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Formulation And Evaluation Of Metformin Hydrochloride Sustained Release Capsule

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ABSTRACT

Metformin Hydrochloride (MH) is a synthesis of N, N -dimethyl guanidine, a type of medicament which is used to treat type II diabetes. Emil Worner and James Belt in the year 1922 were the first to synthesized dimethyl guanidine. MH has various other advantages such as; weight loss, improper fertility, slowing down the tumour growth and few more. The current work is focused on, to sustain the release of the drug in the body for a larger period of time. To perform this study various factor were taken into consideration such as drug, Excipients (HPMC, PVP K30, Magnesium stearate, MCC, NaCMC and Starch) compatibility study, Preformulation studies of raw material and granules. The granules were prepared using wet granulation method, and all the quality control parameter study for formulated 10 capsules were performed. Out of these 10 formulations, formulation 7 (F7) was subjected to have sustain release. Further, F7 was subjected to comparative study with other marketed available tablet and was found out that our formulation has sustained release up to the 13th hr and were as marketed tablet up to 11th hr. Finally accelerated stability study was performed till 3 months and was found that there were no significant changes.

Keywords: *Metformin hydrochloride (MH); polyvinylpyrrolidone (PVP K30); Fourier Transform Infrared Spectroscopy (FTIR); Sustained release*

1. INTRODUCTION

Metformin Hydrochloride (MH) is a biguanide antihyperglycemic drug that is a cornerstone of current therapy for the management of non-insulin dependent diabetic mellitus. It exhibits notable efficacy in reducing the risk of disease development MH (1,1-dimethylbiguanide hydrochloride) has been the most regularly used glucose lowering drug(01).MH was first described in scientific literature in 1922 by Emil Werner and Jams Bell .Later french physician Jean Stearne began the study in humans in 1950s and in 1957 it was used to treat diabetes and came into surveillance(02).MH decreases hepatic glucose production and intestinal absorption of glucose(03).

Conventional dosage form of MH is released immediately after ingestion, providing a rapid onset of action. In contrast, sustained release capsules release the medication gradually over an extended period, allowing for a more prolonged and controlled release of the drug by using suitable polymers and lubricants, which can lead to a smoother blood glucose-lowering effect and potentially fewer side effects(04).

This study aims to formulate and evaluate sustained release capsules of metformin hydrochloride, leveraging various pharmaceutical excipients and formulation techniques. By controlling the release kinetics, these capsules aim to maintain therapeutic drug levels over an extended period, thus improving patient adherence and minimizing adverse effects associated with peak plasma concentrations(05).

Key aspects of this investigation include the selection and optimization of excipients to modulate drug release kinetics, characterization of the physical and chemical properties of the formulated capsules, and evaluation of in vitro/in vivo

performance parameters(06). Through systematic formulation development and rigorous evaluation, this study seeks to contribute to the advancement of sustained release formulations of metformin hydrochloride, with the ultimate goal of enhancing patient outcomes in the management of type 2 diabetes mellitus(07).

2. MATERIALS AND EXPERIMENTAL METHODS

MATERIALS

Table 1: Instruments

S.No	Name	Manufacturer
1.	Electronic weighing balance	ScaleTec. Gujarat, India
2.	Sieve	Gloson Test Sieve, Gujarat, India
3.	Bulk density apparatus	DBK Instruments Mumbai, India
4.	Disintegration apparatus	Lab India Analytical Pvt Ltd, Mumbai, India
5.	Dissolution apparatus	DURALAB, Parlin, New Jersey
6.	Ultraviolet spectrophotometer	SHIMADZU, Japan
7.	FTIR Spectrophotometer	BRUKER, USA
8.	Manual Capsule filling machine	Adinath Machines, Gujarat, India
9.	pH meter	King Lab Instrument Pvt Ltd, Tamilnadu, India
10.	Mortar and pestle	Jain scientific suppliers, Ambala, India
11.	Screw gauge	Zoom, Scientific world, Ambala, India
12.	Melting point apparatus	VSI Electronic Pvt Ltd Mohali, Punjab

Table 2: Chemicals

S.No	Materials	Supplier
1.	Metformin Hydrochloride	Cadila Pharmaceuticals, Gujarat, India
2.	Polyvinylpyrolidine	Fine Chemicals Bangalouru, Karnataka, India
3.	Magnesium stearate	Nice Chemicals P Ltd. Kerala, India
4.	Hydroxypropylmethyl cellulose	HIMEDIA Laboratories P Ltd Maharashtra, India
5.	SodiumCarboxymethylcellulose	Nice Chemicals P Ltd. Kerala, India
6.	Microcrystalline cellulose	HIMEDIA Laboratories P Ltd Maharashtra, India
7.	Starch	ISCO Research Laboratories P Ltd. Maharashtra, India

Freshly prepared distilled water was used in research work.

Glassware

Glassware is an essential equipment for the formulation of MH capsules. Some of the glassware used in the

formulation of MH capsules are Beakers, Graduated cylinders, volumetric flasks, pipettes, burette, conical flasks. All the glasswares are of class A (Borosil Ltd., Mumbai, India)

EXPERIMENTAL METHODS

Preformulation studies

For the Preformulation studies, the physicochemical characterization of drug substance, selection of excipients, compatibility studies, estimation of drug content in MH by UV-Visible Spectroscopy were carried out.

Physicochemical characterization:

MH was characterized and identified by its physical appearance, melting point, ultraviolet (UV) spectroscopy, solubility profile and infrared (IR) spectroscopy.

Physical appearance (08)

Description of the drug is the first line indication for purity for its identification.

1.0 g of MH was weighed and transferred into a clean, dry petridish and physical appearance, colour was observed visually

Melting point

Checking the melting point is the fundamental physical property very often used to identify compounds. Melting point of MH was carried out by capillary method using melting point apparatus. (09) A little amount of MH was added into a glass capillary tube, sealed one end and open at other end; slowly the temperature was increased and observed. The temperature at which melting starts was observed in the attached laboratory thermometer. Average of three readings were taken and compared with the standard melting point of MH, the results are shown in the Table 5.

Solubility studies

The solubility of MH in various solvents like distilled water, methanol, ethanol, and phosphate buffer PB (pH 6.8) were carried out individually. (10) MH 100 mg was added in 100 mL of the various solvents in a volumetric flask and sonicated for 30 min. It was considered as stock solution; from it 1mL was taken and diluted to 10mL with same solvent and filtered through, 0.2 µm Whatman's filter paper. The absorbance was measured at 233 nm by UV- Visible spectrophotometer. The results are shown in the Table 6.

Ultraviolet (UV) absorption maxima (λ max)

A standard stock solution I was prepared by dissolving 100 mg of MH in 100 mL of PB. Subsequently, 1 mL was extracted from stock solution I and diluted with PB (pH 6.8) to a final volume of 100 mL, resulting in a concentration of 10 µg/mL. The resulting solution was then filtered using a 0.2 µm Whatman filter paper. The solution of MH was scanned at 233nm, using PB (pH 6.8), as blank. The R^2 value was calculated; and the λ max was found. The result is shown in Table 7.

Fourier Transform Infrared (FTIR) spectroscopy

Spectra were taken after preparing the pellet with 2-3 mg of sample using potassium bromide in the ratio of 1:100 and were scanned from 4000-400 cm^{-1}. The FTIR spectra were scanned for pure MH was detected and the characteristic peaks are shown in Table 8. (11)

Selection of Excipients for Preformulation Studies of MH

Starch (12)

Starch is abundant in nature, primarily found in plants. It serves as a major form of stored energy in carbohydrates. It is a desirable raw material for many applications due to its accessibility

and affordable price. It is biodegradable, non-toxic and can be modified into diverse biomaterials.

Sodium Carboxymethyl cellulose (CMC)

Its water-solubility makes it easy to incorporate into various formulations. CMC is a good thickening agent, stabilizer, and has film-forming properties. Additionally, its biocompatibility and non-toxic nature contribute to its widespread use.

The specific interactions could involve binding metformin particles, providing controlled release, or facilitating better dispersion.

Hydroxypropyl Methylcellulose (HPMC)

It has sustained Release Properties. HPMC K100 is an excellent release retardant polymer. It is Biocompatible and Safe. It has other properties like water solubility, film formation, stabilization and thickening.

Microcrystalline Cellulose (MCC)

MCC being biocompatible, it is widely used in pharmaceuticals. MCC acts as a binder, stabilizer and as a disintegrant. It is inert and non-toxic.

Polyvinyl pyrrolidone (PVP)

PVP is often chosen as a binder in pharmaceutical formulations due to its excellent binding properties. It forms a strong film around the active pharmaceutical ingredient (API) particles, promoting cohesion. PVP is also water-soluble, facilitating disintegration upon ingestion, which is crucial for drug absorption.

Magnesium Stearate

It exhibits good lubricating properties, reducing friction between particles and facilitating the manufacturing process of tablets or capsules. Anti-Adhesive Properties: Magnesium stearate helps prevent sticking during the tablet compression process, ensuring smooth and efficient production.

Preparation of standard curve for MH by UV method

The calibration curve for MH was established as follows: Initially, 100 mg of MH was dissolved in 100 mL of PB (pH 6.8), constituting the working standard stock I. Subsequently, 1 mL was withdrawn from Stock-I and diluted to 100 mL with PB (pH6.8), forming the working standard stock II. From Stock-II, aliquots of 2, 4, 6, 8, and 10 mL were measured and adjusted to a total volume of 10 mL with PB (pH 6.8), resulting in concentrations of 2, 4, 6, 8, and 10 µg/mL.

The absorbance of these solutions was measured at 233 nm using a spectrophotometer, with PB (pH 6.8) serving as the blank. Data processing was carried out using Microsoft Excel, and a calibration curve for MH was generated by plotting absorbance values against concentrations (µg/mL).

Formulation Development of MH sustain release capsule Purification procedure for MH

MH was purified by recrystallization by centrifugation method to reduce the contain of N- nitrosodimethylamine.

Procedure

500mg MH was taken and the excipients PVP K30, Sodium CMC, HPMC K100 and MCC were taken in the mortar and pestle and was triturated slowly. Prepared starch solution was added until a mass formed. This prepared mass was kept for drying for 10 minutes. Further it was sieved using sieve size 10 to get an uniform sized granules. To this Mg Stearate was added as a lubricating agent further these granules were filled in empty zero size hard gelatin capsules using manual capsule filling machine.

Table 3: Formulation development of MH sustain release capsule

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Metformin HCl	500	500	500	500	500	500	500	500	500	500
PVP K30	16.5	10	23	5	28	14	10	18	5	23
Mg Stearate	2	2	2	2	2	2	2	2	2	2
Sodium CMC	5	5	5	5	5	10	10	10	10	10
HPMC K100	16.5	23	10	28	5	14	18	10	23	5
MCC	10	10	10	10	10	10	10	10	10	10
Starch	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs
TOTAL WEIGHT	550	550	550	550	550	550	550	550	550	550

3. METHODS FOR OPTIMIZATION

The flow properties of formulated MH sustain release blend were characterized by measuring

(General chapter, powder flow <1174>, USP 42).

Angle of repose

To determine the angle of repose, the following were followed

Setup: Choose a clean, flat surface. Place a funnel or a similar device at a fixed height above the surface. Material Placement: Pour the granular or powdered material through the funnel onto the surface. Allow the material to form a cone-shaped pile naturally.

Measurement: Measure the height (h) of the cone from the base to the tip. Measure the radius (r) of the base of the cone.

Use the tangent of the angle of repose formula:

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

Where, θ = Angle of repose, h = height of blend and r = radius of blend heap.

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk Density

Procedure: Allow an excess of powder to flow through the apparatus into the sample receiving cup until it over-flows, using a minimum of 25 cm^3 of powder with the square cup and 35 cm^3 of powder with the cylindrical cup. Carefully scrape excess powder from the top of the cup by Cylinder smoothly moving the

edge of the blade of a spatula perpendicular to and in contact with the top surface of the cup, taking care to keep the spatula perpendicular to prevent packing or removal of powder from the cup. Remove any material from the sides of the cup, and determine the weight, M, of the powder to the nearest 0.1%. Calculate the bulk density, in g/mL, by the formula:

Bulk Density (g/mL) = M/V0

in which V0 is the volume, in mL, of the cup. Record the average of three determinations using three different powder samples.

Tapped Bulk Density:

Procedure: Tapped density of a powder is the ratio of the mass of the powder to the volume occupied by the powder after it has been tapped for a defined period of time. The tapped density of a powder represents its random dense packing. Tapped density can be calculated using the formula;

Tapped Bulk Density (g/mL) = M / Vf

where M=mass in grams, and Vf =the tapped volume in milliliters.

Carr's compressibility index:

Procedure: Carr's Compressibility Index, also known as the Carr Index or Carr's index, is a parameter used to quantify the compressibility and flowability of a powdered or granular material. It is calculated from bulk density and tapped bulk density measurements and is expressed as a percentage.

Calculation:

Carr's Index (%) = (Tapped Bulk Density−Bulk Density/Tapped Bulk Density) × 100

Carr's index (%)	Properties
5 – 15	Excellent
12 – 16	Good
18 – 25	Fair to passable
26 – 32	Poor
33 – 38	Very poor
>40	Very very poor

Hausner's ratio:

Procedure: Hausner's Ratio is a parameter used to assess the flowability of powdered or granular materials. It is calculated from bulk density and tapped bulk density measurements and is expressed as a ratio.

Calculation:

Hausner's Ratio=Bulk Density/Tapped Bulk Density

Evaluation of MH sustain release capsule

The filles capsules are subjected to various quality control tests such as visual inspection, weight variation, content uniformity, friability, disintegration and dissolution.

Visual Inspection:

- Inspect for various defects, including dirt, scratches, foreign particles, cracks, chips, deformation, different colors or discoloration, blurred or scratched print, coating and embossing defects.
- Ensure the consistency of capsule size. Check the fill level inside the capsules whether they are adequately filled with the medication.
- Shape inspection: collapsed, dent, length, double capping, bent, etc.

Weight Variation:

- Ten hard gelatin capsules are usually weighed individually and the contents are removed.
- The emptied shells are individually weighed and the net weight of the contents is calculated by subtracting the weight of the shell from the respective gross weight.
- The content of active ingredient in each capsule may be determined by calculation based on the percent drug content in the formulation

Content Uniformity:

- This test is performed only when the content is specified in the individual monographs and when capsules fail weight variation test. If the weight of capsules is completely filled no need of this test.
- Unless otherwise stated in the monograph for an individual capsule, the amount of drug substance, determined by assay, is within the range of 85.0 % to 115.0% of the label claim for nine (9) of ten (10) dosage units assayed, with no unit outside the range of 75.0 % to 125.0 % of the labelled drug content.
- Additional tests are prescribed when two or three dosage units are outside of the desired range but within the stated extremes.

Disintegration Test:

- The capsules are placed in the basket-rack assembly, which is repeatedly lowered 30 times per minute into a thermostatically controlled bath of fluid at 37± 2 ˚C and observed over the time described in the individual monograph.
- To fully satisfy the test, the capsules disintegrate completely into a soft mass with no firm core and only

some fragments of the capsule shell.

Dissolution Test:

- The dissolution test for capsules evaluates how well they release the drug substance in a specified medium, contributing to their therapeutic efficacy.
- A cylindrical vessel made of borosilicate glass or other transparent material and a motor with a speed regulator that rotates the basket within the vessel.
- The basket ensures smooth rotation without significant wobble.
- The dissolution medium is typically PB (Ph 6.8) and the temperature of the medium should be maintained at 36.5 to 37.5°C.

Release kinetics studies of the optimized formulation

The in vitro release data of the MH F7 was fitted to various kinetic mode (Zero- order, First-order, Higuchi, and Korsemeyer-Peppas models). The best fit was found out to describe the kinetics of drug

release. Release kinetics study of various equations was incorporated in the release data of MH F7. Cumulative percent drug released vs. time (zero order rate kinetics)

$Q = K_0t$

Where Q is the fraction of drug release at time t & K0 is the Zero order release rate constant. A plot of fraction of drug release against time will be linear, if the release obeys Zero order release kinetics. (Unit-concentration/time) Log cumulative percent drug retained vs. time (First order rate kinetics)

Log C= Log C0 - Kt

2.303

C0 is the initial concentration of drug, K is the first order constant and t are time Log cumulative percent drug released vs. square root of time (Higuchi's classical diffusion equation)

$Q = KHt_{1/2}$

KH is the Higuchi's square root of time kinetic drug release constant

Log of cumulative % release Vs log time (Korsmeyer Peppas exponential equation)

Mt/Ma= K x tn

Mt is the amount of drug released at time t and Ma is the amount released at time.

Table 4: Release kinetics study of the optimized formulation

Sl. No.	Model	Graph	Diffusion exponent (n)	Overall solute diffusion mechanism
1.	Zero order	Cumulative release Vs time	0.45	Fickian diffusion
2.	First order	Log Cumulative release Vs time	0.45 < n< 0.89	Non Fickian (Anomalous) diffusion
3.	Higuchi model	% Cumulative release Vst1/2	0.89	Case- II transport
4.	Korsemeyer- Peppas model	% CRt/CR∞Vst1/2	n > 0.89	Super case -II transport

Stability Studies

The MH F7 was subjected for the stability study by placing the sample at 25°C ± 2°C/60% RH ± 5% for three months in the humidity chamber and was examined on 0, 1, 2 and 3 months and checked for changes in physical appearance, disintegration test, dissolution test, weight variation (mg) and %drug content (mg) as per ICH guidelines for the stability testing of new substance and products.

4. RESULTS

Results of formulation, in vitro evaluation of MH sustain release capsule Results of preformulation studies

Results of physical appearance

The physical appearance of MH was found to be white crystalline powder which meets the criteria as per IP monograph, 2007 specification.

Result of melting point

The melting point of MH by capillary method was found in the range of 219- 223°C and the average of three reading was found to be 220.9° which meets the criteria as per IP monograph, 2007 specification.

Table 5: Results of melting point of MH

S. No	Melting point of MH (°C)
1	220.4
2	221.3
3	221.0
Average	220.9

Results of solubility studies

The results of the solubility studies were performed in the selected solvents/media such as distilled water, methanol, ethanol and PB (pH 6.8) based on the solubility data it can be inferred that the solubility in distilled water < methanol < PH (pH 6.8) < ethanol.

Table 6: Results of solubility studies of MH

Solvents /media	Solubility
Distilled water	Freely soluble
Methanol	Freely soluble
Phosphate buffer pH 6.8	soluble
Ethanol	Insoluble

Results of Ultraviolet (UV) absorption maximum (λ max)

The spectral scanning was carried out by using PB (pH 6.8) as solvent by using UV-Visible spectrophotometer. The UV-visible spectrum of MH was shown in Table 7 and Figure 1. The spectra

showed a sharp peak at 233 nm. The wavelength provided sensitivity and high repeatability in absorbance values as mentioned by the earlier authors λ max of 233 nm was selected for all further studies.

Table 7: Results of determination of λ max

S.no	Solvent	λ max
1	PB (pH 6.8)	233

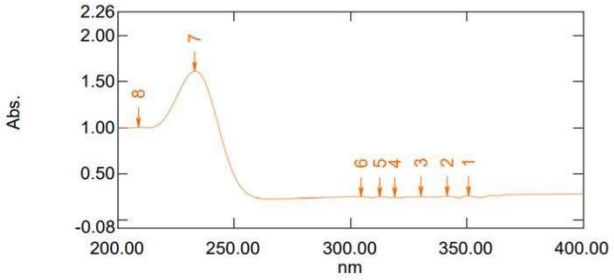

Figure 1: Results of UV Spectrum scanning for MH

Fourier Transform Infra-Red (FTIR) spectroscopy

MH was characterized by FTIR; the MH working standard was compared with reference standard of MH with their spectral data from the scanned sample at 4000- 400 cm^{-1}. It was observed that the presence of N-H stretching amide, C=O carboxylic acid stretching, C=O amide stretching, C=O ester stretching, and COOH stretching were characteristic peaks of MH which were similar to that of the working sample. MH indicating that both the working standard and reference standard of MH were similar. The FTIR values of MH results were coinciding with the works of earlier authors. The result are shown in the Figure 2(a)(b) interpretation data of FTIR Spectrum of pure drug was mentioned in the Table 8

Table 8: Interpretation data of FTIR Spectrum of pure drug

Characteristic peak	Standard range (cm^{1})	MH peaks(cm^{-1})
N-H stretching amide	3500-3310	3367.01
C=O carboxylic acid stretching	1760-1720	1729.83
C=O amide stretching	1681-1613	1621.84
C=O Stretching ester	1200-1100	1166.72
COOH	3300-2500	3147.57

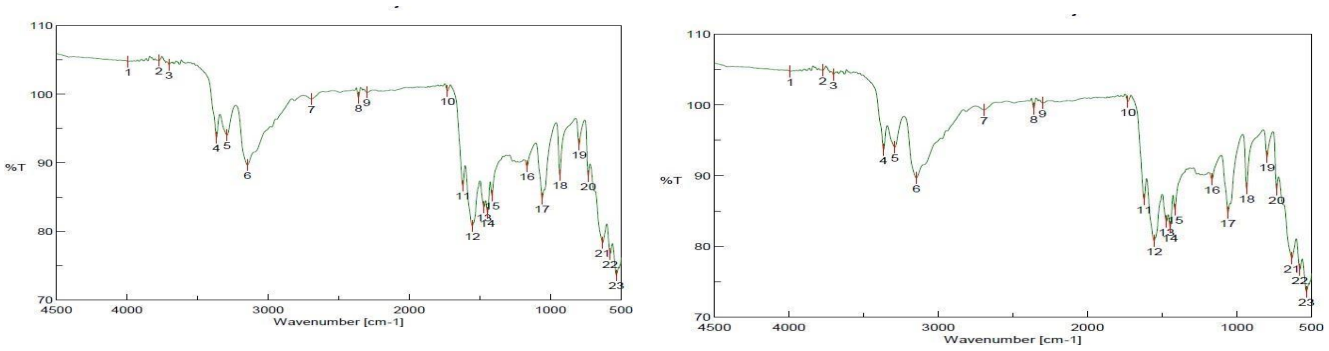

Figure 2: (a)Results of FTIR of working standard (b)Results of FTIR of reference standard

Results of selection of excipients in the preformulation studies of MH

The selection of the polymer for the preparation of the MH was based on the literature and following the criteria of the earlier authors Y Luo et al., 2021 summarised that Polyvinylpyrrolidone has a notable enhancement in its bioavailability, stability and modified release rate. S Lakio et al.,2013 explained that the Magnesium stearate prevents sticking and clumping, acts as a lubricant, and can reduce friction between particles []. Ibrahim SM et al., 2014 explained that Sodium carboxymethylcellulose is very hydrophilic in nature and has a significant affinity for water, making it an effective stabilizer and emulsifier []. Saigal N et al.,2009 were summarised that the Microcrystalline cellulose functions as a flexible binder, binding the constituents precisely and acting as disintegrants []. Ghadermazi R et al.,2019 had explained that the HPMC as a film coating agent, acting as a binder and disintegrant.

Study of analytical method for estimation of MH by UV

The calibration curve of MH was prepared using PB (pH6.8), the absorbance values were found in the range of 2-10 µg/ml are provided in Table 9. The standard calibration curve of MH was shown in Figure 3. From the least square regression analysis, a linear response was obtained over a range of 2 to 10 µg/ml with a regression coefficient (R2) value of 0.996. The best-fit linear equation obtained was y= 0.205x - 0.011, y is the absorbance (AU) and x is the concentration of MH in µg/ml as reported by Dange et al.,

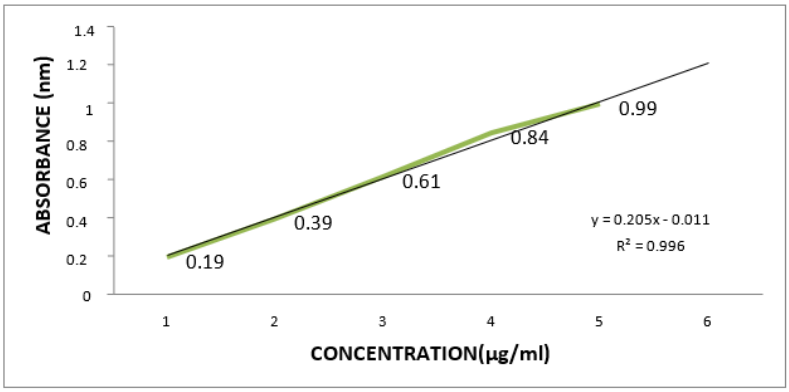

Figure 3: Results of standard graph of MH in PB (pH 6.8)

Table 9: Results of calibration data of MH in UV spectrophotometer

S.no	Concentration (µg/mL)	Absorbance (nm)
1.	0	0
2.	2	0.19
3.	4	0.39
4.	6	0.61
5.	8	0.84
6.	10	0.99

Drug-excipients compatibility studies by FTIR

The compatibility between the MH and excipient was evaluated using FTIR peak matching method. The IR spectra of physical mixture of MH, MCC, HPMC K100, PVP, Na CMC and Magnesium Stearate were super imposable with that of MH, which confirmed the absence of any chemical interaction between the drug with excipients. Further, it can be found that it involves only weak physical bonding interaction of and studied excipients which was confirmed by the shifting of FTIR spectrum of pure drug was recorded and interpretation was done. The original characteristics IR absorption peaks of pure drug (MH) at 3367.1cm^{-1} (N-H stretching amide), 1729.83cm^{-1} (C=O carboxylic acid stretching), 1621.84cm^{-1} (C=O amide stretching), 1166.72cm^{-1} (C=O Stretching ester), 3147.26cm^{-1}(COOH), these peaks are observed in physical mixture spectra, with less intensity. The compatibility studies were coinciding the previous author work of Panda BP et al., 2018. The result was shown in the Table 10 and Figure 4-10.

Table 10: Drug-excipients compatibility studies by FTIR

Characteristic peaks	Frequency cm-1	
	MH	MH + Physical mixture
N-H stretching amide	3367.01	3291.89
C=O carboxylic acid stretching	1729.83	1627.63
C=O amide stretching	1621.84	1561.09
C=O Stretching ester	1166.72	1203.36
COOH	3147.26	2917.77

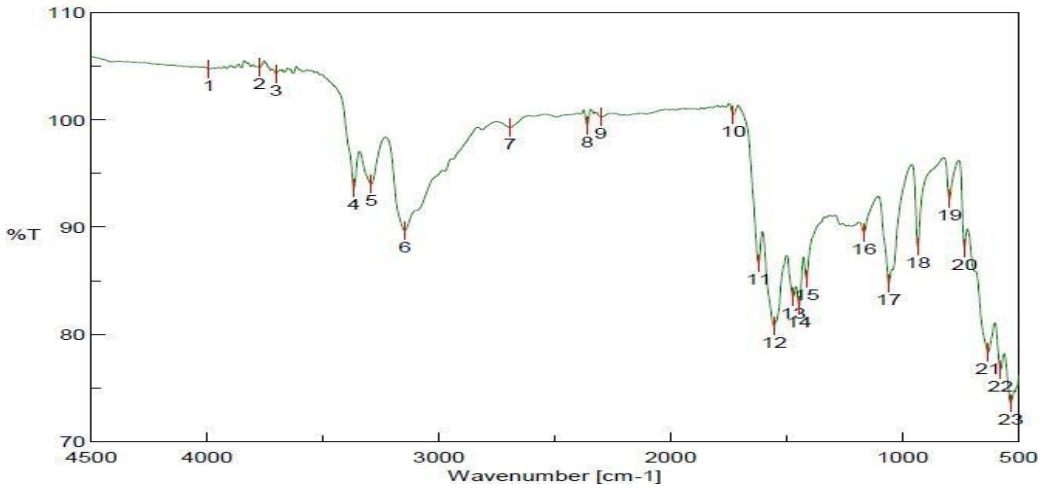

Figure 4: Result of FTIR spectra of pure drug MH

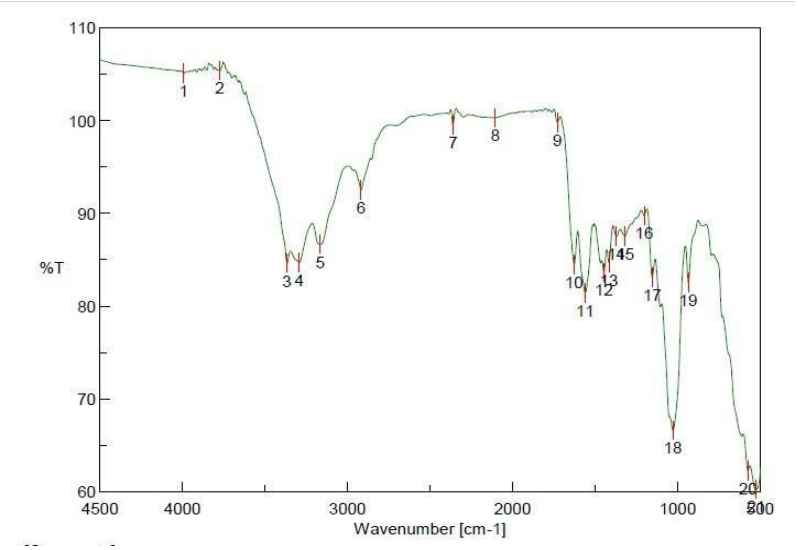

Figure 5: Result of FTIR spectra of pure

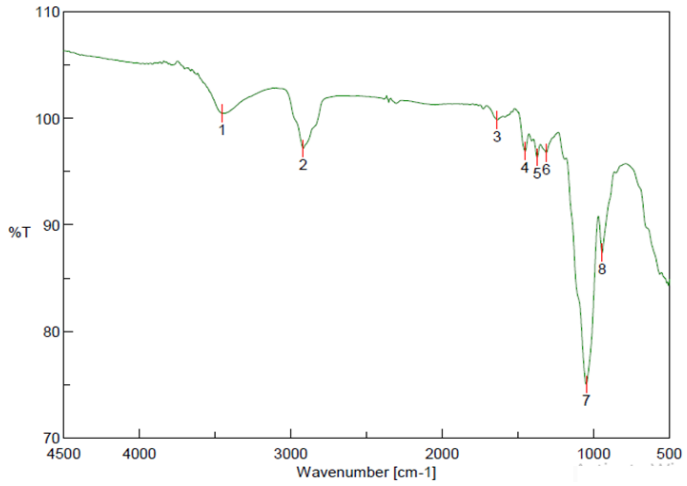

Figure 6: Result of FTIR of HPMC K100 drug MH & physical mixture

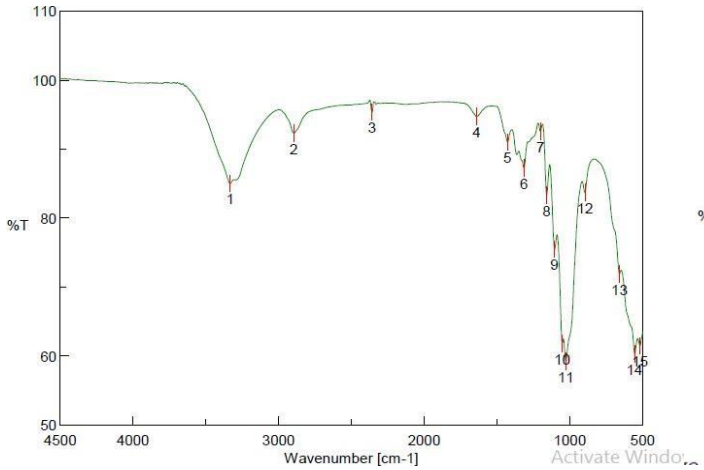

Figure 7: Result of FTIR spectra of MCC

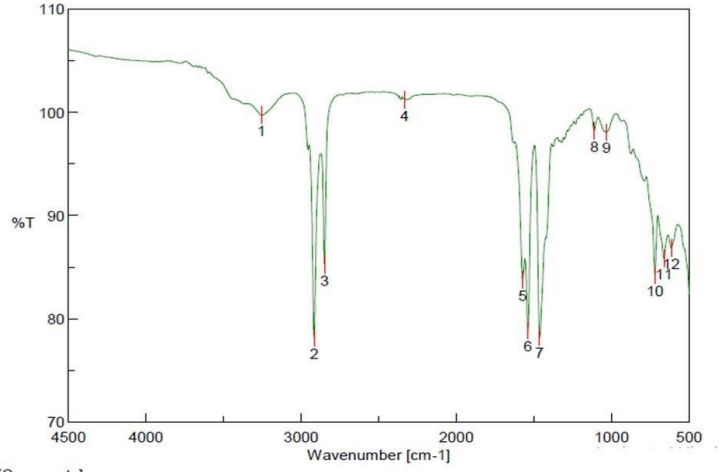

Figure 8: Result of FTIR spectra of Magnesium stearate

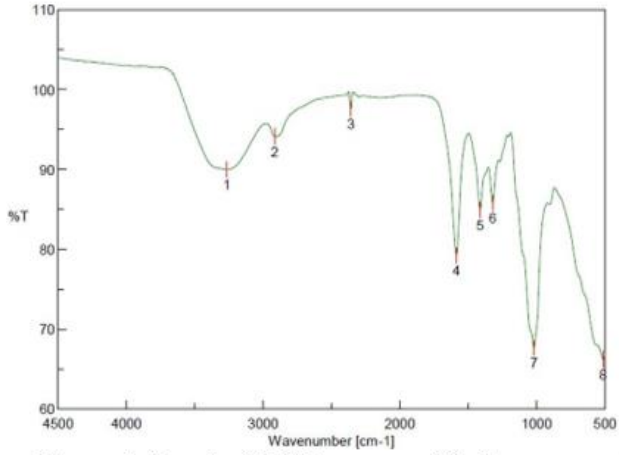

Figure 9: Result of FTIR spectra of Sodium CMC

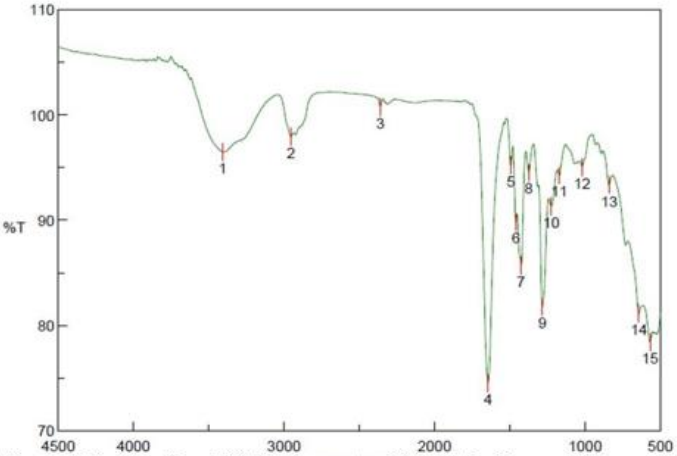

Figure 10: Result of FTIR spectra of Polyvinylpyrrolidone

Results of MH sustain release

In vitro evaluation of MH sustain release blend

The flow properties of formulated MH sustain release blend were characterized by measuring (General chapter, powder flow <1174>, USP 42).

Figure 11: Metformin Hydrochloride granules (F7)

- Angle of repose
- Bulk density and tapped density
- Carr's compressibility index
- Hausner's ratio and the results are tabulated in Table 11

Table 11: Results of Preformulation studies of MH powder blend

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Bulk Density	0.27	0.26	0.25	0.27	0.25	0.25	0.26	0.27	0.26	0.28
Tapped Density	0.33	0.32	0.31	0.33	0.31	0.31	0.32	0.33	0.32	0.35
Carr's compressibility index	18.18	18.75	19.35	18.18	19.35	19.35	18.75	18.18	21.21	20
Hausner's ratio	1.22	1.23	1.29	1.22	1.32	1.24	1.23	1.22	1.23	1.25
Angle of repose	31.20	31.95	32.54	33.07	32.54	33.58	32.24	33.26	32.66	34.19

In vitro evaluation of MH sustain release capsule

The in vitro evaluation study for MH sustain release capsule results are shown in Table 12.

Figure 12: Metformin hydrochloride capsule (F7)

Table 12: Evaluation for the formulated capsule

	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Uniformity of content (%)	98.24	102.98	99.21	97.92	101.5	99.71	103.41	97.33	99.01	101.8
Disintegration time (min)	36.2	37.4	37.7	35.1	37.4	34.8	37.9	35.4	36.8	38.2
Dissolution test (%) at 13th hr	99.74	99.12	98.45	98.57	97.09	99.54	96.23	99.27	98.54	97.22
Uniformity of weight	512.45	498.55	547.71	531	487.92	497.20	514.68	487	541.71	480.54

Out of the 10 formulation it was found out that F7 had better sustain release when compared with other formulation. Hence, F7 was subjected to comparative study.

Comparative study

F7 was taken and the comparative study with two different brand of Metformin hydrochloride 500 mg SR was performed. The results are shown in Table 13 and Figure 12.

Table 13: Comparative study with two different brand of Metformin hydrochloride 500 mg SR

Time (min)	F7(%)	Brand 1(%)	Brand 2(%)
5	0.45	1.87	0.97
10	3.46	5.89	1.54
15	5.51	6.74	4.75
30	11.76	19.75	18.54
60	12.61	28.48	19.89
90	16.64	32.07	20.61
120	22.13	33.72	34.75
180	37.42	46.30	42.46

240	40.87	50.18	47.94
300	47.64	57.31	58.42
360	54.78	60.77	65.48
420	67.56	77.05	80.33
480	71.97	83.68	88.04
540	77.50	89.	96.08
600	85.46	99.75	98.94
660	96.23		
720	99.10		
780	99.21		

Result of release kinetic studies of the optimized formulation

The in vitro release data for F7 was fitted to various model, the best fit was founded to be first order rate kinetics.

Results of Stability studies

The descriptions of the F7 at 0, 1, 2, and 3 months we checked and results are the shown in Table 14. During the stability studies, there was no significant change.

Table 14: Result of the Stability studies for F7 on storage at (25 °C ± 2 and 60% ± 5%RH)

Description	Storage conditions (25°C ± 2°C/60% RH ± 5%)			
	Initial	After 1 month	After 2 months	After 3 months
Physical appearance	Violet and pink color capsule	Violet and pink color capsule	Violet and pink color capsule	Violet and pink color capsule
Weight variation (mg)	497.20	489.20	497	498.12
Disintegration time (min)	37.9	37.9	36.45	36.87
Dissolution test (%) Abs. at 13th hr	99.21	98.90	98.85	99.13
Uniformity of content (%)	103.41	103.17	101.56	101.32

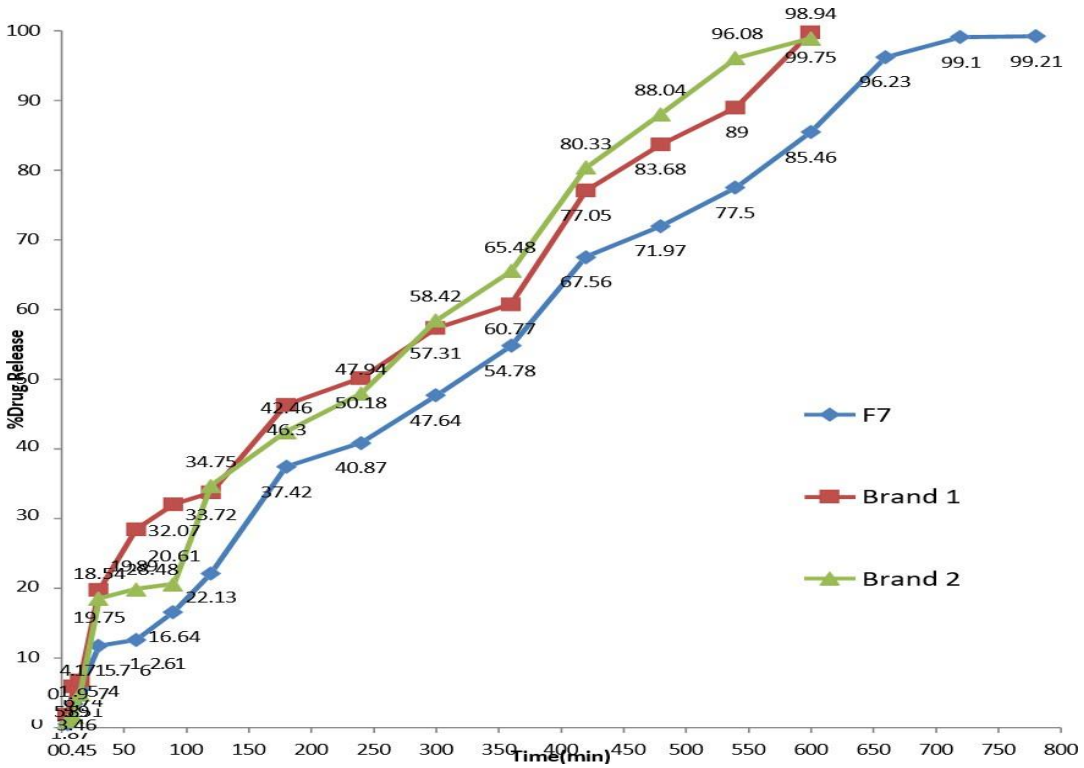

Figure 13: Comparative study with two different brand of Metformin hydrochloride 500 mg SR

This dissolution study demonstrates F7, exhibit a sustained release pattern, from the initial to the end of 13th hr at a constant rate. Drug release may be attributed to presence the combination of Starch, PVP K30, HPMC, MCC, Magnesium stearate and Na CMC polymers which may tend to sustained and extended the drug release up to 13th hr. When compared with marketed MH tablet it showed that brand 1 had release upto 10th hr, brand 2 upto 11th hr and our formulation F7 had a release upto 13th hr.

5. CONCLUSION

India is home to 7.7 million diabetes, making its second highest in the world. The formulation and evaluation of MH sustained release capsules have shown positive outcomes. The meticulous formulation process has resulted in a controlled release product, as evidenced by thorough evaluation criteria such as stability, dissolution characteristics. These findings suggest the potential of the sustained release capsule to enhance therapeutic outcomes and patient adherence in the context of diabetes treatment. Further research and clinical studies may be warranted to validate the long-term effectiveness and real-world application of this formulation.

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REFERENCES

[1] Hernández-Velázquez ED, Alba-Betancourt C, Alonso-Castro ÁJ, Ortizalvarado R, López JA, Meza- Carmen V, Solorio-Alvarado CR. Metformin, A Biological And Synthetic Overview. Bioorganic & Medicinal Chemistry Letters. 2023 Mar 16:129241

[2] FU Y. Historical Story On Natural Medicinal Chemistry: 60 Years History Of Metformin, A Classical Antidiabetic Drug Originated From Galega Officinalis. Chinese Traditional And Herbal Drugs. 2017:4591-600.

[3] Owen MR, Doran E, Halestrap AP. Evidence That Metformin Exerts Its Antidiabetic Effects Through Inhibition Of Complex 1 Of The Mitochondrial Respiratory Chain. Biochem J 2000; 348:607-614

[4] Yüksel N, Tinçer T, Baykara T. Interaction Between Nicardipine Hydrochloride And Polymeric Microspheres For A Controlled Release System. International Journal Of Pharmaceutics. 1996 Aug 30;140(2):145-54.

[5] Siavash M, Tabbakhian M, Sabzghabaee AM, Razavi N. Severity Of Gastrointestinal Side Effects Of

Metformin Tablet Compared To Metformin Capsule In Type 2 Diabetes Mellitus Patients. Journal Of Research In Pharmacy Practice. 2017 Apr 1;6(2):73-6.

[6] Hu LD, Liu Y, Tang X, Zhang Q. Preparation And In Vitro/In Vivo Evaluation Of Sustained-Release Metformin Hydrochloride Pellets. European Journal Of Pharmaceutics And Biopharmaceutics. 2006 Oct 1;64(2):185-92.

[7] Panda BP, Krishnamoorthy R, Shivashekaregowda NK, Patnaik S. Influence Of Poloxamer 188 On Design And Develop-Ment Of Second Generation PLGA Nanocrystals Of Metformin Hydrochloride. Nano Biomedicine And Engineering. 2018 Dec31;10(4):334-4

[8] ICH Harmonised Tripartite Guideline, Impurities In New Drug Substances, Q3A(R2) (2016);

[9] Tomar A, Wadhwani S, Bhadauria RS. A PREFORMULATION STUDY OF PURE METFORMIN Hcl

[10] Yu C, Sun X, Wang Y, Du S, Shu L, Sun Q, Xue F. Determination And Correlation Of Solubility Of Metformin Hydrochloride In Aqueous Binary Solvents From 283.15 To 323.15 K. ACS Omega. 2022 Mar 1;7(10):8591-600.

[11] Jordan, S., Katz, J.S., Yezer, B. (2021). Excipients: Characterization, Purpose, And Selection. In: Li, J., Krause, M.E., Tu, R. (Eds) Protein Instability At Interfaces During Drug Product Development. AAPS Advances In The Pharmaceutical Sciences Series, Vol 43. Springer, Cham. Https://Doi.Org/10.1007/978-3-030-57177-1-10

[12] Wei Q, Deng NN, Guo J, Deng J. Synthetic Polymers For Biomedical Applications. Int J Biomater. 2018 Apr 24;2018:7158621.Doi: 10.1155/2018/7158621. PMID: 29849645; PMCID: PMC5941756.

[13] Sahoo, Chinmaya & Rao, S.R.M. & Sudhakar, M.. (2015). HPMC A Biomedical Polymer In Pharmaceutical Dosage Forms. Journal Of Chemical And Pharmaceutical Sciences. 8. 875-881.

[14] Moosavi SM, Ghassabian S. Linearity Of Calibration Curves For Analytical Methods: A Review Of Criteria For Assessment Of Method Reliability, Calibration And Validation Of Analytical Methods - A Sampling Of Current Approaches. Intech; 2018. Dx.Doi.Org/10.5772/Intechopen.72932

[15] Choudhary, A., Preparation Of Buffer Solutions (Phosphate, Acetate And Other Buffers. 2023, June 18 12248-011-(12)58774-J.

[16] DAIICHI JITSUGYO VISWILL CO., LTD. Tablet / Capsule Visual Inspection System Healthcare Products. DAIICHI JITSUGYO VISWILL CO., LTD.; 2021.

[17] Aliyu RS, Lawal AM, Chasta P, Sharma GK. CAPSULES: TYPES, MANUFACTURING, FORMULATION, QUALITY CONTROL TESTS AND, PACKAGING AND STORAGE – A COMPREHENSIVE REVIEW. World Journal Of Pharmaceutical And Life Sciences; 2020

[18] Ghadermazi R, Hamdipour S, Sadeghi K, Ghadermazi R, Khosrowshahi Asl A. Effect Of Various Additives On The Properties Of The Films And Coatings Derived From Hydroxypropyl Methylcellulose—A Review. Food Science & Nutrition. 2019 Nov;7(11):3363-77.

[19] Dange, Yuvraj Dilip, Et Al. "Development And Validation Of UV- Spectrophotometric Method For Estimation Of Metformin In Bulk And Tablet Dosage Form." Indian Journal Of Pharmaceutical Education And Research 51.4S (2017): S754- S760.)