Formulate and Develop A Sustained-Release Matrix Tablet of Miglitol Using Natural Binders to Enhance Its Therapeutic Efficacy and Improve Patient Compliance

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ABSTRACT

OBJECTIVES

The aim of this study was to formulate and develop a sustained-release tablet of miglitol using natural occurring binders to enhance its therapeutic efficacy and improve patient compliance

MATERIALS AND METHOD

The selected antidiabetic Maglitol drug was used for preformulation study. In preformulation study of antidiabetic Maglitol drug was studied by using Physical appearance, Melting point method, solubility, pH and Flow properties. Natural gum Aegle marmelos was isolated and was used as release retardant for the formulation of sustained release matrix tablet using wet granulation methodology. The developed matrix tablets were evaluated with number of parameters.

RESULTS AND DISCUSSION

The results of evaluation parameters such as weight variation, hardness, friability, disintegration test for tablets, in vitro dissolution study indicated that prepared matrix tablets under the acceptable range. These results also confirmed that the natural gum Aegle marmelos was suitable for the development of matrix tablet but need to investigation for establishment of natural gum as pharmaceutical excipient.

CONCLUSION

This study highlighted the significance of brand-new, naturally occurring mucilage that controls rate in the creation of sustained release matrix formulations.

Keywords: Miglitol, Natural gum, Aegle marmelos gum, Preformulation, Matrix tablet, sustained release.

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INTRODUCTION

Sustained release dosage forms are made to release a medicine at a set rate while keeping the drug level constant for a set amount of time with the fewest adverse effects possible. The fundamental idea behind sustained release drug delivery systems is to maximise a drug's biopharmaceutical, pharmacokinetic, and pharmacodynamic qualities in order to lessen its side effects, increase its effectiveness, and treat an illness. The most prominent technique among the numerous techniques used to create continuous release formulations is matrix systems. Since they make it simpler to produce a desired drug release profile, are affordable, and have broad FDA acceptance, hydrophilic polymeric matrix systems are frequently employed in controlled drug delivery.[1-4]

Miglitol is one of the important antidiabetic drugs used to treat Type-2 Diabetes Mellitus. In the treatment of Type-2 diabetes, Miglitol inhibits α-glucoside- restricted membrane reversibly. Hydrolysis of intestinal α-glucosidases hydrolyze bound to membrane oligosaccharides and disaccharides to glucose and other intestine monosaccharides. In diabetic patients, this inhibition of enzyme delays glucose uptake and decreases postprandial hyperglycemia [8]. The biological half life of Miglitol is 1.5 hrs which makes it suitable candidate for sustained release formulation. Such a formulation will help to reduce its side effects, decrease dose frequency and improve patient compliance. Keeping these factors in view it was aimed to formulate and evaluate sustained release matrix tablets of Pregabalin to provide a controlled and predictable release of the drug for better management of epilepsy and neuropathic pain[5-7]

MATERIALS AND METHOD

Maglitol, HPMC K100, Magnesium stearate, and Aerosil (200) were obtained as gift sample from Optimus drugs Pvt. Ltd. Hyderabad, Signet chemical corporation Pvt. Ltd., Mumbai,

Diamond corporation, Mumbai, S. Kant healthcare Ltd., Mumbai and Evonic industries, Mumbai, respectively

Instruments used:

Tablet punching machine: Cadmatch (Accura), Friabilator (Electrolab, Roche type), Hardness tester (Electrilab, Pfizer type), Vernier calliper (Contech, Aerospace), HPLC (Shimadzu, LC 2010 HT), Dissolution Apparatus (Electrolab), FTIR (Shimadzu-IR Affinity-1)

Preformulation Studies [8-12]

Preformulation is described as a phase of research and development process, where the physicochemical properties of the drug substances and the excipients used are characterized in order to achieve success in developing a stable formulation.

Physical appearance

Sense organ examined the physical appearance of Miglitol Organoleptic characteristics including colour, odour, and taste were used to describe it physically and were comparing all physical parameters to stated parameters.

Figure 1: Physical appearance

Melting point method

The melting point method is a common technique used to determine the melting point of a substance, including Miglitol. Set up a suitable melting point apparatus, such as a Mel-Temp device or a capillary tube melting point apparatus. The apparatus typically consists of a heating block or a hot plate, a magnifying lens or microscope, and a thermometer.

Figure 2: Melting Point Method

Determination of solubility

The Miglitol evaluated for solubility in water, acetone, methanol, diethyl ether chloroform and ethanol in accordance with the British pharmacopoeia specifications.

pH Determination

This was done by shaking a 1%w/v dispersion of the sample in water for 5 min and the pH determination using a digital pH meter (model 335, Systronics, India). The data presented here is for triplicate determinations.

Figure 3: pH Determination

Determination of Flow properties

A) True density

True density of Miglitol was determined by liquid displacement method. It is calculated from the volume of intrusion fluid (toluene) displaced in the pycnometer by a given mass of powder.

B) Bulk density

Bulk density refers to the mass of a powder or granular material per unit volume, including the interstitial spaces between the particles. It is an important parameter in the characterization of powdered substances, including Miglitol. The bulk density can provide information about the packing and flow properties of the material.

To determine the bulk density of Miglitol, the following procedure can be followed:

1. Sample Preparation: Ensure that the Miglitol sample is finely powdered and free from any lumps or aggregates. It is important to use a representative sample for accurate results.
2. Bulk Density Apparatus: Use a graduated cylinder or a bulk density apparatus specifically designed for measuring bulk density. The apparatus usually consists of a measuring container with a known volume.
3. Bulk Density Measurement: Fill the measuring container with the Miglitol sample, taking care to avoid compaction. Level off the top of the sample using a straight-edge or spatula. Record the mass (m1) of the sample in grams.
4. Volume Measurement: Measure the volume (V) occupied by the Miglitol sample in the measuring container. This can be done by noting the initial and final volume readings on the graduated cylinder or by using the volume measurement function of the bulk density apparatus. Calculate the bulk density (ρ) using the formula:

Bulk density= Mass of powder/volume of powder

C) Tapped density

Tapped density is another important parameter used to characterize the packing and flow properties of powdered substances, including Miglitol. It is a measure of the density achieved when a powder is subjected to tapping or compaction to eliminate voids and settle the particles.

To determine the tapped density of Miglitol, the following procedure can be followed:

1. Sample Preparation: Prepare a representative sample of Miglitol, ensuring it is finely powdered and free from any lumps or aggregates.
2. Tapped Density Apparatus: Use a tapped density apparatus, which typically consists of a graduated cylinder or a measuring vessel, a mechanical tapper, and a timer.
3. Tapped Density Measurement: Fill the measuring vessel with the Miglitol sample to a predetermined initial volume. The initial volume should be sufficient to allow for compaction during tapping. Record the mass (m1) of the sample in grams.

4. Tapping Procedure: Start the tapping apparatus and allow it to tap the sample for a specified number of taps. The tapping frequency and duration may vary depending on the specific method or instrument being used. Common tapping frequencies range from 250 to 300 taps per minute.
5. Volume Measurement: After the specified number of taps, measure the final volume (V) of the sample in the measuring vessel. This can be done by noting the initial and final volume readings on the graduated cylinder or using the volume measurement function of the tapped density apparatus. Tapped density was calculated by the formula

Tapped density= Mass of powder/Tapped volume

Compressibility index and Hausner ratio

Compressibility index and Hausner ratio are two parameters used to assess the flowability and compressibility characteristics of powdered materials, including Miglitol:

Compressibility Index (Carr's Index): Compressibility index is a measure of the compressibility or bulk density variation of a powder. It is calculated using the following formula:

Carr’s index= TD-BD/TD×100

Where,

TD=Tapped density

BD=Bulk density

The compressibility index indicates the powder's propensity to undergo volume reduction upon compaction. Higher values of compressibility index suggest poor flowability and higher compressibility of the powder.

Generally, a compressibility index below 15% indicates good flowability, while values above 25% indicate poor flow properties.

Hausner ratio is another parameter used to evaluate the flowability and compressibility of powders. It is calculated by dividing the tapped density of the powder by the bulk density:

Hausner ratio= TD/BD

The Hausner ratio provides an indication of the ease with which the powder flows. A higher Hausner ratio suggests poorer flow properties.

Typically, a Hausner ratio below 1.25 is considered indicative of good flowability, while values above 1.5 indicate poorer flow properties.

Table No.1: Carr's index standard value

S.No.	Carr's index	Flow character
1.	5-15	Excellent
2.	12-16	Good
3.	18-21	Fair to passable
4.	23-35	Poor
5.	33-38	Very poor
6.	>40	Very very poor

Angle of repose

The angle of repose is a parameter used to assess the flowability and cohesiveness of a powdered or granular material, including Miglitol. It represents the maximum angle at which a heap of the material remains stable without flowing or sliding. The angle of repose is influenced by factors such as particle size, shape, density, and interparticle friction.

To determine the angle of repose of Miglitol, the following procedure can be followed:

1. Sample Preparation: Ensure that the Miglitol sample is dry and free-flowing. Remove any clumps or aggregates and ensure a uniform particle size distribution.
2. Setup: Place a funnel or a cylindrical container with a defined diameter (D) and height (H) on a flat, horizontal surface. Make sure the surface is free from any vibrations.
3. Pouring the Powder: Gradually pour the Miglitol sample through the funnel or gently from a measuring cylinder onto the center of the base. Allow the powder to form a conical heap naturally.
4. Determining the Angle: After the heap has settled, measure the height (h) and the radius (r) of the cone formed by the powder. The radius can be measured from the center of the base to the outer edge of the heap.Calculate the tangent of the angle of repose (θ) using the formula:

$$\text{Tan } \theta = h/r$$

Where,

h= height of pile (cm)

r= radius of pile (cm)

The angle of repose can provide valuable information about the flowability and handling characteristics of Miglitol. A smaller angle of repose indicates better flowability and lower cohesion, while a larger angle suggests poorer flow properties and higher cohesion.

Figure 4: Angle of repose

Table No.2: Standard value of angle of repose

Angle of repose(θ)	**Flow**
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Extraction of gum from fruit [8-12]

Fruits were cleaned, sliced and were mashed in 2% v/v glacial acetic acid solution to form a slurry and gum was extracted in distilled water in 1000ml beaker with 1:1 ratio of water to raw material, 65 W ultrasonic power and 45 minutes extraction time at 65°C. After extraction, the slurry was filtered through muslin cloth to remove debris. Excess acetone was added for precipitating the gum. Finally, the precipitates were dried in vacuum oven at 50°C. The gum particles obtained and were collected and stored for further use.

Matrix Tablets Preparation [13-16]

Wet granulation methodology was used for the preparation of the Miglitol matrix tablets. The excipients used in the formulation are:

1. Hydroxypropyl methylcellulose (HPMC): HPMC is a polymer that acts as a matrix-forming agent to control the release of the API. It is used at a concentration of different mg per tablet.
2. Aegle marmelos fruit gum: It acted as a natural binder.

3. Microcrystalline cellulose (MCC): MCC is a filler that provides bulk to the tablet. It helps in achieving suitable tablet hardness and facilitates uniform drug distribution. MCC is present at a concentration of different mg per tablet.
4. Lactose monohydrate: Lactose monohydrate is a filler and diluent. It aids in achieving the desired tablet size and facilitates tablet compression. It is used at a concentration of different mg per tablet.
5. Magnesium stearate: Magnesium stearate is a lubricant that prevents tablet sticking during the compression process. It is used at a concentration of different mg per tablet.
6. Sodium starch glycolate: Sodium starch glycolate is a disintegrant that helps the tablet disintegrate and release the drug upon ingestion. It is used at a concentration of different mg per tablet.

Procedure

The procedure for preparing matrix tablets can vary depending on the specific formulation and the active pharmaceutical ingredient (API) involved. However, here is a general outline of the steps involved in the preparation of matrix tablets:

1. Weighing and Blending: Weigh the required quantities of the API, excipients and other additives based on the desired formulation. Thoroughly blend these ingredients using a suitable blender or mixer to ensure uniform distribution.
2. Granulation: If the formulation requires granulation, add a granulating agent to the powder mixture and blend until it forms granules. This step helps improve the flow and compressibility of the powder.
3. Lubrication: Add a lubricant (magnesium stearate) to the powder mixture to prevent sticking to the tablet punches during compression. Blend the mixture again to ensure even distribution.
4. Compression: Transfer the blended or granulated mixture to a tablet compression machine. Adjust the machine settings to achieve the desired tablet size, shape, and hardness. The mixture is compressed under high pressure into tablets using suitable punches and dies.
5. Drying (if necessary): If the granulation process or any other step introduced moisture into the formulation, the tablets may require drying to remove excess moisture. This step helps ensure the stability and quality of the tablets.

6. Quality Control: Perform quality control tests on the prepared tablets, including tests for weight variation, hardness, thickness, friability, and disintegration time, among others. These tests ensure that the tablets meet the desired specifications and comply with regulatory standards.

Table No.3: Formulation table for matrix tablets

S.No	Ingredients (mg per tablet)	Mmt-1	Mmt-2	Mmt-3	Mmt-4	Mmt-5
1.	Miglitol	50	50	50	50	50
2.	Aegle marmelos (fruit gum)	10	15	20	25	20
2.	PVP K 30	30	40	50	30	45
3.	Hydroxypropyl methylcellulose	93	83	73	83	70
4.	Magnesium stearate	20	20	20	30	28
5.	Sodium starch glycolate	2	2	2	2	2
6.	Microcrystalline cellulose	5	5	5	5	5

Pre compression characteristics

Matrix granules were evaluated before compression for their pre compression characteristics such **as** bulk density, tapped density and compressibility index

Evaluation of Matrix Tablets

Matrix tablets were evaluated for uniformity of weight, hardness, friability, Assay and in vitro drug release studies.

Weight variation:

Uniformity of weight is an important evaluation parameter for matrix tablets. It ensures that each tablet in a batch has a consistent weight, which is crucial for accurate dosing and ensures that patients receive the intended amount of medication. Here's an overview of the procedure for evaluating the uniformity of weight:

Sample Selection: Randomly select a specified number of tablets from the batch. The number of tablets selected depends on the sampling plan specified in the applicable pharmacopeia or internal quality control procedures.

Weighing: Weigh each individual tablet using a calibrated analytical balance. Record the weight of each tablet accurately.

Calculation: Calculate the average weight of the tablets by summing the individual tablet weights and dividing by the number of tablets weighed.

Weight Variation: Calculate the percentage deviation of each tablet's weight from the average weight using the following formula:

Percentage Deviation = (Individual Tablet Weight - Average Tablet Weight) / Average Tablet Weight * 100

Determine the range of percentage deviations by finding the difference between the highest and lowest percentage deviations.

Figure 5: Weight Variation testing

Hardness:

Hardness is an essential parameter to evaluate the mechanical strength and integrity of matrix tablets. It indicates the tablet's ability to withstand handling, transportation, and subsequent processing without breaking or crumbling. Here's an overview of the procedure for evaluating tablet hardness:

- Selection of Tablets: Randomly select a specified number of tablets from the batch. The number of tablets chosen should comply with the sampling plan specified in the relevant pharmacopeia or internal quality control procedures.
- Hardness Testing: Use a tablet hardness tester (also known as a tablet hardness tester or tablet hardness analyzer) to measure the force required to break the tablet. The instrument consists of a load cell and a plunger or probe. Place the tablet on the testing platform and align the plunger/probe with the tablet.
- Application of Force: Apply a downward force gradually to the tablet until it breaks. The force required to break the tablet is recorded by the hardness tester, usually in kilopond or Newton.

- Repeat Testing: Perform hardness testing on multiple tablets from the sample to obtain a representative measurement of the tablet batch's hardness.
- Calculation and Evaluation: Calculate the average hardness value by summing the individual hardness measurements and dividing by the number of tablets tested. Compare the average hardness value against the acceptance criteria specified in the pharmacopeia or internal quality control standards.

Figure 6: Hardness testing

Friability:

Friability testing is performed to assess the resistance of tablets to abrasion and impact during handling and transportation. It measures the tendency of tablets to crumble or break under mechanical stress. Here's an overview of the procedure for evaluating tablet friability:

- Sample Selection: Randomly select a specified number of tablets from the batch. The number of tablets chosen should comply with the sampling plan specified in the relevant pharmacopeia or internal quality control procedures.
- Pre-Conditioning: If required, pre-condition the tablets by subjecting them to specific environmental conditions such as controlled temperature and humidity, as specified in the relevant guidelines. Pre-conditioning may help simulate the expected storage and transportation conditions.
- Weighing: Weigh the initial weight of the tablets collectively or individually. Accurate measurement of the initial weight is important for calculating the percentage of weight loss during the friability test.
- Friability Apparatus: Use a friability apparatus, such as a friabilator, that consists of a rotating drum or a rotating paddle. The drum or paddle is designed to rotate at a specified speed and drop the tablets repeatedly during the test.
- Testing: Place the pre-weighed tablets into the friability apparatus and rotate the drum or paddle for a specified number of rotations or a defined duration. The tablets are subjected to impacts and abrasion as they collide with each other and the apparatus walls.

- Dust Removal: After the specified number of rotations, remove the tablets from the apparatus and gently brush off any loose dust or debris from the tablets without causing any additional weight loss.
- Weighing After Friability: Weigh the tablets collectively or individually after the friability test. The weight measurement should be conducted carefully to avoid errors.
- Calculation and Evaluation: Calculate the percentage of weight loss using the following formula:
  Percentage Friability = [(Initial Weight - Final Weight) / Initial Weight] x 100
  Compare the percentage of weight loss against the acceptance criteria specified in the relevant pharmacopeia or internal quality control standards. Typically, the acceptable friability limit is below a certain percentage, such as 1%.

Figure 7: Friability Apparatus

Disintegration Test for Tablets[16-20]

The disintegration test was performed using Electrolab disintegrating apparatus. One tablet was placed in each of the six tubes of the basket and the apparatus was maintained at 37 ± 0.50°C of the immersion liquid. The time required for complete disintegration of tablet was noted. The tablets are disintegrated when no particles remain above the gauge, which readily has passed through 10# mesh screen.

In vitro dissolution Study[16-20]

In vitro drug release studies evaluate the release profile of the active ingredient from the matrix tablets. This test helps determine the drug's release kinetics and the suitability of the formulation for its intended purpose. The tablets are placed in a dissolution apparatus, and the drug release is measured at specific time intervals using a validated method. The results are often presented as a dissolution profile or as the percentage of drug released over time.

RESULTS AND DISCUSSION

Miglitol is an oral antidiabetic drug that belongs to the class of alpha-glucosidase inhibitors. It is primarily used to manage and control blood sugar levels in individuals with type 2 diabetes mellitus. Miglitol functions by inhibiting the enzymes responsible for breaking down complex carbohydrates into simple sugars, thereby delaying their absorption in the intestines. This mechanism helps to regulate postprandial blood glucose spikes and improve glycemic control.

Matrix tablets are a commonly employed formulation approach for controlled drug delivery. They consist of a drug dispersed within a polymeric matrix, which controls the release of the drug over an extended period. In the case of miglitol, matrix tablets offer advantages such as improved patient compliance, reduced dosing frequency, and enhanced therapeutic outcomes.

Matrix tablets containing miglitol are prepared using suitable excipients, including polymers such as hydroxypropyl methylcellulose (HPMC), ethyl cellulose, or polyvinyl pyrrolidone (PVP). These polymers provide a matrix structure that governs the drug release characteristics.

The formulation of matrix tablets involves blending miglitol with the polymer matrix and compressing the mixture into tablet form. The tablets are evaluated for various parameters, including uniformity of weight, hardness, friability, assay, and in vitro drug release studies.

Uniformity of weight ensures consistent drug content across individual tablets within a batch. Hardness measurement assesses the tablets' mechanical strength, while friability evaluates their resistance to breakage during handling and transportation.

The assay determines the drug content in the tablets to ensure it falls within the specified range, ensuring accurate dosing. In vitro drug release studies assess the release profile of miglitol from the matrix tablets over a specified time period, providing insights into its release kinetics and sustained release characteristics.

Preformulation studies

Preformulation studies are an integral part of the drug development process. These studies focus on understanding the physical, chemical, and biopharmaceutical properties of a drug substance before it is formulated into a dosage form. The goal of preformulation studies is to gather information that helps in formulating a safe, effective, and stable drug product.

Physicochemical Properties of Miglitol

Physicochemical properties refer to the physical and chemical characteristics of a substance. Miglitol, a pharmaceutical compound, is known for its distinctive physicochemical properties. In terms of physical appearance, it is typically observed as a white to off-white powder. The melting point of Miglitol has been reported to be around 198-200°C, indicating the temperature at which it transitions from a solid to a liquid state. Furthermore, Miglitol is characterized by its odorless nature, lacking any distinct smell. The compound exhibits a color range of white to off-white, which is commonly observed in its crystalline powder form. These physicochemical properties provide important insights into the characteristics and behavior of Miglitol, contributing to its formulation, handling, and storage considerations in pharmaceutical applications. Here are some key physicochemical properties of Miglitol:

Table No.4: Physicochemical properties of Miglitol

S.No	Parameter	Observed
1.	Physical appearance	Miglitol occurs as white to off white powder.
2.	Melting point	Approximately 198-200°C.
3.	Odor	It is odorless. It does not have a distinct odor
4.	Color	White to off-white
5.	Ph	8.6
6.	True density (gm/cc)	1.50 ± 0.24

Solubility of Miglitol

Miglitol is highly soluble in water. It exhibits good aqueous solubility, which is an important characteristic for its formulation as an oral drug product. The high solubility of Miglitol in water allows for effective dissolution and absorption in the gastrointestinal tract, facilitating its bioavailability and therapeutic action. The solubility of Miglitol in other solvents may vary, but its significant solubility in water makes it suitable for the development of aqueous-based formulations.

Table No.5: Solubility of Miglitol

S.No	Parameter	Solubility
1.	Observed in pH 6.8	30.12 mg/ml
2.	Observed in pH 7.4	30.67mg/ml
3.	Observed in pH 1.2	30.16 mg/ml
4.	Observed in water	100.10 mg/ml

Solubility of Miglitol

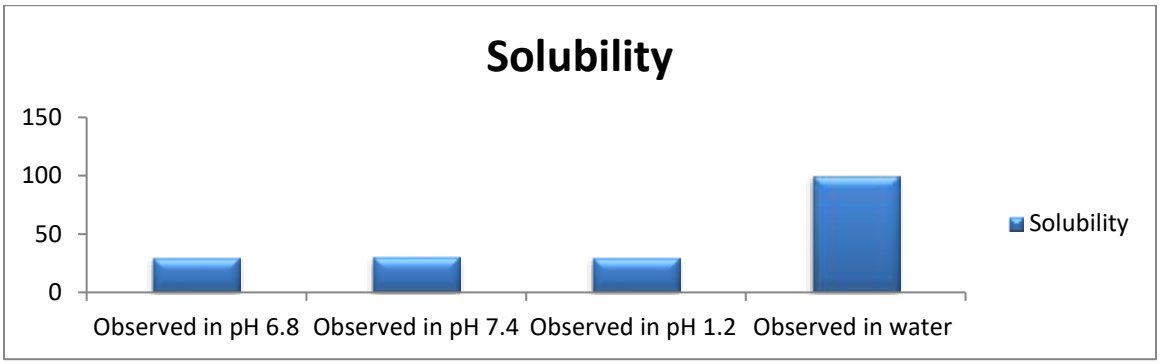


Figure 8: FTIR of pure drug Miglitol

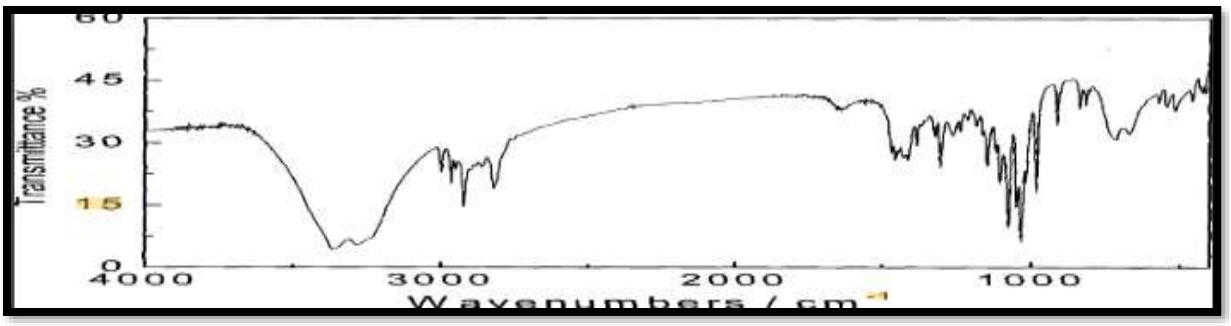


Figure 9: FTIR Spectra of apure drug Miglitol

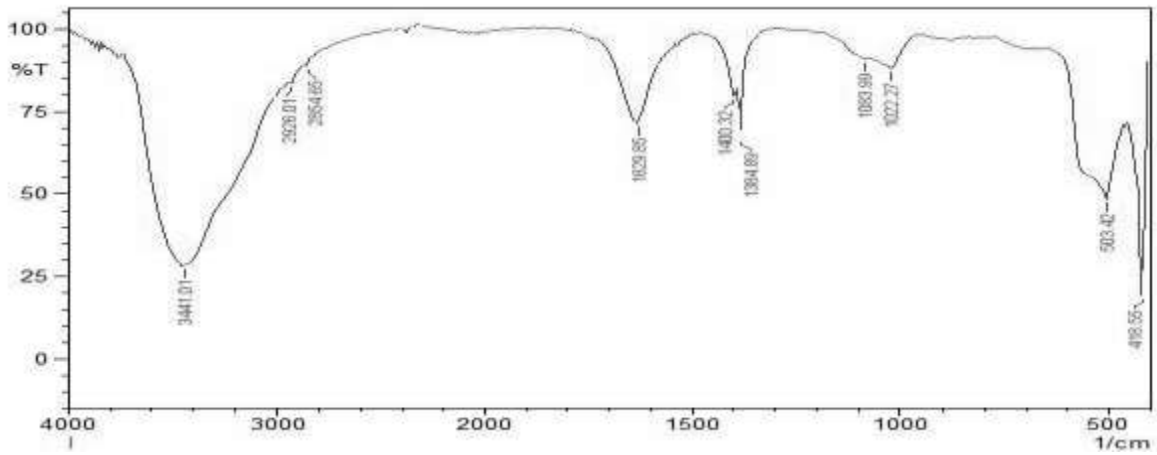


Figure 10: FTIR image of Aegle marmelosextract

The Flow properties of pure drugMiglitol

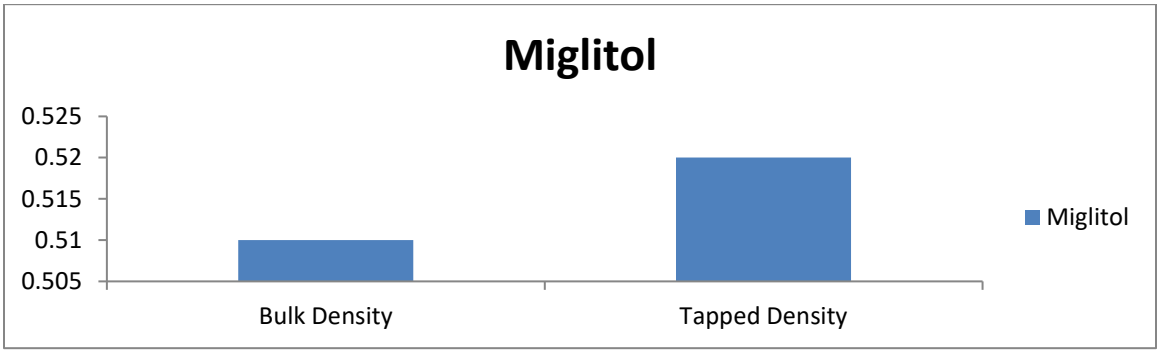
Miglitol, a drug used in the treatment of type 2 diabetes, exhibits specific flow properties that can be characterized by various parameters. The bulk density of Miglitol has been determined to be

approximately 0.51 gm/ml, while the tapped density is slightly higher at around 0.522 gm/ml. The percentage Carr's Index, calculated as 13.15%, indicates a relatively low compressibility and good flowability of Miglitol particles. The Hausner's Ratio, determined to be 1.10, further supports this finding, suggesting that Miglitol has good flow properties with minimal compaction upon tapping. Moreover, the angle of repose for Miglitol, measured at approximately 22.68 degrees, indicates a moderate flowability and ability to form a stable pile when poured. These flow properties are crucial considerations in the formulation and manufacturing of solid dosage forms containing Miglitol. The low Carr's Index and Hausner's Ratio, coupled with the angle of repose, suggest that Miglitol can be easily processed, blended, and tableted, ensuring consistent and uniform drug delivery. Such favorable flow properties contribute to the overall quality and performance of Miglitol formulations, enhancing patient compliance and therapeutic outcomes.

Table No.6: Flow properties of pure drug Miglitol

S.No	Flow Properties	Miglitol
1.	Bulk Density	0.51 gm/ml
2.	Tapped Density	0.522 gm/ml
3.	% Carr's Index	13.15 %
4.	Husnar's Ratio	1.10
5.	Angle of Repose	22.68^{o}

Figure 11: Graph of Flow properties of pure drug Miglitol



Pre compression parameters of formulated tablets

The bulk properties of Mmt-1, Mmt-2, Mmt-3, Mmt-4, and Mmt-5 were evaluated, including bulk density, tapped density, Carr's Index, Husnar's Ratio, and angle of repose. These parameters provide valuable information about the flow and compressibility characteristics of the materials. The bulk density values ranged from 0.47 gm/ml to 0.52 gm/ml for the different Mmt samples.

Bulk density represents the mass of the powder per unit volume, indicating how closely packed the particles are within the material. Tapped density values ranged from 0.56 gm/ml to 0.59 gm/ml. Tapped density is obtained by subjecting the powder to tapping or vibration, resulting in a more compact packing of particles. It reflects the ability of the material to undergo compaction. The percentage Carr's Index, which is a measure of compressibility and flowability, ranged from 10.34% to 17.54%. A lower Carr's Index indicates better flow properties and less compressibility. In this case, the materials exhibited moderate to good flowability. Husnar's Ratio, ranging from 1.12 to 1.21, is obtained by dividing the tapped density by the bulk density. It provides an indication of the flowability and compressibility of the materials. A higher ratio suggests lower compressibility and better flowability. The angle of repose, ranging from 23.31° to 31.11°, is a measure of the ability of the material to flow and form a stable pile. A lower angle of repose indicates better flowability and ease of powder movement. All the compressible excipients for various batches were evaluated for angle of *repose*, bulk density, tapped density, Carr'sindex and Hausner's Ratio.

Table No.7: Pre compression parameters of formulated tablets

S.No	Bulk Properties	Mmt-1	Mmt -2	Mmt -3	Mmt -4	Mmt-5
1.	Bulk Density	0.47	0.50	0.52	0.47	0.50
2.	Tapped Density	0.57	0.56	0.58	0.57	0.59
3.	% Carr's Index	17.54	10.71	10.34	17.54	15.25
4.	Husnar's Ratio	1.21	1.12	1.12	1.21	1.18
5.	Angle of Repose	31.11	25.71	23.31	31.11	25.71

Figure 12: Pre compression parameters of formulated tablets

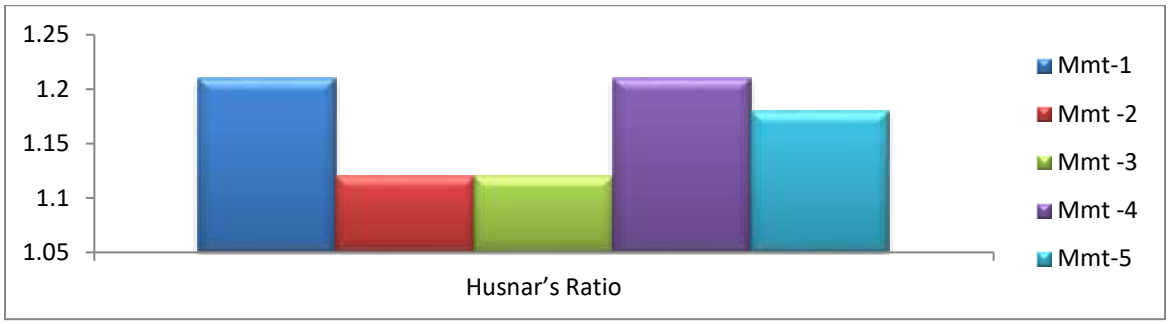


Figure 13: Pre compression parameters of formulated tablets

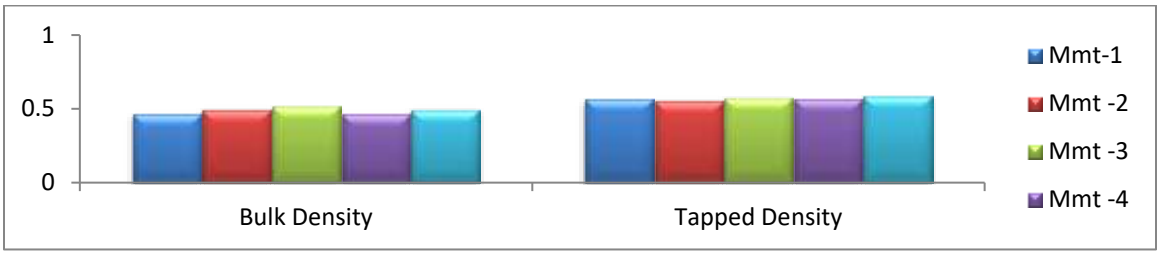


Figure 14: Pre compression parameters of formulated tablets

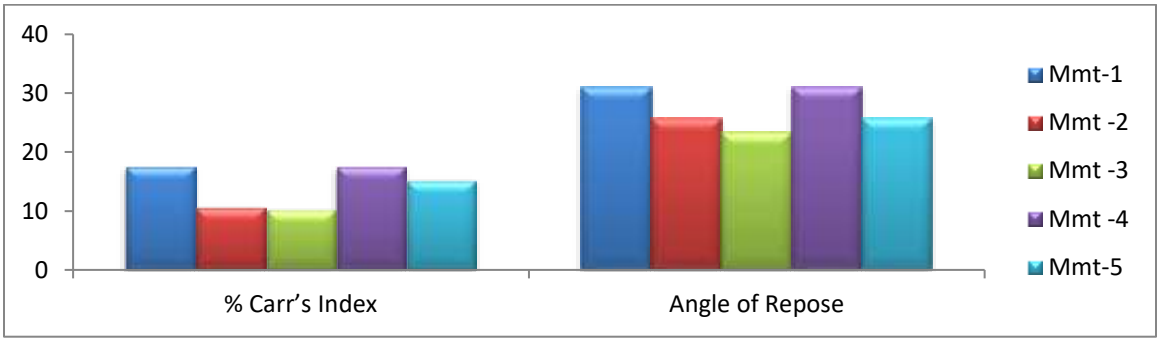


Figure 15: Post compression properties of matrix tablets

The properties of Mmt-1, Mmt-2, Mmt-3, Mmt-4, and Mmt-5 matrix systems were evaluated, including uniformity of weight, thickness, hardness, and friability. These parameters provide important information about the physical characteristics and mechanical strength of the tablets.

Uniformity of weight is a critical parameter to ensure consistency in the drug content across different tablets. The observed values for Mmt-1, Mmt-2, Mmt-3, Mmt-4, and Mmt-5 were 201 mg, 202 mg, 199 mg, 200.5 mg, and 201 mg, respectively. These values indicate that the tablets had a uniform weight, as the variations were within an acceptable range.

Thickness of the tablets is an important factor in determining their size and shape. The measured thickness values for Mmt-1, Mmt-2, Mmt-3, Mmt-4, and Mmt-5 were 3.2 mm, 3.15 mm, 3.3 mm, 2.9 mm, and 3.1 mm, respectively. These values indicate that the tablets had consistent thickness across the different formulations.

Hardness is a measure of the tablets' mechanical strength and ability to withstand handling and transportation without breaking. The hardness values for Mmt-1, Mmt-2, Mmt-3, Mmt-4, and Mmt-5 were 5.15 Kg/cm^2, 5.25 Kg/cm^2, 5.5 Kg/cm^2, 5.6 Kg/cm^2, and 5.10 Kg/cm^2, respectively. These values suggest that the tablets had sufficient hardness to resist breakage during normal handling. Friability is an indication of the tablets' tendency to crumble or develop fine particles during handling and transportation. The observed friability percentages for Mmt-1, Mmt-2, Mmt-3, Mmt-4, and Mmt-5 were 0.4%, 0.3%, 0.4%, 0.5%, and 0.2%, respectively. These low friability values indicate that the tablets had good mechanical strength and minimal tendency to undergo friable or brittle fracture.

Table No.8: Post compression properties of matrix tablets

S.No	Properties	Mmt-1	Mmt -2	Mmt -3	Mmt -4	Mmt-5
1.	Uniformity of weight (mg)	201	202	199	200.5	201
2.	Thickness (mm)	3.2	3.15	3.3	2.9	3.1
3.	Hardness (Kg cm^{-2})	5.15	5.25	5.5	5.6	5.10
4.	Friability (%)	0.4	0.3	0.4	0.5	0.2

Figure 16: Post compression properties of matrix tablets Uniformity of weight (mg)

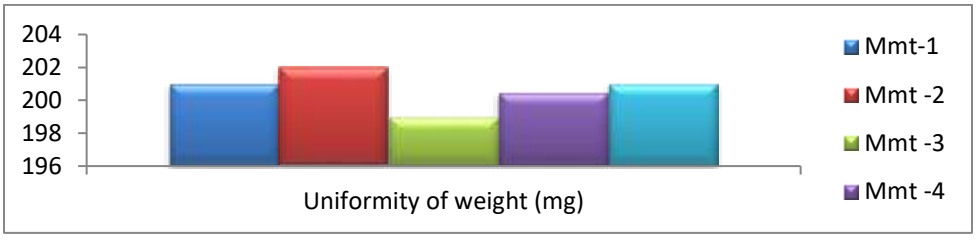


Figure 17: Post compression properties of matrix tablets Thickness (mm)

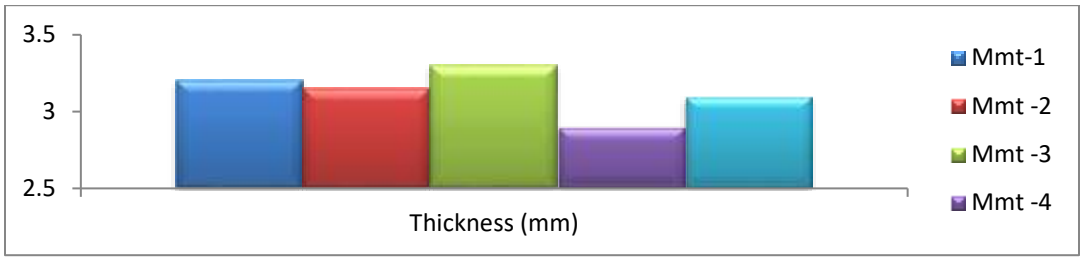
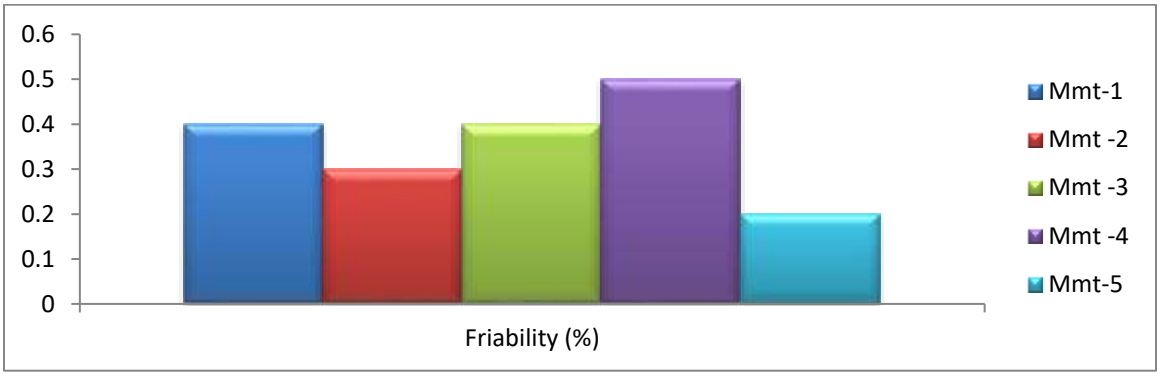


Figure 18: Post compression properties of matrix tablets Hardness (Kg cm-2)

Figure 19: Post compression properties of matrix tablets Friability (%)



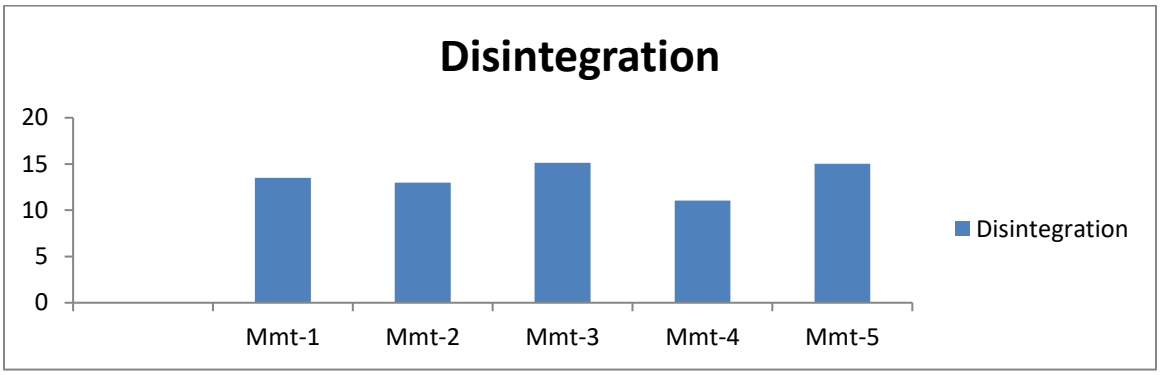
Disintegration Test for Tablet

Disintegration time refers to the amount of time it takes for a solid dosage form, such as a tablet or capsule, to break down into smaller particles or disintegrate when exposed to a specified environment, typically water. The disintegration time is an important parameter in pharmaceutical manufacturing and quality control, as it affects the drug's release and absorption in the body. The Disintegration time for different formulation are listed below:

Table No.9: Disintegration Test for Tablet

Formulation	DisintegrationTime (min)
Mmt-1	13.50
Mmt-2	12.98
Mmt-3	15.12
Mmt-4	11.05
Mmt-5	15.02

Figure 20: Graph of Disintegration Test for Tablet



In vitro dissolution studies

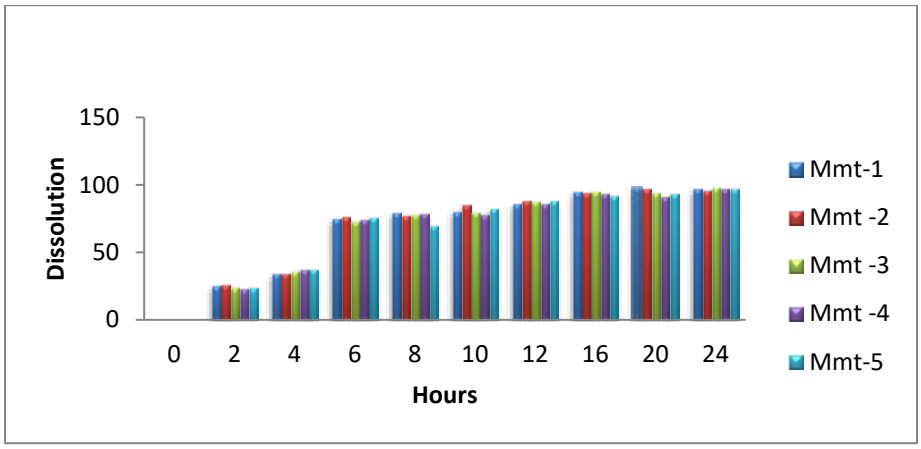
The in vitro dissolution profiles of Mmt-1, Mmt-2, Mmt-3, Mmt-4, and Mmt-5 matrix systems were evaluated over a period of 24 hours. The dissolution results provide insights into the release behavior and drug release kinetics of these formulations. At the start of the dissolution study (0 hours), all formulations showed no drug release, as indicated by the 0% drug release values. This indicates that the drug was effectively entrapped within the matrix systems and had not yet started to dissolve. After 2 hours, a gradual release of the drug was observed in all formulations. The drug release percentages ranged from 23.45% to 26.45%. These initial release rates suggest that the matrix systems began to disintegrate, allowing the drug to be released from the matrices into the dissolution medium. Over the next 4 to 6 hours, the drug release continued to increase. The release percentages ranged from 34.24% to 76.45% at 4 hours and from 69.75% to 88.64% at 6 hours. These results indicate a sustained and controlled release of the drug from the matrix systems. Between 8 and 10 hours, the drug release reached higher levels, with percentages

ranging from 77.84% to 88.64% at 8 hours and from 86.32% to 95.64% at 12 hours. This sustained release profile suggests that the matrix systems provided a prolonged release of the drug over an extended period. At 10 hours, the drug release percentages ranged from 92.65% to 95.64%, indicating that the majority of the drug had been released from the matrix systems. The sustained release behavior demonstrated by these formulations suggests their potential for achieving prolonged therapeutic drug levels. Finally, at the end of the 24-hour dissolution study, the drug release percentages ranged from 96.15% to 98.45%. These high release percentages indicate that the matrix systems had effectively released the majority of the drug.

Table No.10: In vitro dissolution of matrix systems

S.No	Time (Hours)	Mmt-1	Mmt -2	Mmt -3	Mmt -4	Mmt-5
1.	0	0	0	0	0	0
2.	2	25.65	26.45	24.50	23.45	24.45
3.	4	34.25	34.24	36.45	37.45	37.56
4.	6	75.45	76.45	73.24	74.23	76.24
5.	8	79.86	77.84	78.54	79.10	69.75
6.	10	80.65	85.45	79.86	78.42	82.35
7.	12	86.32	88.64	87.45	86.45	88.34
8.	16	95.64	94.23	95.47	93.45	92.65
9.	20	98.45	97.52	94.32	91.24	93.45
10.	24	97.65	96.15	98.31	97.41	97.65

Graph of In vitro dissolution of matrix systems



CONCLUSION

From the current study authors team concluded that the developed SRMT formulation with Aegle marmelos gum polymer retarded drug release for 10hrs. The optimized drug natural gum rations of SRMRT formulation retarded the drug release up-to desired time period. The hydrophilic matrix tablets containing polymer blend of Aegle marmelos gum retard the drug release rate of drug since both are swell-able natural polymer. From the results of in-vitro release experiment found that as increases the concentration of natural gum such as Aegle marmelos polymer decreased the release rate of drug. These studies confirm that this is possible due to slower erosion of gum higher viscosity. The higher viscosity of natural gum might have helped to keep the hydrated gel intact thus releasing the drug for extended period 10 hrs. Among all developed SRMRT especially F3 exhibited best 98.3111% drug release drug release rate.

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