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FABRICATION AND EVALUATION OF METFORMIN HCL TABLETS USING NATURAL POLYMERS AND EXCIPIENTS

MATHEW A. M* AND KASLIWAL R. H.

J.L.Chaturvedi College of Pharmacy, Electronic Building, Hingna Road, Nagpur-440016

ABSTRACT

The oral route of administration of drugs is the most important method for achieving systemic effects. In the process of absorption of drug from oral route dissolution is the rate limiting step. Since the drug belongs to BCS class III, it is necessary to retard dissolution to ensure extended release of drug[1]. Metformin hydrochloride[2] is an anti diabetic, having an elimination half-life of 5±2 hrs. The objective of the study is to prepare Metformin HCl Tablets using Natural Polymers and different concentrations of excipients. The tablets were subjected to thickness, weight variation test, drug content, hardness, friability, and *in vitro* release studies. All the tablet formulations showed acceptable properties and complied with in-house specifications for tested parameters. The results of dissolution[3] studies indicated that formulation MF3 and MF4 could extend the drug release up to 12 hours. The successful formulation of the study, exhibited satisfactory drug release (MF3 and MF4) was compared with the marketed formulation (Bigomet SR® and showed very close to release profile, which suggests sustained/controlled release profile.

KEYWORDS: Metformin HCl, Natural Polymers, Excipients, Bigomet SR®

MATHEW A. M

J.L.Chaturvedi College of Pharmacy, Electronic Building, Hingna Road, Nagpur-440016

Corresponding author

INTRODUCTION

The oral route is the route most often used for administration of drugs. Tablets are the most popular oral formulations available in the market and are preferred by patients and physicians alike. The controlled release systems for oral use are mostly solids based on dissolution, diffusion or a combination of both mechanisms in the control of release rate of drug[4].The goal behind the development of oral controlled-release formulations at that time was the achievement of a constant release rate of the entrapped drug. The industry has seen a number of innovative oral controlled-release dosage forms patented at a rapid pace, but the main drawback of these technologies continues to be the lack of *in-vitro & in-vivo* correlation. Ideally, oral controlled-release[5] systems are reliant upon the dosage form to control the rate of drug release with little or no effect from the intrinsic properties of the drug or the conditions prevailing within the gastro intestinal (GI) tract. Natural polymers[6] are biodegradable and nontoxic, which hydrate and swell on contact with aqueous media, and these have been used for the preparation of dosage form. The release rate of the drug from natural polymers depends upon several factors such as the physicochemical properties of drugs and the polymers, biodegradation rate of polymers, morphology and size of the particles, thermodynamic compatibility that exist between the polymers and the drugs, and the shape of the delivery devices. Hydrophilic matrices[7] are commonly used for oral drug delivery system and are sustained for their good compatibility. Drug release form hydrophilic matrix tablet are sustained by formation of hydrated viscous layer around the tablet which acts as a barrier to drug release by opposing penetration of water into the tablet and also the movement of dissolved solute out of matrix tablet. Hydrophilic polymer have attracted considerable attraction in recent years as sustained controlled release devices for the delivery of water soluble and water insoluble agents, this characteristics and their ability to hydrate and form a gel layer are well known and essential to sustained and controlled drug release from matrices. The hydrated gel layer thickness determines the diffusion path of the drug molecule through the polymer mass into dissolution medium. Controlled release[8] (CR) tablet formulation are preferred for such therapy because they offer better patient compliance, maintain uniform drug level, reduce dose and side effect and increase the safety margin for high potency drugs. A controlled oral delivery may be needed to achieve prolonged exposure or time-based release for a water-insoluble drug under certain circumstances. Matrix systems[9] are widely used in oral controlled drug delivery because of their flexibility, cost effectiveness, low influence of the physiological variables on its release behavior and broad regulatory acceptance. In drug administration, controlled release dosage forms offer numerous advantages compared to conventional immediate release dosage forms, including potential for greater effectiveness in the treatment of chronic conditions through more predictable kinetics, reduced side effects and toxicity by minimizing peak plasma concentrations, greater convenience and higher levels of patient compliance due to simplified dosage schedule.

MATERIALS AND METHODS

Drug

Metformin HCl (Abhilash Pharmaceuticals, Madurai, Zim Laboratories, Nagpur)

Polymer

Guar Gum (Zim Laboratories, Nagpur), Pectin (Alka Scientific, Nagpur)

Excipients

Microcrystalline Cellulose (Avicel-101) (Hanau Chemicals); Polyvinyl pyrrolidone (Povidone K-30) (Hanau Chemicals Ltd); Colloidal anhydrous silica (Aerosil 200) (Hanau Chemicals Ltd); Magnesium stearate (Hanau Chemicals Ltd); Lecithin (Perfect Industries, Mumbai); Lactose (Zim Laboratories, Nagpur)

Solvents and Reagents

Potassium di hydrogen phosphate (Merck, Germany); Sodium hydroxide (Merck, Germany)

Equipments

Single punch tablet press (Shanghai-Tianhe Pharmaceutical Machinery Company), UV Spectrophometer (Shimadzu, Japan); Digital pH meter (Hach Company, USA), Electronic Hardness tester (Pfizer Tester), Friability Tester (Roche Friabilator), Digital Weighing Balance (Wensar PGB-1000/PGB-200, Mumbai), Tablet Dissolution Tester (VDA 8-D**,** Veego Scientific Devices, Mumbai)

1. PREPARATION OF MATRIX TABLET OF METFORMIN HCl[10]

In the initial study, three different ratios of drug to polymer were selected, in case on Metformin HCl, drug to polymer 1:0.5, 1:1, 1:2 ratios were selected. The best results were found in the ratio of 1:0.5 for Metformin HCl respectively. Preparation of Controlled/Sustained Release Matrix Tablets of Metformin HCl with Guar Gum and Pectin alone and in combination with different concentration of excipients.

PROCESSING METHOD

The composition of tablets is shown in Table 1 and 2. Drug, Guar Gum, Pectin along with different concentrations of excipients were weighed properly and mixed for 10 minute in a poly bag and then the blend was transferred into mortar. Distilled water was gradually added to the mixture and the wet mass was prepared with hand. The wet mass was then passed through a sieve 14 screen and was spread on flat paper to dry overnight at 50^0C.The dry granules was forcedly passed through a sieve 18 screen and mixed with the lubricants for 5minutes in the poly bag.The granules of Metformin HCl were compressed by a single punch hand operated machine fitted with 12mm punch.

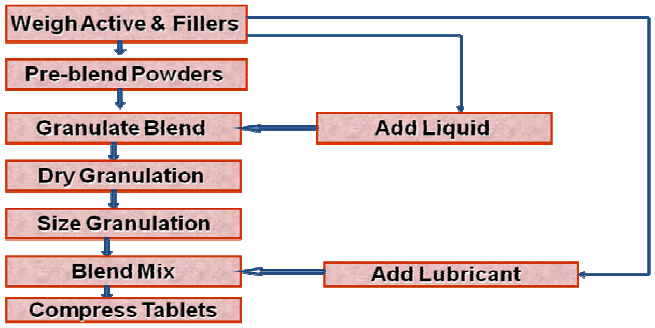


FIGURE 1

Schematic Representation of Controlled/Sustained Release Matrix Tablets of Metformin HCl by Wet Granulation Technique.

Table 1

Composition of Metformin HCl Matrix Tablets

Sr.No.	Ingredients	Formulation Batch (mg)		
		MF1	MF2	MF3
1.	Metformin HCl	250	250	250
2.	Guar Gum	250	----------	125
3.	Pectin	----------	250	125
4.	Mg. Stearate	10	10	10
5.	Talc	10	10	10
	Total	520	520	520

2) EFFECT OF EXCIPIENTS:[11]

To study the effect of excipients, tablets were prepared by Wet Granulation Method as described earlier using Lecithin, Lactose, Micro Crystalline Cellulose (Avicel pH 101), Starch, DCP (Emcompress) at three different concentrations (10%, 15% and 20%) respectively.

Table 2
Composition of Metformin HCl Matrix Tablets along with different Excipients

Sr.No.	Ingredients	Formulation Batch (mg)				
		MF4	MF5	MF6	MF7	MF8
1.	Metformin HCl	250	250	250	250	250
2.	Guar Gum	125	125	125	125	125
3.	Pectin	125	125	125	125	125
4.	Lecithin	50	---	---	---	---
5.	Lactose	---	50	---	---	---
6.	MCC	---	---	50	---	---
7.	Starch	---	---	---	50	---
8.	DCP	---	---	---	---	50
9.	Mg. Stearate	10	10	10	10	10
10.	Talc	10	10	10	10	10
	Total	570	570	570	570	570

3) DISSOLUTION STUDIES:[12]

The *in-vitro* release of Metformin HCl from formulated tablets was carried out in acid buffer pH 1.2 for 2 hours and then continued in phosphate buffer pH 6.8 for 10 hours.

Sr. No.	Contents	Specifications
1.	Dissolution Apparatus	USP-23 Basket (Type-I)
2.	Dissolution Medium	900ml of Phosphate pH 6.8 Buffer
3.	Temperature	37±0.5^{0}C
4.	Paddle Speed	100rpm
5.	Sampling Time	10ml/hr
6.	Wavelength	233nm

The studies were performed in USP dissolution apparatus I, (Dissolution Test Apparatus, Model No.VDA 8-D, Veego Scientific Devices, Mumbai) and analyzed for Metformin HCl content at 234.0 nm (in acid buffer) and (in pH 6.8 buffer) by using UV–visible spectrophotometer, (Model No. UV 601 PC, Shimadzu Corporation, Singapore).

4) CALCULATION OF SIMILARITY FACTOR (f_2)[13]

Similarity Factor (f_2)[14]

The similarity factor (f2) was defined by CDER, FDA and EMEA as the logarithmic reciprocal square root transformation of one plus the mean squared differences in percent dissolved between the test and the references products. This was calculated to compare the test with the references release profiles. It was calculated from the mean dissolution data according to the following equation:

$$\left\{ \left[1 + (1/n) \sum_{t=1}^{n} (R_t - T_t)^2 \right]^{-0.5} \times \right\} 100$$

Where,
f_2= 50 log
n = No. of full points
R_t = The reference profile at the time point t
T_t = the test profile at the same point

Similarity Factor (f_2)	Significance
< 50	Test and Reference release profiles are dis-similar
50-100	Test and Reference release profiles are similar
100	Test and Reference release profiles are identical
> 100	The equation yields a negative value

The method is more adequate to compare dissolution profiles when more than three or four dissolution time points are available and can only be applied if the average difference between R_t and T_t is less than 100. If this differences is higher than 100, normalization of data is required.

5) DRUG – EXCIPIENTS COMPATIBILITY STUDIES: [15]

Drug-Excipients Compatibility were done by

1) Fourier Transform Infrared Spectroscopy (FTIR)
2) Differential Scanning Calorimetry (DSC)

FOURIER TRANSFORM INFRARED SPECTROSCOPY (FTIR)

FTIR spectra of Metformin HCl, Guar Gum, Pectin along with different Excipients were recorded with FTIR spectrometer (FTIR-8001, Shimadzu, Japan), operated with Omnic Software on sample prepared by KBr pellets method.

DIFFERENTIAL SCANNING CALORIMETRY (DSC)

Thermal analysis of Metformin HCl, Guar Gum, Pectin along with different Excipients were assessed by DSC using DSC Q 10 V9 Instrument.

6) STABILITY STUDIES

The stability studies were performed on the most promising tablet formulation batch MF3, MF4. The study has done to know the effect of aging and temperature on the *in-vitro drug* release. The study was performed by keeping the prepared tablets in the airtight, high-density polyethylene bottles at 40^0C and relative humidity of 75%.

RESULTS AND DISSCUSSION

1. PHYSICAL EVALUATION OF DRUG LOADED GRANULES

Granulation Bulk Density, Tapped Density, Houser Ratio, % Compressibility and Angle of Repose are reported in the Table No. 3

Table 3
Physical Evaluation of Metformin HCl Granules (Mean ± S.D. n=3)

Sr.No	Angle of Rep	Bulk Density g/ı	Tapped Density g/ml	% Compressibility	Hounser Ratio
MF1	30.1^0 ± 0.33	0.4296 ± 0.007	0.5313 ± 0.006	19.14	1.23
MF2	30.4^0 ± 0.94	0.4637 ± 0.008	0.4873 ± 0.007	4.84	1.0.5
MF3	26.5^0 ± 1.25	0.5168 ± 0.005	0.5731 ± 0.005	9.82	1.1

2. IN – VITRO DRUG DISSOLUTION STUDIES

Table 4
In- Vitro Drug Release from Metformin HCl Matrix Tablet using Guar Gum, Pectin and 1:1 Combination

Time (Hrs.)	Cumulative % Drug Release (Mean ± S.D; n=3) MF1	MF2	MF3
1.	28.61 ± 0.64	36.76 ± 1.24	18.34 ± 0.58
2.	39.12 ± 0.34	64. 03 ± 1.54	24.63 ± 1.22
3.	48.62 ± 0.47	75.46 ± 0.43	33.49 ± 0.33
4.	58.68 ± 0.80	91.86 ± 1.64	45.27 ± 1.23
5.	66.77 ± 0.77	101.4 ± 1.23	51. 98 ± 1.36
6.	74.82 ±0.33		64. 51 ± 0.19
7.	80.28 ± 0.79		76.85 ± 1.27
8.			84. 22 ± 0.54
9.			90. 63 ± 1.26
10.			94. 57 ± 1.76
11.			97.43 ± 0.47
12.			99.95 ± 1.11

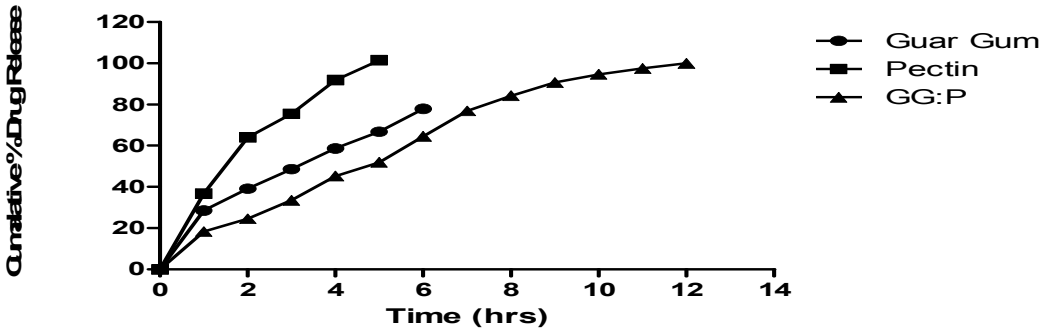


FIGURE 2
In-Vitro Drug Release from Metformin HCl Matrix Tablets using Guar Gum, Pectin and (1:1) combinations.

3. EFFECT OF EXCIPIENTS ON METFORMIN HCl MATRIX TABLETS

Excipient are generally a pharmacologically inactive substance formulated with the active ingredient ("API") of a medication. Excipients are commonly used to bulk up formulations that contain potent active ingredients to allow convenient and accurate dispensation of a drug substance when producing a dosage form.

Table 5
Effect of Excipients in 10% Concentration

Time	Cumulative % Drug Release (Mean ± S.D; n=3)				
In hrs	MF4	MF5	MF6	MF7	MF8
1.	12.37±0.60	11.04±0.53	9.12±0.85	7.46±0.45	5.09±0.76
2.	21.45±0.64	21.27±0.81	18.17±0.62	14.91±0.75	13.01±0.42
3.	35.55±1.01	35.14±0.70	29.1±0.61	23.84±0.82	21.65±0.30
4.	45.62±1.13	44.29±0.61	36.48±0.42	31.71±1.04	36.30±1.30
5.	56.08±0.31	58.29±0.84	52.78±0.47	48.92±0.47	43.19±0.62
6.	65.56±0.54	62.05±0.63	58.83±0.62	53.45±0.54	51.44±0.64
7.	72.71±0.53	67.97±0.31	64.88±0.33	59.15±0.36	55.72±0.42
8.	78.33±0.63	73.45±0.34	70.82±0.44	64.62±0.43	59.41±1.21
9.	84.78±0.52	77.63±0.63	74.74±0.33	70.05±0.63	65.91±1.09
10.	87.04±0.35	81.54±0.63	76.93±0.41	74.01±0.62	69.63±0.44
11.	93.97±0.62	87.78±0.46	82.96±0.43	78.99±0.56	75.12±0.33
12.	98.78±0.34	93.67±0.53	88.77±0.63	85.57±0.63	80.52±0.36

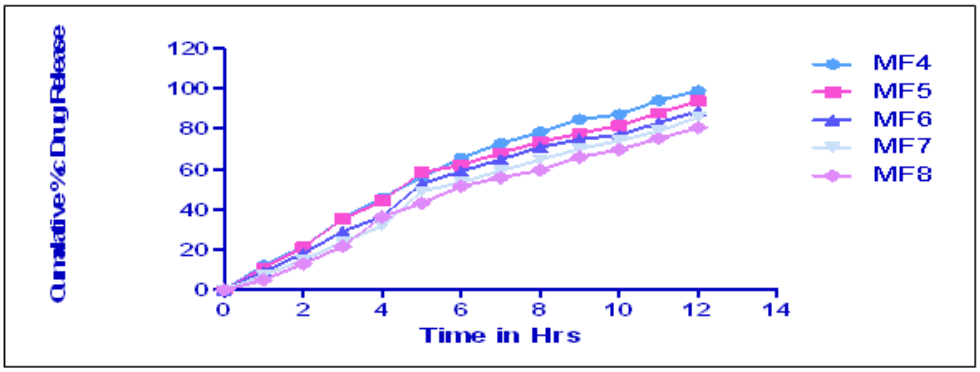


FIGURE 3
Effect of Excipients on In-Vitro Drug Release for 10% Concentration

Table 6
Effect of Excipients in 15% Concentration

Time In Hrs	Cumulative % Drug Release (Mean ± S.D; n = 3)				
	MF4	MF5	MF6	MF7	MF8
1.	14 ± 0.43	15 ± 0.60	12 ± 0.75	11 ± 1.11	11 ± 1.29
2.	21 ± 0.31	23 ± 0.33	19 ± 0.63	16 ± 0.63	14 ± 1.08
3.	29 ± 0.32	31 ± 0.34	26 ± 0.30	24 ± 0.66	20 ± 0.63
4.	36 ± 0.62	44 ± 0.30	32 ± 0.036	30 ± 0.45	27 ± 0.45
5.	47 ± 0.45	54 ± 1.29	40 ± 0.24	35 ± 0.41	32 ± 0.36
6.	53 ± 1.11	62 ± 1.09	44 ± 0.61	39 ± 0.48	36 ± 0.30
7.	61 ± 0.31	68 ± 1.11	53 ± 0.62	45 ± 0.36	41 ± 0.62
8.	69 ± 0.30	74 ± 0.75	59 ± 0.66	53 ± 0.66	49 ± 0.41
9.	77 ± 1.08	80 ± 0.30	67 ± 1.05	60 ± 0.33	54 ± 0.36
10.	83 ± 1.11	87 ± 0.41	72 ± 0.30	67 ± 0.34	60 ± 0.34
11.	90 ± 1.29	93 ± 0.44	80 ± 0.36	75 ± 0.41	67 ± 0.30
12.	93 ± 0.30	97 ± 0.30	82 ± 0.30	82 ± 0.30	73 ± 1.11

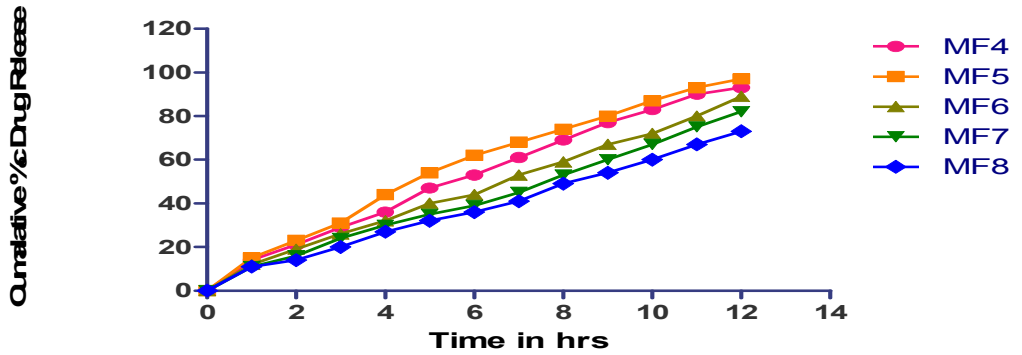


Figure 4
Effect of Excipients on In-Vitro Drug Release for 15% Concentration

Table 7
Effect of Excipients in 20% Concentration

Time In Hrs	Cumulative % Drug Release (Mean ± S.D; n = 3)				
	MF4	MF5	MF6	MF7	MF8
1.	13.6± 1.32	18.0 ± 1.0	12.4 ± 0.34	17.5 ± 1.26	11.0 ± 1.26
2.	21.9± 0.34	31.4 ± 1.29	20.1 ± 0.66	24.2 ± 1.11	17.6 ± 0.44
3.	25.9± 0.66	45.9 ± 0.30	24.8 ± 1.72	28.7 ± 0.78	23.4 ± 0.65
4.	31 ± 1.11	55.3 ± 0.44	30.6 ± 0.33	36.2 ± 2.21	29.4 ± 0.44
5.	43.6± 0.33	64.9 ± 1.47	45.4 ± 0.76	49.3 ± 0.34	34.4 ± 0.67
6.	56.4± 0.45	67.1 ± 0.66	52. 1 ± 1.11	57.3 ± 1.72	42.7 ± 2.1
7.	63 ± 0.45	74.4 ± 0.44	61.9 ± 0.33	66.5 ± 0.66	55.2 ± 0.33
8.	69 ± 0.67	77.2 ± 1.12	70. 3 ± 1.26	73.9 ± 0.44	63.8 ± 1.92
9.	73 ± 1.23	82.7 ± 0.30	75.12 ± 1.65	79.6 ± 0.34	70.5 ± 0.56
10.	79.5± 0.67	88.3 ± 0.46	81.9 ± 1.41	83.7 ± 0.63	74.2 ± 0.53
11.	81.9± 1.11	94. 7 ± 1.23	84. 5 ± 1.0	87.3 ± 1.28	79.8 ± 0.76
12.	86.3± 0.45	98.7 ± 1.65	93.2 ± 0.65	90.9 ± 1.11	85. 7 ± 1.98

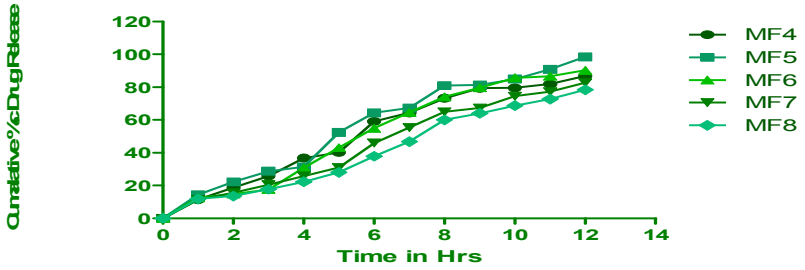


Figure 5
Effect of Excipients on In-Vitro Drug Release for 20% Concentration

4. EVALUATION OF PHYSICAL PROPERTIES OF METFORMIN HCl TABLETS

Table 6
Physical Parameters of Tablets (Mean ± S.D., n = 3)

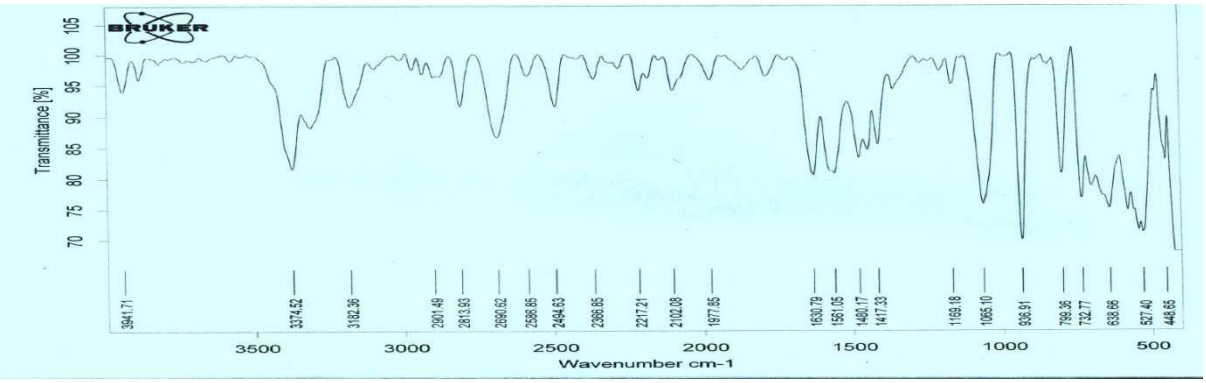
Batch No.	Weight Variation(mg) (Mean ± S.D.)	Hardness (kg/cm^2) (Mean ± S.D.)	Thickness (Mean ± S.D.)	Friability (%)	Drug Content (%) (Mean± S.D.)
MF1	577± 2.82	5.2± 0.070	4.39 ± 0.44	0.303±0.063	80.28±0.79
MF2	534± 3.53	5.1± 0.353	4.38 ± 0.67	0.543±0.091	101.4±1.23
MF3	503± 3.55	3.5± 0.212	4.36 ± 1.11	0.553±0.120	99.5±1.11

Batch No.	Weight Variation (mg) (Mean ± S.D)	Hardness (Kg/cm2) (Mean ± S.D)	Thickness (Mean ± S.D)	Friability (%)	Drug Content (%) (Mean ± S.D)
MF4	535 ± 5.32	5.1 ± 0.069	4.38 ± 0.34	0.57 ± 0.019	98.78 ± 0.65
MF5	558± 2.12	5.3± 0.070	4.33 ± 1.02	0.59± 0.021	93.67 ± 1.29
MF6	511± 1.41	4.1± 0.28	3.89 ± 0.47	0.4± 0.141	88.77 ± 0.65
MF7	585± 7.77	5.4± 0.14	4.32 ± 0.33	0.38± 0.325	85.77 ± 0.34
MF8	560± 3.55	4.9± 0.21	4.36 ± 0.66	0.37± 0.282	80.52 ± 0.45

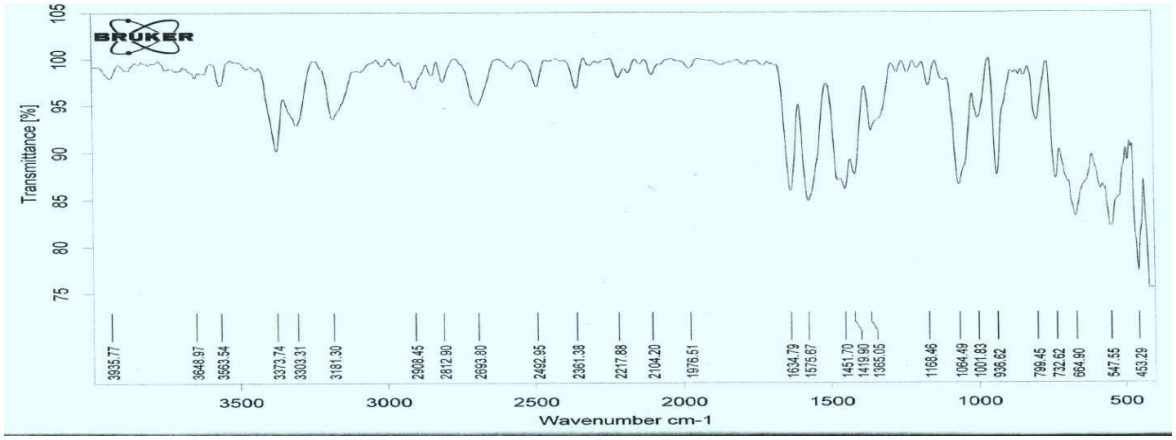
5. DRUG – EXCIPIENTS COMPATIBILITY STUDIES

1. FOURIER TRANSFORM INFRARED SPECTROSCOPY (FTIR)

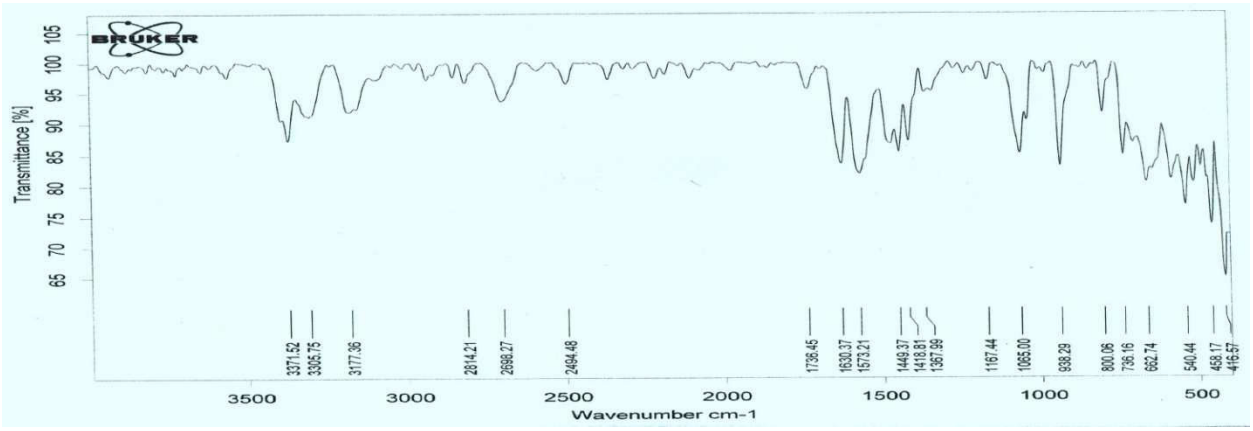
FTIR spectra of pure drug Metformin HCl and granules of Guar Gum and Pectin along with the different excipients.



Metformin HCl



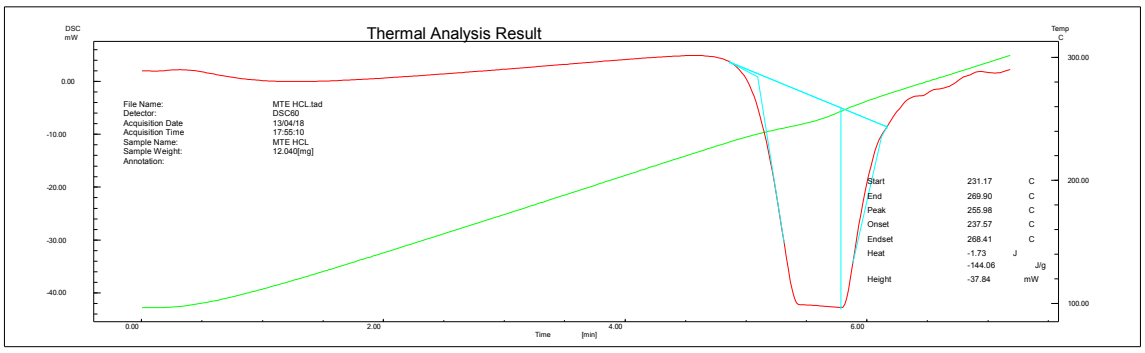
Metformin HCl, Guar Gum and Pectin (1:0.5:0.5)



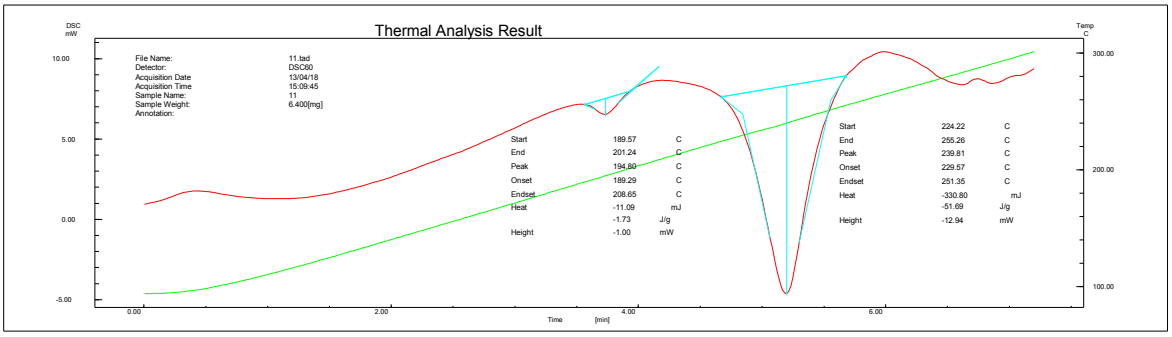
Metformin HCl (1:0.5:0.5): Lecithin

2. DIFFERENTIAL SCANNING CALORIMETRY (DSC)

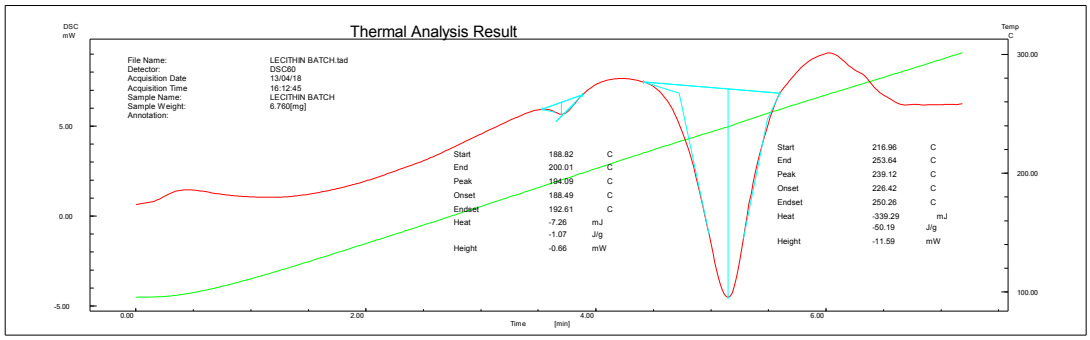
DSC thermo gram of pure drug Metformin HCl and granules of Metformin HCl with Guar Gum and Pectin along with different excipients are shown



Metformin HCl



Metformin HCl: Guar Gum: Pectin (1:0.5:0.5)



Metformin HCl (1:0.5:0.5): Lecithin

6. STABILITY STUDIES

Stability Studies of Formulation Batch MF3

The effect of temperature and humidity (40^0C and 75% RH) on in-vitro drug release of the most promising formulation batch MF3 and MF4 were performed.

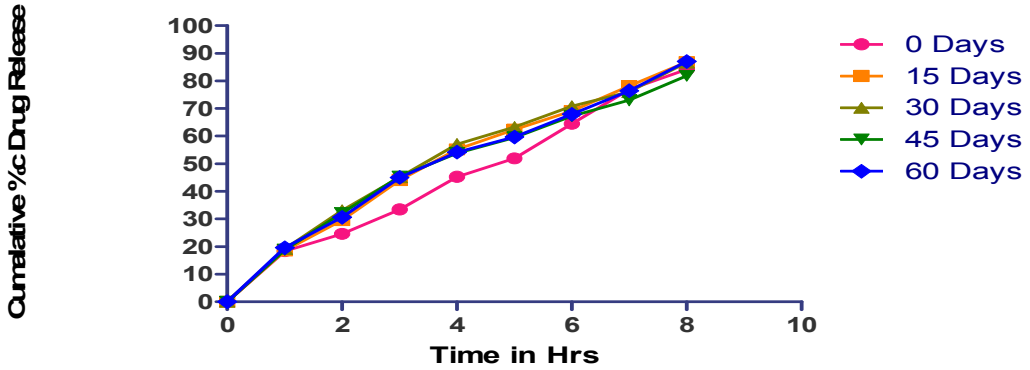


FIGURE 6

Effect of temperature and humidity on in-vitro drug release from the formulation batch MF3

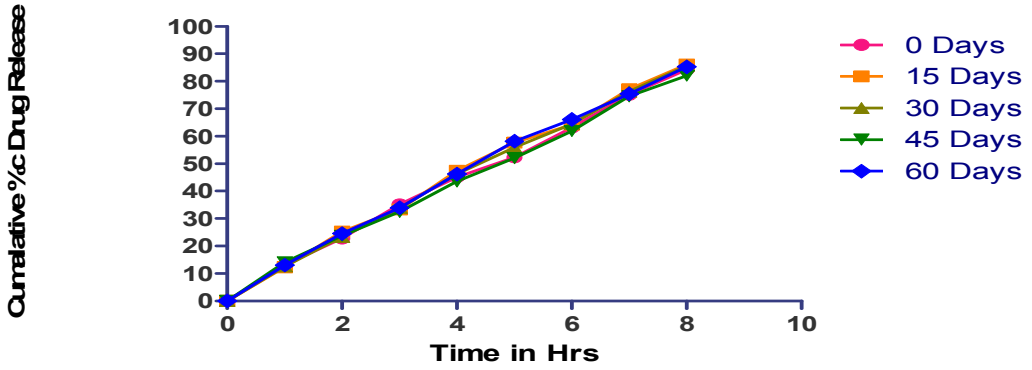


FIGURE 7

Effect of temperature and humidity on in-vitro drug release from formulation batch MF4.

7. CALCULATION OF SIMILARITY FACTOR (f_2)

A statistical comparison of dissolution data was carried out using a model independent method (f_2). The comparison of MF3 and MF4 batch release profile with marketed tablet (BIGOMET SR-250®) respectively.

Table 9

Comparison of formulation batch MF3 and MF4 with marketed product

Time In Hrs.	Cumulative % Drug Release (Mean ± S.D; n = 3)		
	Bigomet SR	MF3	MF4
1.	20.53 ± 0.46	18.62 ± 0.48	12.32 ± 0.95
2.	38.85 ± 0.88	29.61 ± 0.81	25.32 ± 0.64
3.	53.42 ± 1.02	44.09 ± 0.74	33.32 ± 0.36
4.	61.12 ± 0.33	55.22 ± 1.02	47.34 ± 1.14
5.	70. 44 ± 0.66	62.34 ± 1.12	57.72 ± 1.02
6.	76.62 ± 0.45	69.12 ± 1.24	64.22 ± 0.56
7.	83.87 ± 1.08	78.12 ± 0.81	77.14 ± 0.36
8.	88.13 ± 0.34	86.89 ± 1.18	86.12 ± 0.76

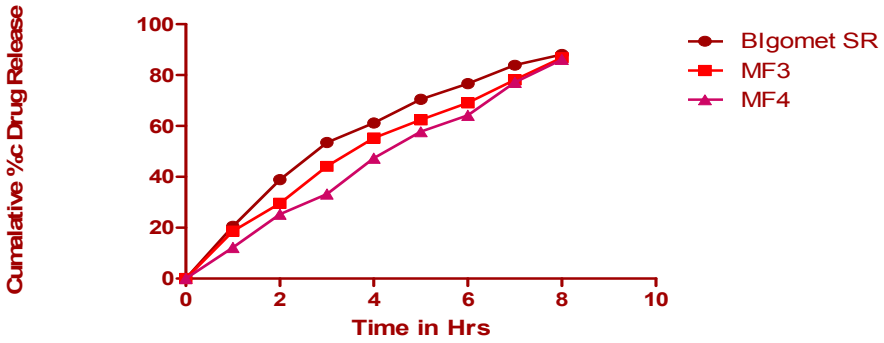


FIGURE 8

Comparison of MF3 and MF4 batches with Bigomet SR®

DISCUSSIONS

- ♣ All Batch Granules have passable Flowability and Good Compression Properties.
- ♣ No Color changes in granules were observed, indicating that the active ingredients and excipients were stable during granulation process.
- ♣ In- Vitro Release profile of formulation batch MF1 showed the initial burst effect and is dissolved in 5-6hrs. After this period no further release is seen in the case of, Guar Gum because it gets swells and blocks the release.
- ♣ In- Vitro Release profile of formulation batch MF2 showed the initial burst effect and the drug is 100% released in case for Pectin when used alone. It is due to high erosion rate of Pectin as compared to Guar Gum.
- ♣ The study was carried out for 12 hrs and the best results were found with the polymers and the excipients.
- ♣ At 10%, Concentration the lowest release was seen with tablets containing DCP (Emcompress®) while tablets containing Lecithin showed high drug release rate.
- ♣ DCP < Starch < MCC < Lactose < Lecithin
- ♣ At 15%, Concentration the lowest release was seen with tablets containing DCP (Emcompress®) while tablets containing Lactose showed high drug release rate.
- ♣ DCP < Starch < MCC < Lecithin < Lactose
- ♣ At 20%, Concentration the lowest release was seen with tablets containing DCP (Emcompress®) while tablets containing Lactose showed high drug release rate.
- ♣ DCP < Starch < MCC < Lecithin < Lactose
- ♣ Lactose containing tablets exhibited a single crack on the sides of tablets during dissolution process. Drug diffusion was promoted due to the pores and channels that were created following the solubilization of the lactose.
- ♣ Tablets containing MCC and Starch absorbed water through the capillaries leading to swelling and disintegration. New surface were thus created for drug diffusion to occur.
- ♣ Emcompress® (Di-calcium Phosphate) is in-soluble, non-swelling and tablets are intact throughout the dissolution process. Drug release was through diffusion via small inter and intra granular spaces.
- ♣ The observed differences in dissolution profiles due to differences in the solubility, swellability and density of the Excipients.
- ♣ The formulation batch MF4 (Lecithin) showed promising results at 10% concentration.
- ♣ The formulation batch MF5 (Lactose) is water soluble polymer and thus it enhances and modifies the drug release rate, while MF8 (Emcompress®) is a hydrophobic (Water- Hating) polymer in nature and thus decreases the drug release rate.
- ♣ The formulation batch MF6 (MCC) and MF7 (Starch) containing MCC and Starch are water swellable in nature. The presence of MCC and Starch in combination to Guar Gum and Pectin (1:1) matrix tablets modifies the release rate due to the disintegration phenomenon based on the water uptake capacity and the swelling properties of Guar Gum and Pectin in water.
- ♣ From the above figure, it was concluded that there were no changes in the peak shape and no shift of peaks.
- ♣ Therefore, the drug was compatible with the polymers (Guar Gum and Pectin) along with the Excipients (Lactose, Lecithin, Starch, MCC, and DCP)
- ♣ These thermo grams indicated that no significant change in peak shape, area and no shift of peaks were formed.
- ♣ Therefore, this study revealed that there were no interactions between the drug, polymers and Excipients or may be little interactions because Guar Gum and Pectin are hydrocolloids and they do-not melt to give the sharp peaks.
- ♣ Accelerated stability studies were designed to increase the rate of chemical degradation

or physical changes of an active substances or drug formulation.

- ♣ No significant variation (1 to 5%) in drug release was observed from the above table. Therefore it was concluded that the batch MF3 and MF4 were stable over the chosen temperature and humidity for 2 months.
- ♣ Therefore, it was concluded that the optimized batch formulations (MF3 and MF6) were stable over chosen temperature and humidity for 2 months.

CONCLUSIONS

- ♣ Metformin HCl sustained release matrix tablet was successfully formulated by using the combination of Guar Gum and Pectin (HM) in the ratio of 1:0.5:0.5 (Drug: Polymer).
- ♣ Combination of Guar Gum and Pectin (HM) is an interesting polymer mixture for the preparation of CR/SR matrix tablet because of high water swellability, non-toxicity and low cost of Guar Gum and good binding and gelling capacity of Pectin.
- ♣ All the formulation batches fulfill the I.P. limit for physical parameters like weight variation, hardness, friability and drug content uniformity.
- ♣ The in-vitro drug release studies indicated that the optimum release profile was found to be by the formulation batch MF3 and MF4.
- ♣ At 10%, concentration the in-vitro drug release decreased in the order of lecithin, lactose, MCC, Starch and Emcompress as Excipients with batch MF3.
- ♣ At 15% concentration the in-vitro drug release decreased in the order of lactose, lecithin, MCC, Starch and Emcompress as Excipients with batch MF3.
- ♣ At 20% concentration the in-vitro drug release decreased in the order of lactose, lecithin, MCC, Starch and Emcompress as Excipients with batch MF3.
- ♣ By Drug-Excipients interaction studies, no significant interactions were found.
- ♣ Formulation batch MF3 and MF4 were found to be stable over the chosen temperature and humidity for 2 months.
- ♣ Formulation batch MF3 and MF4 has better CR/SR release profile as compared to the marketed preparation.
- ♣ Therefore, it can be concluded that the formulation batch MF3 and MF4 were optimized by using Guar Gum and Pectin as polymers and Lecithin, Lactose, MCC, Starch, DCP as excipients at three different concentrations and the matrix tablets were formulated.

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