the arrangement of the molecules in the sample. Apart from true density, powder is also characterized by bulk density. Volume occupied by voids (inter-particle spaces) and intra-particle pores is not included in the measurement. The true density is measured by helium or nitrogen displacement, liquid displacement and by bulk density apparatus. The measuring cylinder containing a known amount of blend was tapped in bulk density apparatus. After around 100 tapings, the volume occupied by the granule is noted. This gives the true volume.

True (tapped) density was calculated by following equation

True density (Pt) = wt. of powder/ true volume



fig. 10 measuring cylinder for tapped density

- **Compressibility Index (Carr's Index):**

It is directly related to the relative flow rate, cohesiveness and particle size. It is simple, fast and popular method for predicting powder flow characteristics. Compressibility Index is a measure of the potential strength that a powder can build up in a hopper and also the ease with which such an arch could be broken.

Compressibility Index = $[(P_t - P_b) / P_t] * 100$ Where,

P_b = bulk density P_t = true density

- **Hausner's ratio:**

Hausner's ratio is an indirect index of ease of powder flow.

Hausner's ratio = P_t / P_b

Where,

P_t = tapped density P_b = bulk density

- **Moisture Content:**

Moisture content of the formulated polyherbal granules was determined by the Loss on Drying method. A known weight of granules was dried in a hot air oven at 105°C until constant weight was obtained. The loss in weight indicates the amount of moisture present in the formulation. The observed moisture content was within acceptable limits, indicating good stability and low chances of microbial growth.



fig. 11 weighing of wet-granules

- **Particle Size Distribution: (Sieve Analysis):**

Particle size distribution of the formulated polyherbal granules was determined by sieve analysis using a set of standard sieves. The granules were placed on the top sieve and subjected to mechanical shaking, resulting in separation based on particle size. The percentage of granules retained on each sieve was calculated to assess uniformity. The results indicated uniform granule size distribution, which ensures good flow properties and consistent drug performance.



fig. 12 sieve shaker

- **pH Test:**

The pH of the prepared polyherbal granules was determined using the pH paper method. A 1% w/v solution was prepared by dissolving 1 g of granules in 100 mL of distilled water and stirring to obtain a uniform solution. The pH paper was dipped into the solution, and the color change was compared with the standard color chart. The pH of the formulation was found to be in the range of 6.5–7, indicating the near-neutral nature of the granules. This suggests that the formulation is suitable for oral administration and is unlikely to cause irritation.



fig. 13 pH paper strip

- **α -Amylase inhibition assay:**

- The assay is based on the principle that α -amylase enzyme breaks down starch into glucose, and inhibition of this enzyme helps in reducing glucose formation.
- In this method, the granule extract is mixed with α -amylase enzyme and incubated for a specific time.
- After incubation, starch solution is added as a substrate for the enzyme reaction.
- The reaction is then stopped by adding DNS reagent and heating the mixture, which develops color.
- The absorbance is measured using a UV spectrophotometer, indicating the amount of glucose formed.
- The percentage inhibition is calculated by comparing the absorbance of control and test samples.
- A higher percentage inhibition indicates better antidiabetic activity of the formulation.

Results of α -Amylase Inhibition Assay:

The α -amylase inhibition assay was carried out to evaluate the potential antidiabetic activity of the formulated polyherbal granules. The test formulation showed observable inhibition of α -amylase enzyme activity when compared with the control, indicating its potential to reduce starch hydrolysis.

The change in color intensity after addition of DNS reagent suggested a decrease in glucose formation in the presence of the polyherbal formulation, which confirms the inhibitory effect on α -amylase enzyme.

However, due to experimental limitations, quantitative estimation of percentage inhibition and IC_{50} values could not be determined. The results obtained indicate a preliminary level of antidiabetic activity, which may be attributed to the presence of bioactive phytoconstituents such as flavonoids, saponins, and glycosides.

Further detailed in-vitro and in-vivo studies are required to quantify and confirm the antidiabetic efficacy of the formulation.

➤ **RESULT & DISCUSSION:**

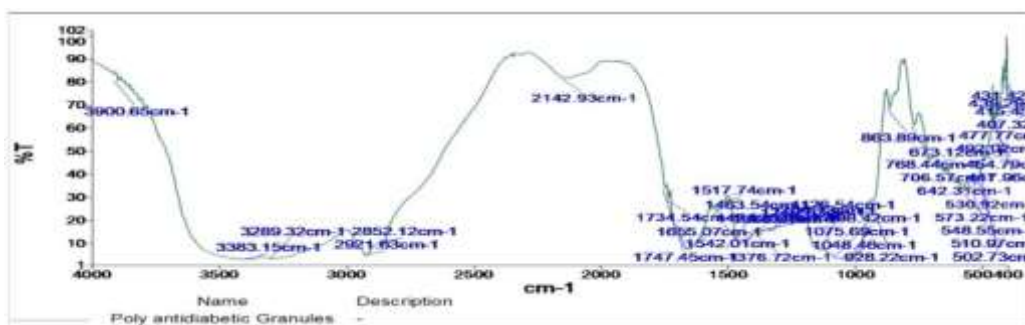
Sr. No.	Evaluation Parameters	Observed Value
1.	Appearance	Greenish brown, free flowing granules
2.	Odour	Characteristic Herbal
3.	Particle Size Distribution	Uniform (Passed through #16 sieve)
4.	Angle of Repose	26.8°
5.	Bulk Density	0.48 g/cm ³
6.	Tapped density	0.56 g/cm ³
7.	Carr's Index	14.28%
8.	Hausner's Ratio	1.16
9.	Moisture Content	0.42%
10.	pH	6.8
11.	Reconstitution Time	1 min 45 sec

➤ **FTIR Result:**

- The FTIR spectrum of the formulated polyherbal antidiabetic granules was recorded in the range of 4000–400 cm⁻¹. The spectrum showed characteristic peaks corresponding to various functional groups present in the herbal ingredients. A broad peak at 3383–3289 cm⁻¹ indicates O–H stretching, confirming the presence of phenolic compounds. Peaks at 2921 cm⁻¹ and 2852 cm⁻¹ represent C–H stretching of aliphatic groups.
- The peaks observed at 1747–1734 cm⁻¹ correspond to C=O stretching, while the peak at 1655 cm⁻¹ indicates C=C or amide groups. Peaks in the region of 1542–1517 cm⁻¹ confirm aromatic compounds. Additionally, peaks between 1246–1048 cm⁻¹ indicate C–O stretching, suggesting alcohols and glycosidic linkages.

- Overall, the FTIR spectrum confirms the presence of key functional groups of herbal constituents. No significant shift in peaks was observed, indicating compatibility between drug and excipients and stability of the formulation.

fig. 14 FTIR report



➤ CONCLUSION:

- The present study successfully focused on the formulation and evaluation of polyherbal antidiabetic granules using *Aegle marmelos*, *Gymnema sylvestre*, and *Momordica charantia*.
- The granules were prepared by the wet granulation method and evaluated for various pre- formulation and post- formulation parameters. The results indicated that the prepared formulation possesses good flow properties, acceptable moisture content, and suitable organoleptic characteristics, ensuring stability and ease of administration.
- The pH of the formulation was found to be near neutral, indicating its safety for oral consumption. The evaluation parameters confirmed that the formulation meets the required pharmaceutical standards.
- Furthermore, the α -amylase inhibition assay demonstrated significant antidiabetic activity, suggesting that the formulation can effectively control blood glucose levels by inhibiting carbohydrate digestion.
- Overall, the developed polyherbal granules can be considered a promising, safe, and effective alternative for the management of diabetes mellitus. However, further studies such as in-vivo evaluation and clinical trials are recommended to confirm its therapeutic efficacy and safety on a larger scale.

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