World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Research Article
ISSN: 2583-6579
SJIF Impact Factor: 6.916
Year - 2026
Volume: 5; Issue: 5
Page: 361-376

OPTIMIZATION OF SUSTAINED RELEASE MATRIX TABLET FOR METFORMIN HYDROCHLORIDE BY USING NATURAL POLYMER

Bhupendra Mourya, Dr. Akash Yadav*, Dr. Dinesh Kumar Jain

IPS Academy College of Pharmacy, Knowledge Village, Rajendra Nagar, A.B. Road, Indore-452012 (M.P.), India.

Article Received: 4 March 2026 | | Article Revised: 26 March 2026 | | Article Accepted: 15 April 2026

***Corresponding Author: Dr. Akash Yadav**
IPS Academy College of Pharmacy, Knowledge Village, Rajendra Nagar, A.B. Road, Indore-452012 (M.P.), India.
DOI: https://doi.org/10.5281/zenodo.19917289

How to cite this Article: Bhupendra Mourya, Dr. Akash Yadav, Dr. Dinesh Kumar Jain (2026) OPTIMIZATION OF SUSTAINED RELEASE MATRIX TABLET FOR METFORMIN HYDROCHLORIDE BY USING NATURAL POLYMER. World Journal of Pharmaceutical Science and Research, 5(5), 361-376.

ABSTRACT

Metformin Hydrochloride has a short half-life, requiring multiple administrations to achieve the maintained control of type 2 Diabetes Mellitus. This may affect adherence to your medication regimen. The goal of this project was to create and optimize matrix tablets made with Metformin Hydrochloride using a sustained-release mechanism with a natural polymer system. To achieve this objective, Fenugreek Gum was chosen as the matrix-forming component and was used to create matrices with other excipients to make the product formulations. To evaluate these formulations, experiments were performed according to the Box–Behnken Method. The studies conducted were used to evaluate how the formulation components of Metformin Hydrochloride matrix tablets (including matrix particle size) affect the overall characteristics of the tablets (hardness, friability, weight variation, and drug content uniformity) as well as the dissolution profile. Statistical tools were used to analyze the data obtained from the experimental treatments to generate a second-order polynomial model for the response variables tested. This research provides an organized method of evaluating the formulation of sustained release dosage forms made using natural polymer materials and how these variables affect the formulation outcome.

KEYWORDS: Metformin Hydrochloride, Sustained release matrix tablet, Box-Behnken Design, Fenugreek Gum.

1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) has become a serious global public health issue, with numbers rapidly growing all over the world. Globally, T2DM accounts for approximately more than 96% of all detected cases of diabetes[1] according to IDF; it has been estimated that total health care costs related to diabetes for people between the ages of 20 and 79 reached approximately $969 billion in 2021 and are projected to be $1054 billion by 2045; and it is currently estimated that approximately 537 million people were living with diabetes in 2021, giving an age-adjusted prevalence of 6.1%. The prevalence rate for diabetes across the world has increased significantly from 3.2% in 1990, with

projections that this will increase to approximately 783 million by the year 2045. Estimates indicate that the overall global prevalence could increase to 9.8%, representing over 1.3 billion people. The most common form of diabetes is T2DM, accounting for nearly 90% of diabetes cases overall.[2,3]

Diabetes mellitus has two types of classifications: insulin-independent and insulin-dependent. Insulin-independent diabetes occurs due primarily to the body's inability to effectively use the available insulin (insulin deficiency) or as the result of insufficient release of insulin from the pancreas (insulin resistance). In either case, continuous oral antidiabetic use is essential for appropriate management of diabetes type II. Good glycemic control depends on drug bioavailability, continuous plasma levels, and patient adherence to therapy to promote better outcomes with type II diabetes.[4,5]

Due to the convenience and effectiveness of its use, oral route continues to be the most popular method for administering drugs. In addition, since most of the medications prescribed for chronic conditions require multiple daily doses, patient compliance with conventional dosage forms is problematic for a variety of reasons. Sustained-release (SR) solid dosage forms have therefore been developed to provide patients with the ability to maintain steady-state plasma levels, decrease the frequency of dosing, and increase the potential for success with therapy.[6]

Natural polymers in sustained-release metformin hydrochloride formulations provide biocompatibility, biodegradability, and safety while enabling efficient matrix formation, swelling-controlled drug release, and prolonged therapeutic action. Their cost-effectiveness, eco-friendly nature, and regulatory acceptability make them suitable alternatives to synthetic polymers, improving patient compliance and ensuring consistent glycemic control in long-term management of type 2 diabetes mellitus.

Metformin hydrochloride is the only available clinical biguanide that is used as the first-line medication for Type 2 diabetes. Metformin reduces both hepatic glucose production and insulin resistance; however, there is little risk of inducing hypoglycemia. The absorption of metformin via the gastrointestinal tract appears to be incomplete; furthermore, metformin has a bioavailability between 50-60% and a relatively short plasma half-life of 1.5-4.5 hours.[7]

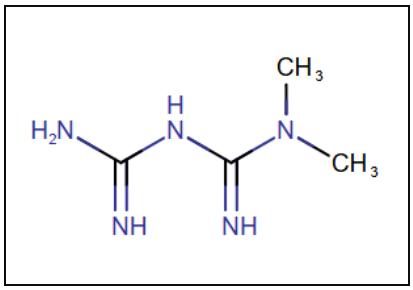


Figure 1: Chemical structure of Metformin Hydrochloride.

Fenugreek seed extract is an all-natural product (made from *Trigonella foenum-graecum* seed) that is rich in galactomannan and has been shown to have antihyperglycemic properties, including reductions in postprandial blood glucose concentrations and attenuation of the hyperglycaemia caused by stress. Fenugreek also has the potential to enhance the overall effects of metformin HCl on glycemic control by exhibiting complementary pharmacodynamic effects. When fenugreek is used in sustained-release metformin HCl tablets as a hydrophilic, matrix-forming polymer, it can modulate drug release via gel-formation and swelling mechanisms.

Box-Behnken Experimental Design

Response Surface Methodology (RSM) is a statistical method that looks at how independent factors affect responses, used to optimize processes. One of the principal components of RSM is designed experimentations that optimize an experimental run and provide a systematic and efficient analysis of several factors at several levels. Full-factorial designs, central-composite designs, and the Box-Behnken design are examples of how RSM is applied in experiments associated with optimization. Box-Behnken Designs (BBD) are often implemented using software packages such as Design-Expert, most commonly with three levels of experimentation. The BBD consists of 15 run replicates with an additional number of centre points to provide a measure of confidence that results can be reproduced reliably. The BBD is derived from a second-order polynomial predicting the interaction between input factors (variables) and output responses. The BBD used in pharmaceutical research has many benefits, including reducing the number of experiments needed while providing enough data for accurate analysis. By using BBD, factor interactions can be evaluated in an efficient manner, data can be interpreted at a higher level of sophistication, and optimized formulations will be developed faster and at a lower cost. By employing RSM and BBD, research productivity and quality is enhanced.[8-10]

Selected Independent variables and Dependent variables

The selected independent variables are displayed in table 1.

Table 1: Independent variables.

Factor	Name	Unit	Minimum	Maximum
A	Fenugreek Gum	%	10	20
B	PVP K30	%	2	5
C	MCC	%	15	25

The selected independent variables are displayed in table 2.

Table 2: Dependent variables.

Response	Variables	Unit
1.	Hardness	Kg/cm^2
2.	*In vitro* Drug release at 4 hrs	Percent (%)
3.	*In vitro* Drug release at 8 hrs	Percent (%)

Table 3: Formulation Runs as per Box-Behnken design.

Std	Runs	Independent Variables			Dependent Variables		
		Fenugreek gum (mg)	PVP K30 (mg)	Microcrystalline cellulose (mg)	Hardness (kg/cm2)	*In vitro* drug release at 4 hours	*In vitro* drug release at 8 hours
14	1	15	3.5	20	4.7	36.8	80.12
6	2	20	3.5	15	5.4	37.1	79.86
10	3	15	5	15	4.8	41.3	85.34
13	4	15	3.5	20	4.6	36.9	80.45
8	5	20	3.5	25	5.3	37.2	79.65
11	6	15	2	25	4.7	33.8	74.28
7	7	10	3.5	25	3.9	37	80.74
9	8	15	2	15	4.8	34.1	73.95
15	9	15	3.5	20	4.6	36.7	81.02
5	10	10	3.5	15	3.8	36.9	80.36
1	11	10	2	20	4	34	74.62
4	12	20	5	20	5.5	41.5	84.92
12	13	15	5	25	4.7	41.1	85.76
2	14	20	2	20	5.3	33.9	73.84
3	15	10	5	20	3.9	41.4	86.18

2. MATERIALS AND METHODS

Materials

Metformin hydrochloride active pharmaceutical ingredient used in the present study, was purchased from Universal Medicament, Nagpur (Maharashtra, India). Fenugreek gum (matrix former) was obtained from Arjuna Natural Extract, (Gujarat, India). Guar gum (release modifier) and Microcrystalline cellulose (MCC) (diluent) were procured from Signet Chemical Corporation in Mumbai (Maharashtra, India). Polyvinylpyrrolidone K30 (PVP K30) was used as a binder. Other chemicals including Magnesium stearate (lubricant) and talc (glidant) were also acquired from Signet Chemical Corporation, Mumbai (Maharashtra, India). All other chemicals and reagents used in the study were of analytical grade.

METHODS

Study of physical interaction between drug and polymer

The FTIR (Fourier Transform Infrared) Spectrophotometer Model: Shimadzu 8400S from Japan was used to obtain the infrared spectra of the pure drug and polymers independently from one another over the wavenumber range of 4000 to 400 cm^{-1}. Comparison of Spectra for the pure drug versus each of the pure polymer samples was conducted to identify potential physical interactions between the drugs and polymers.

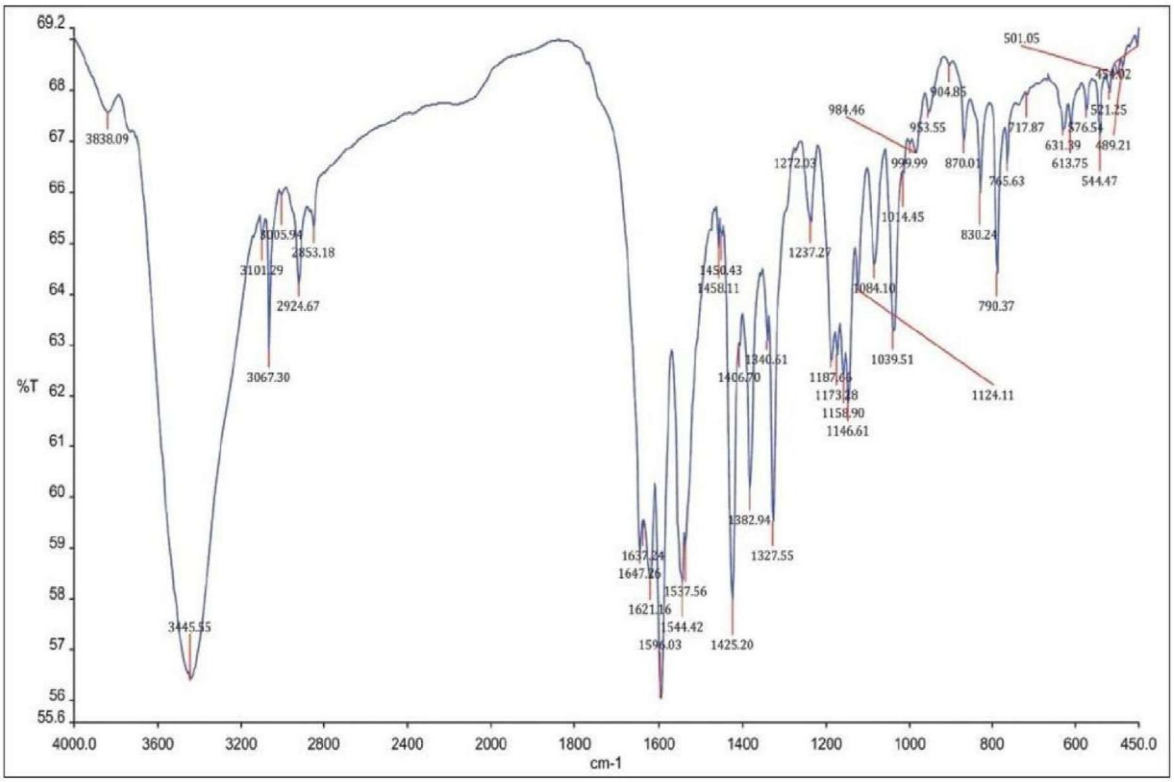


Figure 2: FT-IR spectra of Metformin Hydrochloride.

Wet Granulation Method- Tablet manufacturing employs wet granulation as a common and well-established method of converting smaller sized powders of the desired tablet ingredients into larger, more consistently sized granules by adding a liquid binder. First, the active pharmaceutical ingredient and excipients are blended together as a powder mixture to create a uniform drug distribution. The next step is to add a granulation fluid, typically a binder to the powder mixture in small amounts and with continued mixing to form a cohesive wet mass. After this step, the wet mass

is passed through a sieve or granulator so that it can be granulated into the appropriate size granules. The next processing step is to dry the granules using controlled heating. This removes excess water and aids stability of the granules. Once dry, the granules will be resized to achieve a uniform particle size before blending in lubricants and glidants, usually composed of magnesium stearate and talc, into the granules.

The final processing step is to compress the prepared granules into tablets using a tablet compression machine. Wet granulation improves flow characteristics, compressibility, and content uniformity leading to improved quality and mechanical strength of finished tablets.

Ideal Characteristics of Wet Granulation Method

- **Good flow properties:** The prepared granules should possess adequate flow characteristics to allow smooth movement into the tablet die during compression.
- **Consistent particle size:** Granules should have a relatively uniform size distribution to help maintain consistent tablet weight and dose uniformity.
- **Sufficient granule strength:** The granules should be mechanically strong so they can tolerate handling and processing without excessive breakage or dust formation.
- **Proper compressibility:** Granules must compress effectively to produce tablets with adequate hardness and structural integrity.
- **Uniform drug dispersion:** The active pharmaceutical ingredient should be evenly distributed throughout the granules to ensure accurate drug content in each tablet.[11-13]

Preparation of matrix tablets using drug substances, polymers and other excipients-

Metformin Hydrochloride matrix tablets were formulated through the wet granulation process according to the method of preparation using PVP K30 as a binder. Various formulations were developed using different concentrations of fenugreek gum and guar gum to produce matrix former and release modifier. The tablet ingredients and their role is shown in Table 1. The formulations were prepared using the following steps:

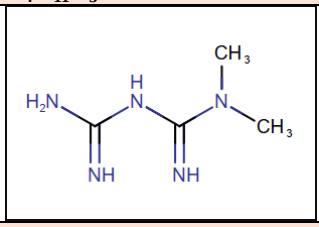
- **Step 1 Sifting:** Accurately weigh and sift metformin hydrochloride, microcrystalline cellulose (MCC), fenugreek gum, and guar gum through a 40# mesh sieve.
- **Step 2 Dry Mixing:** Transfer all sifted materials (except talc and magnesium stearate) into a polybag and mix thoroughly for 20-30 minutes or until a homogeneous mixture of dry components is obtained. Take samples for blend uniformity and loss on drying testing.
- **Step 3 Preparation of Binder Solution:** PVP K30 was dissolved in an appropriate quantity of distilled water with continuous stirring to obtain a clear binder solution.
- **Step 4 Wet Granulation:** Add the binder solution slowly to the dry blend with continuous mixing until a cohesive wet mass is formed. Visually determine the endpoint of granulation using a hand squeeze test.
- **Step 5 Wet Screening:** Pass the wet mass through a 10# mesh sieve to produce uniform wet granules.
- **Step 6 Drying:** Granules were subjected to air drying for a period of approximately 10 minutes and then dried using a tray drier at 45^{o}C until they reached their target moisture level corresponding to a moisture content below 2-3%.
- **Step 7 Dry Screening:** After drying the granules, they were screened using a 20# mesh sieve and collected in double polyethylene-lined containers.

- **Step 8 Lubrication:** Talc (as a glidant) and magnesium stearate (as a lubricant) were incorporated into the granules, and mixed gently for 5 minutes to produce a lubricated blend.
- **Step 9 Compression:** The lubricated granules were compressed using a single rotary tablet press with appropriate punches to produce a tablet with a hardness of 5-7kg/cm², and the tablets were then evaluated for the physical characteristics of the tablets and stored in tightly closed containers for additional testing.

Table 4: List of excipients used in formulation and their role

Excipients	Role
Metformin hydrochloride	Active pharmaceutical ingredients
Fenugreek gum	Matrix former
Guar gum	Release modifier
PVP K30	Binder
MCC	Diluent
Magnesium Stearate	Lubricant
Talc	Glidant

Table 5: Physical and chemical parameters of metformin hydrochloride.

S. No.	Parameter	Predicted value
1.	**Molecular formula**	**$C_4H_{11}N_5$.Hcl**
2.	Molecular structure	
3.	IUPAC name	1-carbamimidamido-N, N-dimethylmethanimidamide hydrochloride
4.	Molecular weight	165.62 g/mol
5.	BCS class	Class III
6.	Ph and pKa	2.8 and 6.8
7.	Crystallinity	Crystalline solid
8.	Melting point	223-226°C
9.	Solubility	Freely soluble in water and 0.1 N HCL

PRE-COMPRESSION STUDIES

Angle of Repose- Angle of repose is the maximum degree an object can stable sit on a slope before sliding. The angle of repose indicates the degrees of flowing freely and stickiness or will affect how fast or slow the powder is going to flow. The angle of repose is measured by building a cone of atleast 1 inch tall above the base and continue building the cone until it collapses to form a heap.

$$\text{Angle of repose}(\tan\theta) = \frac{\text{Height of pile}}{\text{Radius of the base pile}}$$

Bulk Density- Bulk density of a powder is defined as the mass of that powder divided by the entire volume. The bulk density of a powder can be expressed in different units such as g/cm³ or kg/L, and provides an indication of the powder's ability to compact to fill an entire volume. The bulk density can be determined by using a graduated cylinder and weighing (mass) a known volume of the powder in order to provide a valid measurement of the bulk density.

$$\text{Bulk density} = \frac{\text{Mass of bulk powder}}{\text{Volume of bulk powder}}$$

Tapped Density- The maximum bulk density reached by tapping or vibrating a powder sample until voids between particles are minimized is called "Tapped Density". Once reached, tapping or vibrating the sample will continue until the volume is stable, indicating how efficiently the powder can fill space when under compression.

$$\text{Tapped density} = \frac{\text{Weight of Granules}}{\text{Final volume after tapping}}$$

Hausner's Ratio- Hausner's ratio is the ratio of tapped density to bulk density, calculated using the formula:

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

It offers information about the packing efficiency and flow behavior of the powder. Good flowability is indicated by a ratio near 1, and poor flowability is indicated by values greater than 1.

Carr's Index- Carr's index, also referred to as the compressibility index is parameter used to evaluate the compressibility characteristics of a powder. It is determined using the following equation:

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100\%$$

The Carr's Index gives an indication of how well a particular powder flows when it has been compacted or subjected to mechanical vibration. A low Carr's Index corresponds with excellent powder flow properties, while a high Carr's Index represents poor powder flow characteristics and significant interparticle adhesion.

Metformin hydrochloride identification studies- Metformin HCl 100 mg was accurately weighed and dissolved in 100 ml distilled water and subsequent dilution was made to get the required concentrations (1000µg/ml). The wave length of maximum absorbance (λ max) of this clear solution was determined from 200- 400nm and water was used as blank.

- **Preparation of stock solution:** Metformin HCl 100 mg was dissolved in water 100 ml (1000µg/ml) Stock solution I. From this solution 10 ml was pipetted and diluted with water up to 100ml (100µg/ml) Stock solution II was prepared.
- **Preparation of sample solution:** From Stock solution II 1 ml was pipetted and diluted with water up to 10ml (10µg/ml). From Stock solution II was carried out taking 1, 2, 3, 4, 5 and 6 ml and made up to 60 ml to obtain the concentration of 10, 20, 30, 40, 50 and 60 µg/ml respectively. The absorbance was measured at 229 nm against the respective blank solution using UV visible spectrophotometer 1800. The standard curves were plotted by putting the known concentration on X- axis and the obtained absorbance on Y- axis. The absorbance of each diluted solution was then measured at a wavelength of 229 nm using a UV-visible double beam spectrophotometer. This data was used to construct the calibration curve for Metformin HCl, enabling accurate determination of its concentration in subsequent samples based on their absorbance values.

Melting Point of Metformin hydrochloride- The Melting point of Metformin Hydrochloride was determined by using an electric Melting point apparatus. The melting point was determined by sealing a sample of metformin hydrochloride into a capillary tube to construct a sample of metformin hydrochloride and by placing the sealed sample into a digital melting point instrument's chamber. The digital melting point instrument was heated slowly until the first evidence of liquefaction was noted and the melting statement was recorded. The procedure was repeated only 3 times to confirm repeatability and thus establish the average. Therefore, the method results in a consistent and reproducible characterisation of metformin hydrochloride.[14-16]

POST COMPRESSION STUDIES

- **Organoleptic Characteristics-** Tablets were visually checked for overall physical characteristics such as colour, appearance, odour and shape to ensure consistency of individual batches and acceptable aesthetic quality.
- **Thickness & Diameter-** The thickness and diameter of tablets were determined using a vernier calliper. Five tablets from each batch were measured individually, and mean value was calculated and reported in millimeters (mm).
- **Hardness-** Hardness testing of the tablets was conducted via a Monsanto hardness tester using three tablet samples. Average hardness was recorded in kilograms per centimeter square (kg/cm^2).
- **Friability-** Friability of tablet was determined using a Roche friabilator in accordance with Indian Pharmacopoeia (IP) specifications. Initially, 20 tablets were weighed collectively to obtain the initial weight (Wi). The tablets were then subjected to rotation at 25 rpm for 4 minutes. After completion of the test, the tablets were dedusted and reweighed to obtain the final weight (Wf). The percentage friability (%F) for each formulation was subsequently calculated using the appropriate formula.

$$F = \frac{Wi - Wf}{Wi} \times 100$$

- **Weight variation-** The weight of each tablet in each batch was assessed for their uniformity by selecting 20 random tablets from that batch. The next step was to weigh each of them using a calibrated analytical balance and find out what the average weight was based on the weights of these 20 individual tablets. The difference between the individual weight of each tablet and the average was calculated for each of those 20 tablets. All of the evaluations performed according to the Indian Pharmacopoeia. Tablets with an average weight greater than 250 mg will have a variation of ±5% of the average weight, where no more than 2 individual tablets may be outside that tolerance or may not exceed twice that tolerance value.

$$\%\text{Deviation} = \frac{\text{Weight of each tablet} - \text{average weight of tablet}}{\text{Average weight of tablet}} \times 100$$

- ***In-vitro* dissolution studies-** The dissolution profile study using USP Dissolution Apparatus II (Paddle) for metformin hydrochloride tablets was performed. The dissolution was performed in 900 ml of 0.1 N HCl for the first two hours, then in 900 ml of phosphate buffer at pH 6.8 for the next six hours. The rotational speed of the paddle was maintained at 50 rpm, and the temperature was maintained at 37±0.5°C during the entire study. At predetermined intervals samples were withdrawn, and fresh medium was added to replace the withdrawn volume at preset time points. The collected samples were analyzed by using UV Spectrophotometer at 229 nm.[17]

This process is done on all batches. The average percentage of metformin hydrochloride released at different time points was determined from the sample image and plotted against time.

Calculation of % drug release involves the following steps
Determined concentration of drug released by using formula

$$Y = mx + c$$

Y is the absorbance, m is slope, C is intercept, X is concentration (µg/ml)

$$\text{Amount of drug release} = \frac{\text{Conc.} \times \text{dilution factor} \times \text{volume of dissolution medium}}{1000}$$

- **Stability Studies-** All formulations were evaluated for short-term stability according to accelerated study guidelines from the ICH. The tablets were packaged in aluminium foil and put inside sealed glass containers to be stored at different temperatures. There were 3 evaluations (at 10, 20, and 30 days) of the following: physical appearance; drug content; and performance parameters to determine formulation stability.[18-20]

3. RESULTS AND DISCUSSION

Organoleptic properties: Organoleptic properties of the drug sample were found to be as given in table below.

Table 6: Organoleptic Properties of Metformin Hydrochloride.

S. No.	Organoleptic Characteristics	Result
1.	Colour	White or off-white crystalline powder
2.	Nature	Crystalline Powder
3.	Odour	Odourless
4.	Taste	Slightly bitter taste

Melting Point of Metformin Hydrochloride: The final reading was obtained by averaging the results of three independent experiments, resulting in a temperature of 225^{o}C.

pH determination of Metformin Hydrochloride: The pH range of metformin hydrochloride is adjusted to 6.5 to 6.7 during preparation to ensure that it is stable and effective in treating diabetes.

Solubility study of Metformin Hydrochloride: The solubility of Metformin Hydrochloride was tested with distilled water. An excess of the drug was added into a conical flask with some distilled water. The flask was then put onto a magnetic stirrer and continuously stirred at room temperature for about 24 hours or until all of the drug had dissolved to reach equilibrium between the drug and the distilled water. After stirring, the solution was filtered to remove undissolved particles from the mixture, leaving a clear solution.
The amount of drug contained within the obtain filtrate was then determined using a UV-Visible spectrophotometer at the appropriate absorbance max for Metformin Hydrochloride and compared to a pre-determined standard curve thus, giving a concentration of drug in the filtrate (mg/mL). This study will assist in further understanding the solubility properties/metformin hydrochloride, and will help to develop formulation.

Table 7: Solubility of metformin hydrochloride in solvents.

S. No.	Name of solvent	Solubility
1.	Distilled water	Freely soluble
2.	0.1 N HCL	Freely soluble
3.	Methanol	Slightly soluble
4.	Acetone	Practically Insoluble
5.	Ether	Practically Insoluble

Table 8: Flow properties of powder blend.

S. No.	Angle of repose (θ)	Bulk density (g/cm^2)	Tapped density (g/cm^2)	Hausner's Ratio	Carr's Index (%)
1.	31.42	0.5	0.59	1.18	15.25
2.	32.18	0.48	0.56	1.16	14.28
3.	30.95	0.51	0.58	1.13	12.06
4.	33.1	0.47	0.55	1.17	14.54
5.	32.64	0.52	0.6	1.15	13.33
6.	31.87	0.49	0.57	1.16	14.03
7.	30.74	0.5	0.56	1.12	10.71
8.	32.55	0.51	0.59	1.15	13.56
9.	33.22	0.48	0.57	1.18	15.78
10.	31.96	0.53	0.61	1.15	13.11
11.	32.84	0.49	0.58	1.18	15.51
12.	30.68	0.52	0.6	1.15	13.33
13.	31.74	0.54	0.62	1.14	12.9
14.	32.97	0.5	0.59	1.18	15.25
15.	31.55	0.51	0.58	1.14	12.06

Post-compression studies

Organoleptic characters

Table 9: Organoleptic properties of Metformin Hydrochloride Tablets

S. No.	Organoleptic Characteristics	Result
1.	Colour	White or off-white
2.	Shape	Oval
3.	Odour	Odourless
4.	Taste	Slightly bitter and nutty taste

Identification of Metformin Hydrochloride by UV spectrophotometry

Derivation of drug spectrum: The distilled water-based stock solution of Metformin HCl, with a concentration of 10µg/ml, exhibited a peak absorption wavelength (λ max) at 229 nm. The absorbance observed at this wavelength was measured to be 0.0765.

Preparation of calibration curve of Metformin HCl in water: The calibration curve of Metformin HCl dissolved in distilled water was plotted using a UV spectrophotometer and measured at a wavelength of 229 nm. This curve was created from 6 dilutions of stock solution, each at 10 µg/ml. The resulting curve is shown in Table 10.

Table 10: Calibration curve data of Metformin HCl in distilled water.

S. No.	Concentration (µg/ml)	Absorbance at 229 nm
1.	10	0.0765
2.	20	0.1408
3.	30	0.2023
4.	40	0.2676
5.	50	0.3231
6.	60	0.3875

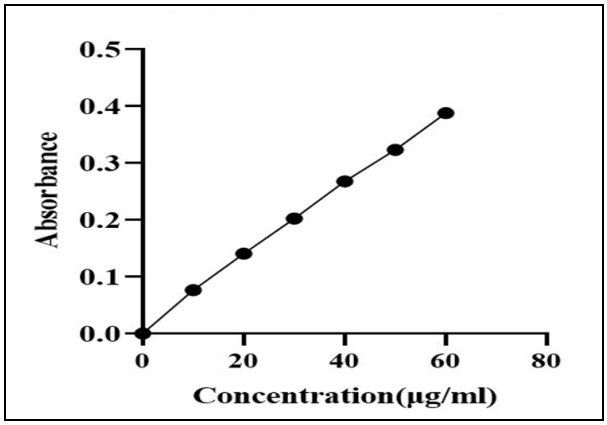


Figure 3: Calibration Curve of Metformin Hydrochloride in Distilled Water.

Table 11: Post-compression parameters of tablets.

Formulation Code	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Weight Variation (mg)
F1	4.62 ± 0.18	4.3 ± 0.36	0.62 ± 0.04	748.16 ± 2.13
F2	4.68 ± 0.10	5.1 ± 0.58	0.58 ± 0.05	752.62 ± 4.13
F3	4.70 ± 0.16	4.5 ± 0.63	0.54 ± 0.03	746.53 ± 3.13
F4	4.75 ± 0.17	4.6 ± 0.12	0.51 ± 0.02	751.92 ± 2.83
F5	4.78 ± 0.19	4.8 ± 0.22	0.49 ± 0.03	744.83 ± 6.84
F6	4.80 ± 0.15	4.6 ± 0.05	0.46 ± 0.02	747.75 ± 3.46
F7	4.85 ± 0.18	4.9 ± 0.03	0.44 ± 0.02	751.31 ± 2.22
F8	4.88 ± 0.16	5.1 ± 0.03	0.41 ± 0.02	746.97 ± 5.88
F9	4.90 ± 0.17	4.2 ± 0.04	0.39 ± 0.01	752.26 ± 3.44
F10	4.92 ± 0.10	4.2 ± 0.54	0.36 ± 0.02	750.61 ± 0.99
F11	4.95 ± 0.18	4.6 ± 0.83	0.35 ± 0.02	747.83 ± 4.44
F12	4.98 ± 0.17	5.1 ± 0.28	0.33 ± 0.01	748.22 ± 2.67
F13	5.00 ± 0.19	4.8 ± 0.62	0.32 ± 0.02	751.31 ± 2.82
F14	5.02 ± 0.16	4.3 ± 0.84	0.31 ± 0.01	749.13 ± 0.92
F15	5.05 ± 0.18	4.6 ± 0.32	0.30 ± 0.02	750.21 ± 0.33

***In-vitro* dissolution studies**

Table 12: Cumulative drug release of Metformin HCL tablets formulations (F1-F15).

Formulation Code	Cumulative Drug Release (%)							
	Time (hr)							
	1 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h
F1	10.5	18.2	27.4	36.8	49.5	61.7	71.4	80.12
F2	11.1	19.3	28.2	37.1	50.3	63.4	72.8	79.86
F3	13.2	21.7	31.5	41.3	55.8	68.6	77.4	85.34
F4	10.8	18.7	27.8	36.9	49.8	62.1	71.9	80.45
F5	11.4	19.6	28.7	37.2	50.1	62.8	71.6	79.65
F6	9.8	17.2	25.6	33.8	45.3	56.9	66.1	74.28
F7	11	18.9	27.9	37	50.4	63.7	72.9	80.74
F8	10.2	17.8	25.9	34.1	46.2	57.8	66.9	73.95
F9	11.3	19.2	28.1	36.7	49.9	63.2	72.6	81.02
F10	11.2	19	27.6	36.9	49.6	62.5	72.1	80.36
F11	9.9	17.4	25.7	34	45.5	56.8	65.7	74.62
F12	13.4	22.3	31.9	41.5	56.7	69.9	78.6	84.92
F13	13.1	21.9	31.6	41.1	56.2	69.3	78.4	85.76
F14	10	17.6	25.8	33.9	46	57.4	66.5	73.84
F15	13.3	22.1	31.8	41.4	56.8	70.2	79.1	86.18

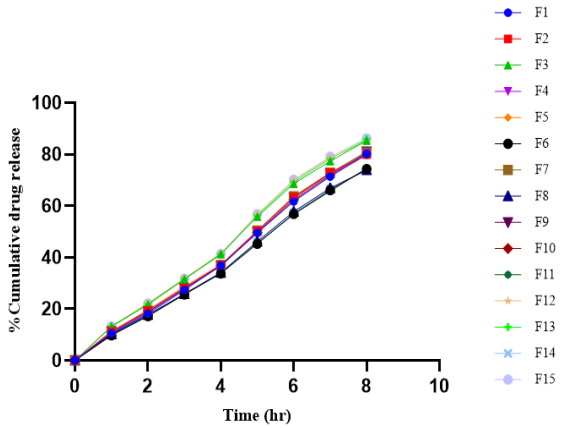
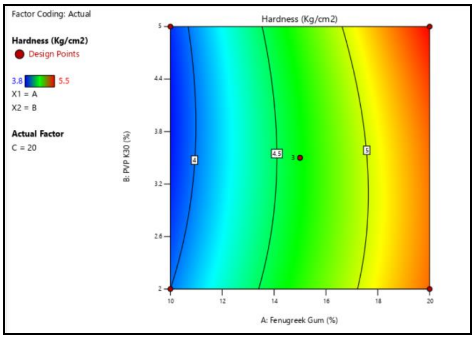


Figure 4: Cumulative drug release of Metformin Hydrochloride tablets.

Response data for all 15 batches by using Box-Behnken Experimental Design (F1-F15).

Response 1 Hardness (kg/cm^2).



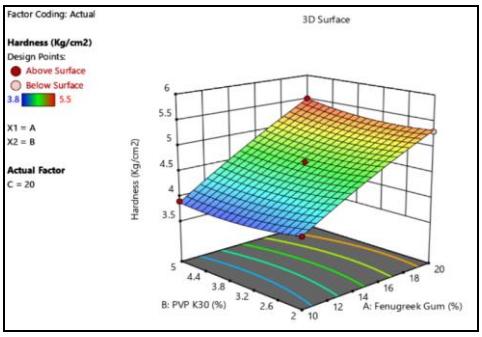


Figure 5: The 2D contour plot and 3D response surface demonstrates the combined influence of Fenugreek Gum and PVP K30 on tablet hardness, indicating a gradual increase in hardness values.

ANOVA for Quadratic model

Response 1: Hardness.

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	4.44	9	0.4932	174.08	< 0.0001	**Significant**
A-Fenugreek Gum	4.35	1	4.35	1535.74	< 0.0001	
B-PVP K30	0.0012	1	0.0012	0.4412	0.536	
C-Microcrystalline cellulose	0.005	1	0.005	1.76	0.2414	
AB	0.0225	1	0.0225	7.94	0.0372	
AC	0.01	1	0.01	3.53	0.1191	
BC	0	1	0	0	1	
A²	0.0108	1	0.0108	3.82	0.1079	
B²	0.0339	1	0.0339	11.97	0.0181	
C²	0.0016	1	0.0016	0.5656	0.4859	
Residual	0.0142	5	0.0028			
Lack of Fit	0.0075	3	0.0025	0.75	0.6148	**Not significant**
Pure Error	0.0067	2	0.0033			
Cor Total	4.45	14				

Response 2: *In-vitro* drug release at 4 hrs (%)

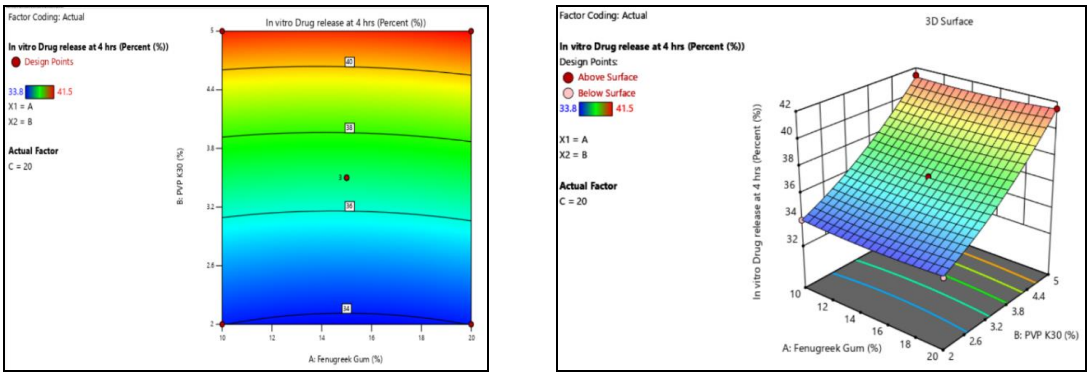


Figure 6: The 2D contour plot and 3D response surface illustrates the combined effect of fenugreek gum and PVP K30 concentrations on *In-vitro* drug release at 4 hrs in sustained release tablets.

ANOVA for Quadratic model

Response 2: *In-vitro* drug release at 4 hrs

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	110.76	9	12.31	464.42	< 0.0001	**Significant**
A-Fenugreek Gum	0.02	1	0.02	0.7547	0.4247	
B-PVP K30	108.78	1	108.78	4104.95	< 0.0001	
C-Microcrystalline cellulose	0.0113	1	0.0113	0.4245	0.5434	
AB	0.01	1	0.01	0.3774	0.5659	
AC	0	1	0	0	1	
BC	0.0025	1	0.0025	0.0943	0.7711	
A^2	0.1298	1	0.1298	4.9	0.0778	
B^2	1.87	1	1.87	70.73	0.0004	
C^2	0.0144	1	0.0144	0.5443	0.4938	
Residual	0.1325	5	0.0265			
Lack of Fit	0.1125	3	0.0375	3.75	0.2176	**Not significant**
Pure Error	0.02	2	0.01			
Cor Total	110.9	14				

Response 3: *In-vitro* drug release at 8 hrs (%)

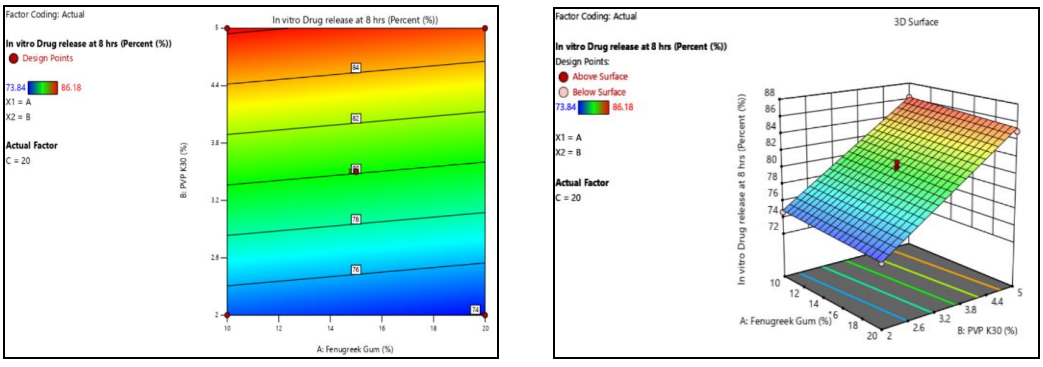


Figure 7: The 2D contour plot and 3D response surface representing the presence of fenugreek gum and PVP K30 concentrations on *In-vitro* drug release at 8 hrs, indicating gradual variation in release percentage.

ANOVA for Linear model

Response 3: *In-vitro* drug release at 8 hrs

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	260.65	3	86.88	578.39	< 0.0001	**Significant**
A-Fenugreek Gum	1.65	1	1.65	10.97	0.0069	
B-PVP K30	258.9	1	258.9	1723.49	< 0.0001	
C- Microcrystalline cellulose	0.1058	1	0.1058	0.7043	0.4192	
Residual	1.65	11	0.1502			
Lack of Fit	1.24	9	0.1375	0.6634	0.7275	**Not significant**
Pure Error	0.4146	2	0.2073			
Cor Total	262.3	14				

Table 13: Pre compressional data of optimized batch (F16).

S. No.	Pre compressional evaluation parameter	Results
1.	Angle of Repose (θ)	31.88
2.	Bulk Density (g/cm^2)	0.51
3.	Tapped Density (g/cm^2)	0.59
4.	Hausner's Ratio	1.15
5.	Carr's Index (%)	13.56 %

Table 14: Post compressional data of optimized batch (F16).

S. No.	Post-compression evaluation Parameter	Results
1.	Thickness (mm)	5.00 ± 0.15
2.	Hardness (kg/cm²)	4.9 ± 0.20
3.	Friability (%)	0.31 ± 0.02
4.	Weight Variation (mg)	750.32 ± 2.10
5.	% Drug release	84.60%

Table 15: *In vitro* drug release for optimized batch (F16).

S. No.	Time (hr)	F16 (% Drug Release)
1.	1 h	12.0
2.	2 h	20.5
3.	3 h	30.2
4.	4 h	39.8
5.	5 h	54.5
6.	6 h	67.8
7.	7 h	76.9
8.	8 h	84.6

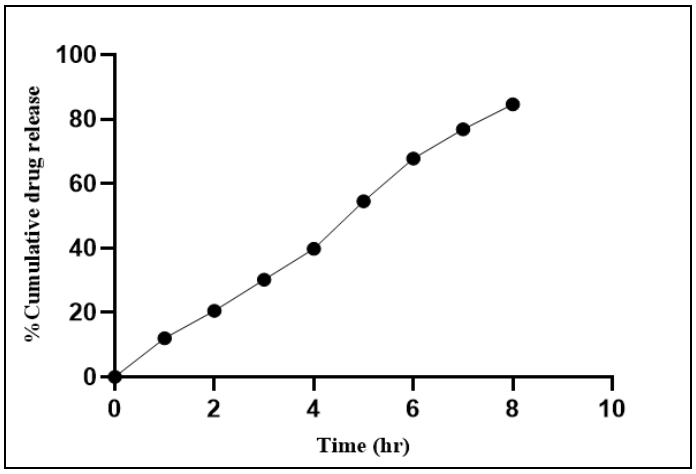


Figure 8: Percent drug release of batch F16 (Optimized Batch).

The optimized formulation F16 exhibited 84.6% cumulative drug release within 8 hours. The batch was further evaluated for all required pre-compression and post-compression parameters to ensure the quality of the dosage form. The obtained results were found within acceptable limits, indicating satisfactory formulation performance.

Stability Studies

According to the ICH guidelines, the stability study of Metformin hydrochloride (F16) optimized sustained-release tablets was performed under recommended stability testing conditions. Tablets were stored at 40 ± 2 °C and 75 ± 5% RH for three 3 months. During the study, samples were evaluated monthly for physical appearance, hardness, friability, drug content, and *in-vitro* drug release profile. The study results showed no significant changes in both physical properties and drug release characteristics of tablets during the storage period. The drug content and dissolution characteristics were found to be within acceptable limits as per the compendial specification, and thus demonstrate that the optimized formulation is stable when stored under recommended conditions.

4. CONCLUSION

Current Study is aimed to design and optimize sustained release Metformin Hydrochloride matrix tablets using natural polymer-based excipients for their potential to control drug release. To achieve this purpose, other pharmaceutical excipients were utilized along with fenugreek gum which served as the main matrix forming agent throughout this study. The Box-Behnken Design was used to formulate each batch and investigate how each of the formulation variables affect tablet hardness and the subsequent release of the drug over four different time points. The flow characteristics of the formulated powders were determined to be acceptable based upon the values obtained for angle of repose, bulk density, tapped density, Hausner’s ratio and Carr's index. In addition, post compression parameters included thickness, hardness, friability, and weight variation which all fell within the acceptable limits set forth by the applicable pharmacopoeial regulations confirming acceptable quality tablets were produced. *In-vitro* dissolution data indicated F16 was the optimized formulation based upon 84.6% cumulative release over 8 hours indicating that sustained drug release occurred with this formulation. Stability testing showed that F16 remains stable under accelerated conditions. Thus, this formulation has great potential to be utilized as an effective sustained release delivery system for long-term treatment of Type 2 Diabetes Mellitus.

5. REFERENCES

1. Ong KL. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet, 2023; 402(10397): 203–234.
2. Sun H, et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Research and Clinical Practice, 2022; 183: 109119.
3. Gieroba B, Kryska A, Sroka-Bartnicka A. Type 2 diabetes mellitus – conventional therapies and future perspectives in innovative treatment. Biochemistry and Biophysics Reports, 2025; 42: 1–16.
4. Kakad SB, Rachh PR. Design, development and characterization of immediate release matrix tablet of vildagliptin. International Journal of Pharmaceutical Quality Assurance, 2021; 12(4): 303–308.
5. Kakad SB, Rachh PR. Effect of hydrophilic polymer and binder on drug release of metformin HCl sustained release tablet. International Journal of Health Sciences, 2022; 6(S3): 6635–6643.

6. Roy H, Brahma CK, Nandi S, Parida KR. Formulation and design of sustained release matrix tablets of metformin hydrochloride: influence of hypromellose and polyacrylate polymers. International Journal of Applied and Basic Medical Research, 2013; 3(1): 55–63.
7. Wadher KJ, Kakde RB, Umekar MJ. Formulation of sustained release metformin hydrochloride matrix tablets: influence of hydrophilic polymers on the release rate and *In- vitro* evaluation. International Journal of Research in Controlled Release, 2011; 1(1): 9–16.
8. Cha KH, Lee N, Kim MS, Kim JS, Park HJ, Park J, et al. Development and optimization of a novel sustained-release tablet formulation for bupropion hydrochloride using Box-Behnken design. Journal of Pharmaceutical Investigation, 2010; 40(5): 313–319.
9. Roy H, Nandi S, Pavani U, Lakshmi U, Reddy TS, Gayatri DV. Optimization and quality by design approach for piroxicam fast dissolving tablet formulations using Box-Behnken design. Current Drug Therapy, 2020; 15(2): 152–165.
10. Sharma S, Chauhan S. A review: an overview of natural superdisintegrants. Research Journal of Topical and Cosmetic Sciences, 2021; 12(1): 13–24.
11. Mulani HT, Patel B, Shah NJ. Development of pH-independent matrix type sustained release drug delivery system of propranolol hydrochloride. Journal of Applied Pharmaceutical Science, 2011; 1(3): 83–92.
12. Agrawal R, Naveen Y. Pharmaceutical processing – a review on wet granulation technology. International Journal of Pharmacy Frontiers Research, 2011; 1(1): 65–83.
13. Hansuld EM, Briens L. A review of monitoring methods for pharmaceutical wet granulation. International Journal of Pharmaceutics, 2014; 472(1–2): 192–201.
14. Butola M, Bhatt V, Nainwal N, Jakhmola V, Dobhal K, Ale Y. Preparation and evaluation of polymer fused metformin hydrochloride sustained release tablet. Indian Journal of Pharmaceutical Education and Research, 2023; 57(3): 711–716.
15. Sonare T, Kumar A, Khadsondni K, Mandloi K, Yadav A, Jain DK. Strategic optimization of rapidly disintegrating tablets utilizing Box–Behnken experimental design. European Journal of Pharmaceutical and Medical Research, 2025; 12(4): 1–13.
16. Tomar A, Wadhwani S, Bhadauria RS. A preformulation study of pure metformin HCl. International Journal of Pharma Erudition, 2019; 8(4): 1–9.
17. Das S, Samanta A, De HS. Formulation, *In-vitro* release kinetics and stability interpretation of sustained release tablets of metformin hydrochloride. International Journal of Pharmacy and Pharmaceutical Sciences, 2015; 7(3): 418–422.
18. Chandira M, Venkateswarlu BS, Shankarrao JA, Bhowmik D, Jayakar B, Narayana TV. Formulation and evaluation of extended-release tablets containing metformin HCl. International Journal of Chemical Technology Research, 2010; 2(2): 1320–1329.
19. Sonare T, Kumar A, Khadsondni K, Mandloi K, Yadav A, Jain DK. Construction and analysis of instant effect formulation involving Box-Behnken. Journal of Clinical Research & Clinical Trials, 2025; 4(3): 1–15.
20. Sonare T, Kumar A, Khadsondni K, Mandloi K, Yadav A, Jain DK. Complication and assessment of time sensitive tablets involving design expert software. Journal of Diabetes Research Review & Reports, 2025; 7(1): 1–11.