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FORMULATION AND EVALUATION OF METFORMIN HCL GASTRORETENTIVE TABLETS

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ABSTRACT:

Generating and evaluating Metformin HCL gastroretentive tablets is the fundamental objective of this present study. Metformin HCL belongs to the biguanide class which is an oral anti-diabetic drug. It is used to treat for type-2 diabetes Metformin HCL is recognised as corresponding to class 3 in the Biopharmaceutical classification system (BSC). It is important to ensure that Metformin HCL tablets must possess low permeability and high solubility. Metformin HCL pills are produced utilising four distinct types of synthetic polymers.They are Hypromellose K6 LV, Hypromellose E15LV, Hypromellose K100MPCR, Hypromellose K100LV. These synthetic polymers will impact the buoyancy mechanism on the tablet. Metformin HCL gastroretentive tablets are prepared by using two techniques.one is wet granulation method, and another one is top spray granulation method. In this study Four formulations were prepared. After formulation of tablets should be subject to different types of evaluation tests like weight variation test, thickness,hardness,friability test, Floating Lag time, total floating time, invitro dissolution studies and kinetic drug release studies. All the results are within the limits. Formulation 2 shows the highest drug release in dissolution studies.Studies on the kinetic discharging of chemical substances have been carried out employing formulation 2, which at first was regarded as to be the optimum formulation. All the results are within the limitation and satisfactory.

Key Words: Key Words: Metformin HCL, gastroretentive tablets, wet granulation method, Top spray granulation method.

INTRODUCTION:

The medication metformin hydrochloride (MH) has a brief half-life and a constrained window for absorption in the upper gastrointestinal system. Additionally, this medication is a part of the BCS III biopharmaceutical classification system. Due to patient compliance, ease of consumption, and cost-effectiveness, the oral route is the most favored method for drug delivery. Many different methods, such as tablets, capsules, syrups, etc., have been developed to deliver a significant amount of medication at a predetermined site and time in a systematic manner. However, this route has many physiological issues, such as the ease with which it can bypass the major absorption zone (the stomach and upper part of the intestine) due to high density and low-density retention times, which causes incomplete drug release and unpredictable low drug efficacy.

Drugs' stomach residence times can be greatly extended by gastro retentive systems since they can stay in the gastric region for several hours. Long-term stomach retention increases bioavailability, lowers drug waste, and increases the solubility of medications that are less soluble in high pH environments. Gastric retention will offer novel treatment opportunities and significant patient advantages. The Metformin HCL Tablet is a Type II Diabetes Mellitus medication that works as an antihyperglycemic agent to lower blood sugar levels.

The wet granulation method is used to create the oral sustained-floating tablet form of metformin HCL. This particular pill is designed to float on top of or within a liquid media. The floating tablet with density less than 1 and the tablet containing both an effervescent and non-effervescent system, where the non-effervescent system's swellable polymer, such as HPMC K 100 is responsible for the floating of the tablet, comes into contact with the GI (Effervescent system) Fluid effervescence is produced The Drug's Bulk is Reduced, and the Tablet is Floated. This tablet is made available for prolonged activity over a longer period of time.

MATERIALS:

Metformin HCL, Povidone(Binder), Microcrystalline cellulose pH 102(Diluent), Hypromellose K100LV(Swelling Matrix Polymer), Hypromellose K15 MPCR (Swelling Matrix polymer), Hypromellose K100 M(Swelling matrix polymer), Hypromellose E6LV(Swelling Matrix polymer), Magnesium stearate(Lubricant), Colloidal silicon Dioxide (Adsorbent), Methacrylate Copolymer Type A, Di Butyl Sebacate, Talc, Carbowax Sentry PEG 1450 NF, Acetone, IPA, Water. Analytical-grade chemicals and solvents were employed throughout the study.

METHODS:

Calibration curve of Metformin HCL with the help of UV spectrophotometer.

1.Standard Graph of Metformin HCL in Methanol

Preparation Stock Solution

- Measure and transfer roughly 100 mg of the metformin HCL standard into a 100 ml volumetric flask. Then, add roughly 60 ml of methanol, sonicate for 20 minutes, then add more methanol to bring the volume up to 100 ml.

Preparation of Test solution from the stock solution,

- A working solution is made by taking 1 ml and diluting it with 10 ml of methanol.
- Utilizing concentrations between 200 and 700 nm, ˙λ max is Calculated.

Standard graph Of Metformin HCL

- Weigh the Metformin HCL standard and transfer about 100 mg into a 100 ml volumetric flask.
- After adding roughly 60 ml of methanol and sonicating for 20 minutes, add enough methanol to make 100 ml of volume
- A working solution is created by taking 1 ml of the stock solution and diluting it with 10 ml of methanol.
- At 233 nm, the absorbance was measured when 2,4,6,8, and 10 µg/ml were produced from the stock solution.

2.Standard graph of Metformin HCL by using PH 6.8 phosphate buffer solution

Standard graph of Metformin HCL in PH 6.8 phosphate buffer:

Preparation of buffers and reagents:

- In order to make a PH 6.8 solution of phosphate buffer, mix 250 ml of 0.2 M potassium dihydrogen orthophosphate and 112 ml of 0.2 M NAOH in a 1000 ml volumetric flask. Next, add distilled water to the flask to bring the volume up to 1000 ml, and use diluted NAOH to adjust the pH to 6.8.

Spectrum of metformin hydrochloride

- A volume of 0.5 ml is pipetted into a 100 ml volumetric flask from the prepared stock solution. A volume of 100 millilitres is created using phosphate buffer solution with a pH of 6.8.A scan at 200–400 nm was performed on the resultant solution, which contained 5 ug/ml. The maximum wavelength (λ) was discovered to be 233 nm.

Metformin hydrochloride calibration curve in pH6.8 phosphate buffer: -

- A precise weight of 50 mg of metformin hydrochloride was dissolved in a little amount of pH 6.8 phosphate buffer solution, and the volume was adjusted to 100 ml. To achieve drug concentrations of 2 to 10 µg/ml, appropriate aliquots were placed into various volumetric flasks and filled to a capacity of 50ml with a pH 6.8 phosphate buffer solution. The blank solution was scanned between 400 and 200 nm, and all absorbance measurements were made at the same wavelength. The greatest absorbance was discovered at 233 nm.

3.Standard graph of Metformin HCL by Using 0.1N HCL

Preparation of Stock Solution

- A precisely weighed quantity of 100 mg was added to a 100 ml volumetric flask. The medication was dissolved in a few ml of water, and then 100 ml of 0.1N HCL were added. The solution that was produced had a concentration of 1 mg/ml and was designated as stock.

Preparation working standard solution

- Using this stock solution, 10 ml were taken and diluted with 0.1N HCL to yield 100ml. which produced a solution with a 100 mcg/ml concentration.

Serial dilutions were prepared by using the working standard solution

- This second solution was used to make the necessary dilutions given the various metformin concentrations (2–10 mcg/ml) solutions.
- The absorbances of the previously mentioned solutions were measured at 233 nm (λ max).

Formulation of Metformin HCL Gastroretentive Tablets:

Formulation of Metformin HCL Gastroretentive Floating Tablets Are Prepared by Using Wet Granulation Method and Top Spray Granulation Method.

In the initial trial, Metformin HCL Tablets are made by combining different ratios of polymers, like HPMC, with NaHCO3 as a gas-generating agent. Metformin HCL is passed through sieve no 20. Mesh number 40 is used to pass through HPMC K4M, MCC 102, NaHCO3, and citric acid. No.60 sieve was used to filter the talc. Sieve number 60 is used to filter out the magnesium stearate. For ten minutes, Metformin HCL was geometrically combined with HPMC K4M, MCC 102, and NaHCO3. Talc was added and stirred for a further 10 minutes. Then, after 5 minutes of mixing, magnesium stearate was added. The rotary tablet press was used to compress the lubricated blend.

Table No:01- Direct compression Ingredients

Ingredients	F1	F2	F3	F4	F5
Metformin HCL	1000	1000	1000	1000	1000
HPMC K4M	50	50	50	40	40
NaHCO3	100	80	120	100	100
MCC 102	50	70	30	60	40
Citric acid	20	20	20	20	20
Magnesium stearate	10	10	10	10	10
Total weight	1230	1230	1230	1230	1230

Result: The tablet is only 4-6kps in hardness. No floating was observed in 0.1N HCl. The tablets immediately developed effervescence when placed in a beaker containing 0.1N HCl, and they soon dissolved. Also, very high weight variation, the pills have a too-soft texture. The breaking of tablets was simple. Also, the required thickness wasn't attained.

Trial 2:

Impact of HPMC k 6LV, HPMC K100M, HPMC E15 LV, and HPMC K100 LV will be studied using the wet granulation method.

Table No:02- Wet Granulation Ingredients

Ingredient	Trade name	Lot No	Quantity mg/unit	Quantity mg/unit	Quantity mg/unit	Quantity mg/unit
Metformin HCL	NA	AMFHVSP20120719	100			
Povidone	Kollidon 90	2279535	30			
Purified water	NA	NA	Q.S			
HPMC 6LV	Methocel K4M	GAR476525	100	---	---	---
HPMC E15 LV	Methocel E15 LV	GAR481193	---	100	---	---
HPMC K100 M	Methocel K100 M	GAR455066	---	---	100	---
HPMC K100 LV	Methocel K100 LV	GAR530188	---	---	---	100
Colloidal silicon dioxide	Aerosil 200 pharma	150082714	10	10	10	10
Microcrystalline cellulose 102	Avicel pH 102	719205	50	50	50	50
Magnesium stearate	Ligamand MF-2V	C919626	10	10	10	10
Total weight of uncoated tablets			1200			

Through a 1.0 mm screen and #20 meshes, guaifenesin was milled. To create the binder solution, 33g of Povidone was continuously stirred into 398.57g of filtered water. Wet granules are created after the binder solution is manually applied to the blend. The 60mesh is used to grind this moist substance. The granules are processed through 20 meshes after being dried in a hot air oven. Four equal portions of the sized granules are divided, and then four more extra-granular materials are added. Aerosil, MCC 102, HPMC K4M, HPMC E15 LV, HPMC K100M, and HPMC K100 LV extra granular material were sorted through #40 meshes and prelubricated for 10 minutes.

Result:

Even when using multiple polymers with a range of viscosities, wet granulation could not produce floating tablets. Top spray granulation is an additional suggestion to assess the impact of the operation. Even when using multiple polymers with a range of viscosities, wet granulation could not produce floating tablets. Top spray granulation is an additional suggestion to assess the impact of the operation.

Trial 3

Formulation Trials of Top spray Granulation

Table No:03

Ingredient	F1	F2	F3	F4
Metformin HCL	1000	1000	1000	1000
HPMC K100 LV	100	---	---	---
HPMC E6 LV	---	100	---	---
HPMC K100 M	---	---	100	---
HPMC K15 MPCR	---	---	---	100
Povidone	30	30	30	30
MCC	50	40	30	20
Magnesium stearate	10	6.5	0	6.5
Colloidal silicon oxide	10	20	20	28
Purified water	Q.S	Q.S	Q.S	Q.S
Unit weight (mg)	1200	1200	1200	1200

Through a 1.0 mm screen and #20 meshes, Metformin HCL was milled. As a binder solution, povidone was dissolved in the necessary amount of water after being sifted through #40 meshes. The transferred sifted API was fluidized for up to five minutes in FBP. 360°C spraying began after the product reached the desired temperature. The spray rate gradually increased while preserving the product's temperature. The spray pump's initial RPM was 2. The spray solution was finished, and the granulated material was left to dry for 15 minutes. At 1050C for 5 minutes, the dried granular material's LOD was NMT 1.5% w/w. Material that had been dried and ground up was filtered through #20 meshes. HPMC E6LV/HPMC K100 M/HPMC K15M/HPMC K100 LV, Aerosil, and MCC PH 102 extra granules material that is equivalent to 100 tablets was sifted through #40 meshes before being charged into a blender with sized granules and prelubricated for 10 minutes at 13RPM. Magnesium stearate was lubricated for five minutes at 13 RPM after being sorted through #60 meshes. Lubricated blend was compressed into tablets using 20.50×9.50mm round punch for 1000mg strength.

Table No:04- Spray parameters

Time (min)	Inlet temp (0C)	Product temp (0C)	Exhaust temp (0C)	Air flow CFM	Atomization (bar)	Spray RPM	Spray rate (g/min)
Initial	40	46	30	63	1.0	4.0	1.0
30 min	48	46	30	38	1.0	6.0	4.0
1 hr	48	36	30	44	1.0	6.0	4.0
1.5 hrs	48	37	30	42	1.0	6.0	4.0
1.75 hrs	48	37	30	43	1.0	6.0	4.0
Drying at 0 minutes	38	37	30	48	---	---	---
Drying (15 minutes)	37	37	30	41	---	---	---

Observation:

With the exception of the formulation comprising HPMC E6 LV, floating was noticed after 30 to 40 minutes in all formulations of various polymers. However, the reduced floating lag time is under a minute.

Way forward:

Polymer coating was then carried out to achieve the ideal floating lag time.

Table No:05- coating ingredient

Ingredients	Quantity (mg per unit)	Trade Name
Methacrylate Copolymer type A	40.00	Eudragit RLPO
Dibutyl Sebacate	4.00	DBS NF
Talc	20.00	Luzenac pharma
Carbowax sentry PEG 1450NF	4.00	Sentry flake PEG 1450 NF
Acetone	38%	NA
IPA	52%	2-Propranalol
Water	10%	NA
Total weight of Coated Tablet	1296.00	

Tablet coating process parameters

Table No:06- Coating process parameters

Time (min)	Inlet temp (0 c)	Product temp (0C)	exhaust temp (0 c)	Pan RPM	Peristaltic pump	Atomization (bar)	Spray pattern
0	29.1	28.5	29.4	12	2.08	0.8	0.5
15	29.6	28.9	29.5	12	3.21	0.8	0.5
30	30.5	29.2	28.7	14	3.98	0.8	0.5
45	30.9	29.3	27.5	14	4.56	0.8	0.5
60	31.2	29.5	28.7	14	4.79	0.8	0.5

EVALUATION OF METFORMIN HCL GASTRORETENTIVE TABLETS

Evaluation of pre-compression parameters:

Bulk Density:

Bulk Density is a proportion of weight mass to bulk volume. The original volume of the powder material is measured, and its bulk density is estimated using the following formula after it has been separately weighed and put into a 100 ml measuring cylinder.

Bulk density = Mass / Volume

Tapped Density:

Tapped Density is defined as the ratio of weight mass to tapped volume. An important evaluation parameter known as "tapped density" is found by setting a graduated cylinder with a known mass of powder. Undergoes manual tapping (100 tapes) and mechanical tapping (using an instrument) when the volume of the powder bed has reached a minimum volume. The following formula is used to compute the tapped density.

Tapped density = Powder weight / tapped volume of Powder

Angle of Repose:

It states that the Angle of Repose refers to the Pile surface of Powder. This method of calculating the angle of repose involves pouring powder into a conical shape onto a level, flat surface, then measuring the resulting angle. The formula which is used to determine the angle of repose is.

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

Where,

θ - Angle of repose,

h - Height of the powder cone,

r - Radius of the powder cone

Compressibility Index or Carr's Index:

Bulk and Tapped densities are used to calculate the compressibility index. Compressibility Index is a ratio of Tapped Density to Bulk Density.

Hausner ratio:

The Hausner ratio is the proportion of tapped density to bulk density.

Evaluation of post compression parameters:

Thickness and Diameter:

Using a thickness gauge Vernier calipers type CD-8" CSX (Mitutoyo, New Delhi, India), the diameter and thickness of the tablets were measured. Average values were computed using five pills from each batch.

Hardness:

The hardness test involved measuring three tablets of each formulation. A Hardness Tester type EH-01 (Electrolab) was used to assess the hardness. In kg/cm2, the hardness was calculated.

Weight variation test:

The USP weight variation test is carried out by weighing each of the 20 tablets separately, determining the average weight, and comparing the weight of each tablet to the average. The following formula is used to calculate the weight variation percentage.

Weight variation - [X/* X] × 100

Where,

X - Individual weight of the tablet,

X -* Average weight of the tablet.

Friability Test:

Using a friability tester, the friability of 20 tablets was ascertained. Twenty pills from each formulation were weighed and tested for four minutes at a speed of 25 rpm. The tablets were reweighed after removal, and the friability % was measured. giving a 20-tablet beginning weight to get the appropriate friability of the 20 tablets, divide these weights by the friability after 20 tablets and multiply by 100. After that, the percentage of friability was determined by using the following formula.

In vitro drug release studies:

It is a process where solid material is dissolved into liquid medium over a certain amount of time. Sink Condition is the basic foundation of it. Paddle Type (USP II) of Dissolution Apparatus controls the dissolution of Floating Tablets. The pill was placed into a cylindrical jar with 900 ml of PH 1.2 Acidic media, 75 rpm, and a temperature of 37 0.5 C, at intervals of 1 to 8 hours. after an hour. A 5 ml sample was taken, and the necessary amount of sample was taken to measure absorbance using the U.V. spectroscopy technique and assess the rate of pill dissolution.

Floating Lag Time:

One tablet is introduced into a beaker filled with a 100ml solution of 0.1N HCL to make it float while the total floating time of the tablet is calculated. If you're using a Metformin HCL tablet, the total floating duration is 10 minutes. In table number 17, it is reported how long the tablet has been in use overall.

RESULT AND DISCUSSION:

Solubility of Metformin HCL in Different Solvents

Table No:07

S.No	Medium	Concentration Of the Drug Soluble (mg/ml)
1	Methanol	16.99
2	0.1N HCL	8.23
3	PH 6.8 Phosphate Buffer Solution	4.28
Result	Class of Drug	BSC Class II

Metformin HCL's solubility in the sample solution are Reported to the table No:7. Concentration of the Drug Soluble (mg/ml) in Methanol is 16.99, in 0.1N HCL is 8.22, and in PH 6.8 Phosphate Buffer Solution is 4.22.

Construction of Calibration Curve by using UV-Visible Spectrophotometer:

Calibration Curve of Metformin HCL by Using Methanol

Table No:08

Concentration(µg/ml)	Absorbance(nm)
2	0.182±0.020
4	0.324±0.0025
6	0.521±0.031
8	0.768±0.039
10	0.918±0.017

Standard Deviations n=3

Calibration curve of Metformin HCL in Methanol

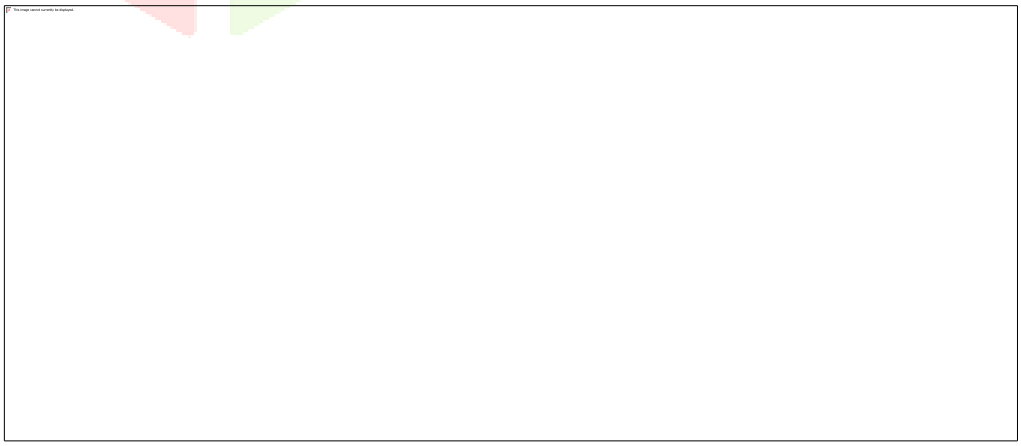

Figure No1: Standard Graph of Metformin HCl By Using 0.1N HCL

Linearity plot of Metformin HCl in the concentration range of 2-10 µg/ml were evaluated. Linear absorbance versus concentration gives regression equation; Y=0.0958x-0.032, with a correlation coefficient (r^2) of more than 0.99 in Methanol.

Calibration Curve of Metformin HCL by Using 0.1N HCL

Table No:9

Concentration(µg/ml)	Absorbance(nm)
2	0.202±0.017
4	0.395±0.024
6	0.558±0.035
8	0.745±0.041
10	0.912±0.013

Standard Deviations n=3

Calibration curve of Metformin HCL in 0.1N HCL

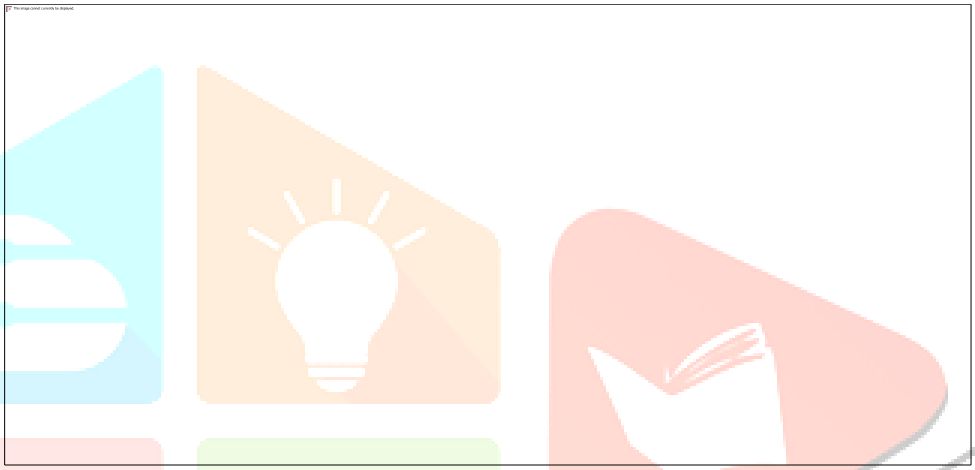

Figure No:2 Calibration Curve of Metformin HCL in 0.1N HCL

Linearity plot of Metformin HCl in the concentration range of 2-10 µg/ml were evaluated. Linear absorbance versus concentration gives regression equation; Y=0.0885x-0.0314, with a correlation coefficient (r^2) of more than 0.99 in 0.1N HCL.

Standard Graph of Metformin HCl By Using PH 6.8 Phosphate Buffer Solution

Table No:10

Concentration(µg/ml)	Absorbance(nm)
2	0.159±0.0197
4	0.319±0.022
6	0.481±0.029
8	0.647±0.038
10	0.802±0.015

Standard Deviations n=3

Calibration curve of Metformin HCL in PH6.8 Phosphate Buffer Solution

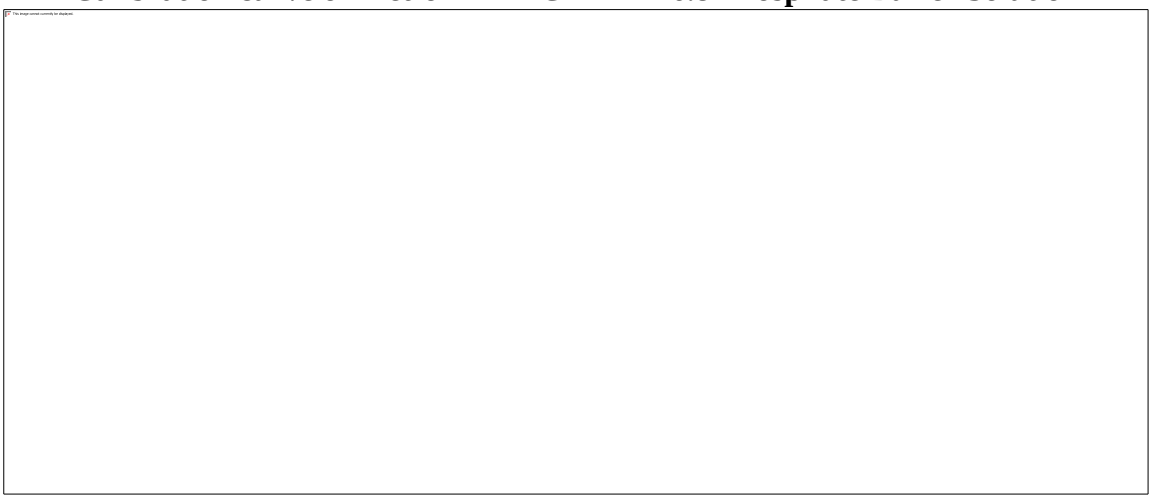

Figure No:3 Calibration Curve of Metformin HCL in PH 6.8 Phosphate Buffer solution

Metformin HCl's linearity plot was determined between 5 and 40 µg/ml of concentration. Linear absorbance versus concentration gives regression equation; Y=0.0807x-0.0026, with a correlation coefficient (r^2) of more than 0.99 in PH 6.8 Phosphate Buffer Solution.

Preformulation Studies:

Drug excipient compatibility studies:

No notable interactions were found between the medications and excipients, based on drug excipient compatibility investigations. The IR spectra of the formulations and the IR spectra of the pure drug were compared in order to verify the drug polymer interaction. The pure drug's IR spectra showed no appreciable shift in its functional groups, and the chosen formulation did not exhibit any new peaks. Proving there isn't a drug-excipient interaction.

Drug Excipient Compatibility Studies of Metformin HCL

Figure No:4 FTIR Spectrum of Metformin Pure Drug

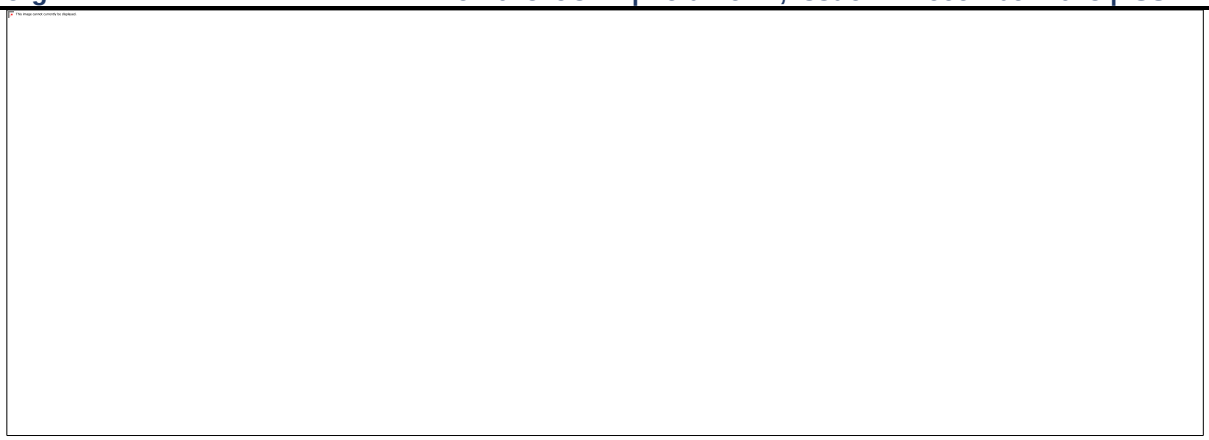

Figure No6: FTIR Spectrum of Drug and Excipient

Comparison of Metformin HCL Pure Drug and Drug+ Excipients

Table No:11

FTIR Band of Metformin HCL (cm-1)	FTIR Band of Drug and Excipients (cm-1)	Functional Group
3370	3367.71	NH-
3290	3294.42	NH-
3174	3170.97	C-H
1420	1418	C-H
1477	1470.47	C=H

Discussion: Pure Metformin HCL spectra showed sharp characteristic peaks at 3370,3290,3174,1420,1477 (cm-1). These Peaks are also which are similar to the Drug and excipients FTIR Spectrum.

Evaluation Of Metformin HCL Tablets

Table No:12

Parameters	F1	F2	F3	F4
Bulk Density(g/ml)	0.50±0.011	0.48±0.006	0.44±0.007	0.40 ±0.005
Tapped Density(g/ml)	0.65 ±0.009	0.54±0.04	0.46±0.013	0.53 ±0.014
Carr's Index (%)	24 ±0.002	12.6 ±0.006	8.2 ±0.016	23 ±0.017
Hausner's Ratio	1.5 ±0.004	1.13±0.013	1.091±0.018	1.317±0.016
Angle of Repose	24.63±0.129	24.04±0.0115	28.35±0.124	22.62±0.0128
Result	Fair	Fair	Fair	Fair

Standard Deviations n=3

The API of were tested by various studies including bulk density (0.50gm/ml), tapped density(0.65gm/ml), Hausner's ratio (1.317), Carr's index (24 %) and Angle of Repose (28.35±0.124). All the results showed Fair.

In Process Parameters:

Table No:13

S.NO	Evaluation tests	F1	F2	F3	F4
1	Weight variation(mg)	1189±1209	1193±1210	1191±1220	1182±1221
2	Hardness (Kg/Cm3)	9.1±12.1	9.6±11.4	9.3±11.5	9.2±12.4
3	Thickness(mm)	9.3±9.2	9.1±9.53	9.5±9.59	9.1±9.61
4	Friability (%)	0.21	0.23	0.22	0.24

Standard Deviations n=3

The API of were tested by various studies including Weight Variation(11939mg), Hardness (9.6 Kg/Cm3), Thickness(9.5mm), and Friability (0.24%). All the results showed Fair.

In Vitro Buoyancy Studies:

According to the protocol outlined by Rosa et al., in vitro buoyancy tests were carried out for each formulation. A 100 ml beaker filled with 0.1 N HCL (pH 1.2) held the tablets that were randomly chosen from each formulation. We called this floating lag time (FLT) the amount of time it took for the tablet to rise to the surface and float. The amount of time the dose form stayed on the medium's surface continuously was calculated as the total floating time (TFT)

Table No:14

S.No	Parameters	F1	F2	F3	F4
1	Floating lag time	Floating was observed immediately in 0.1N HCl	Floating was observed immediately in 0.1N HCl	Floating was observed immediately in 0.1N HCl	Floating was observed immediately in 0.1N HCl

Invitro Drug release Studies:

The USP paddle apparatus type II was used to determine the in vitro release study of 1000 mg of Metformin Hydrochloride from the tablets. The dosage form was fully submerged in 900 ml of 0.1 N Hydrochloric acid, pH 6.8 Phosphate buffer Solution, which served as the dissolution medium. The temperature was maintained at 37±0.5 0C, and the paddle rotation speed was kept at 50 rpm. At predefined intervals, five ml samples were taken (0,1,2,4,6,8,10,12). The samples were swapped out for an equal volume of brand-new dissolving medium. Using a twin beam UV/Visible spectrophotometer, the absorbance of these solutions was examined at 233 nm. A calibration curve was used to determine the drug's content. To calculate the release profile, the proportion of drug release was plotted against time. A graph shows the cumulative % release of Metformin HCL as a function of time for each formulation.

Table No:15 –Dissolution Profile in PH 6.8 Phosphate Buffer

Time(hrs.)	Cummulative % Drug Release			
	F1	F2	F3	F4
0	0	0	0	0
1	8.5±1.3	7.3±0.7	6.5±1.1	7.4±0.7
2	24.8±0.8	23.4±1.2	24.1±0.9	27.0±1.6
4	58.3±0.9	49.3±0.8	35.3±0.8	34.6±0.7
6	75.9±0.9	67.5±0.8	48.5±1.3	51.7±0.4
8	87.59±0.6	79.6±1.2	67.9±1.3	68.8±1.7
10	86.6±1.2	88.3±1.3	76.4±0.4	72.8±0.7
12	89.0± 0.3	94±0.7	86.6±0.3	85.0±0.9

Standard Deviations n=3

Drug release from all formulations in PH 6.8 Phosphate Buffer:

In formulation F1, the total percentage of drug release from tablets at the end of 12 hours is found to be 89.0%

In formulation F2, the total percentage of drug release from tablets at the end of 12 hours is found to be 94%.

In formulation F3, the total percentage of drug release from tablets at the end of 12 hours is found to be 86.6%.

In formulation F4, the total percentage of drug release from tablets at the end of 12 hours is found to be 85.0%.

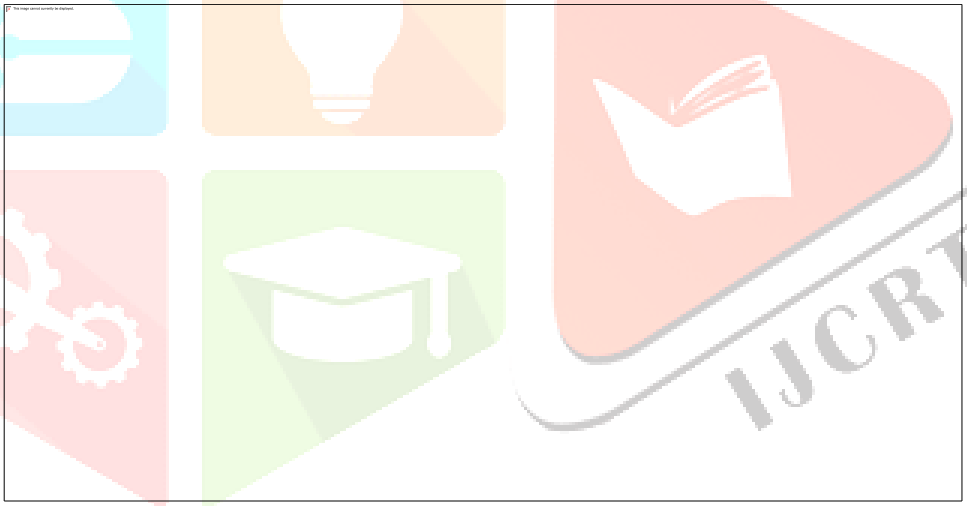

Figure No7: Dissolution Profile in PH 6.8 Phosphate Buffer

Table No:16-Dissolution Profile in 0.1N HCL

Time(hrs.)	Cummulative % Drug Release			
	F1	F2	F3	F4
0	0	0	0	0
1	8.3±1.2	7.4±0.7	6.6±1.1	7.8±0.7
2	24.5±0.9	22.5±1.1	20.4±0.8	27.8±1.1
4	59.6±0.6	48.3±0.9	34.4±0.5	32.4±0.6
6	77.2±1.3	67.0±0.4	49.7±1.2	50.7±0.5
8	84.1±1.4	79.8±1.2	67.6±1.7	69.8±1.4
10	86.4±1.1	89.4±1.2	74.9±0.5	73.8±1.7
12	89.9±0.6	93±0.6	87.6±0.3	88.0±0.6

Standard Deviations n=3

Drug release from all formulations in 0.1N HCL:

In formulation F1, the total percentage of drug release from tablets at the end of 12 hours is found to be 89.9%.

In formulation F2, the total percentage of drug release from tablets at the end of 12 hours is found to be 93%.

In formulation F3, the total percentage of drug release from tablets at the end of 12 hours is found to be 87.6%.

In formulation F4, the total percentage of drug release from tablets at the end of 12 hours is found to be 88.0%.

Figure No:08 Dissolution Profile in PH 0.1N HCL

Drug release kinetics of optimized formulation in PH6.8 Phosphate Buffer Solution

The kinetic characteristics of drug release are represented graphically by models such as the zero-order kinetic model, first order kinetic model, Higuchi model, Hixon and Crowell model, and Korsmeyer-Peppas model. Since the correlation coefficient (R2) value of 0.9908 is higher than that of first order release kinetics, the kinetic results of the optimized formulation followed zero order kinetics. The drug release optimized formulation fits the Hixson and Crowell model the best, with an R2 value of 0.9876.

Table No:17

F.Code	Zero Order R^2 value	First Order R^2 value	Higuchi Kinetic Model R^2 value	Hixson and Crowell Kinetic Model R^2 value	Kors-peppas Kinetic Model R^2 value
F2	0.9908	0.9769	0.9035	0.9876	0.9782

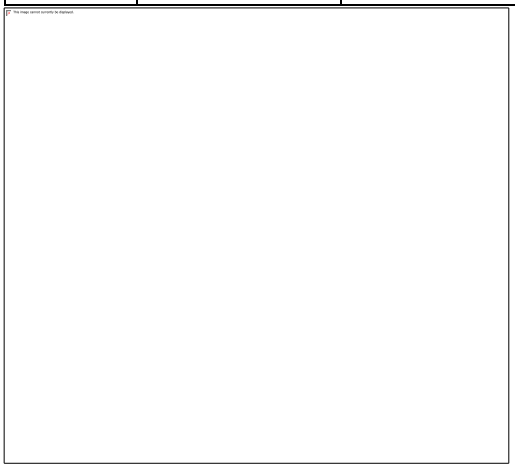

Figure N0:08 Zero Order Kinetic Model

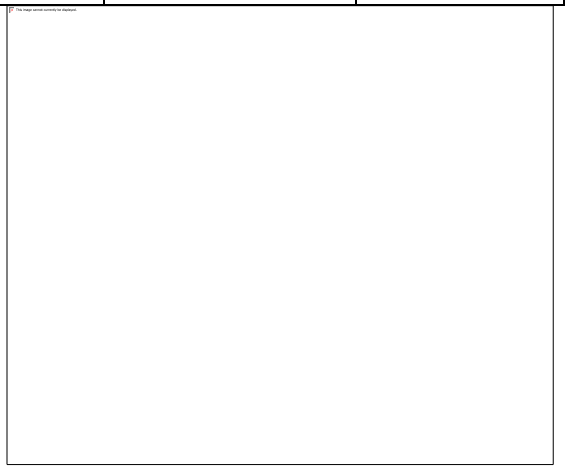

Figure N0:09-First Order Kinetic Model

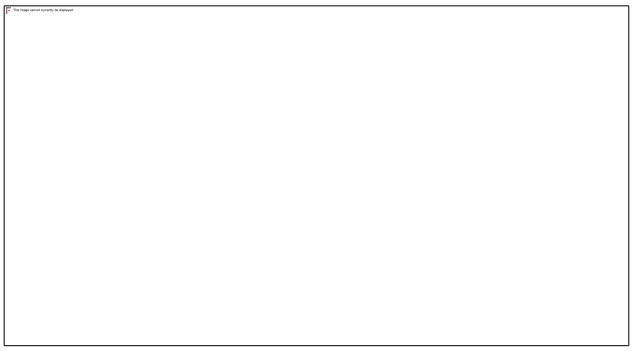

Figure N0:10- Higuchi Kinetic Model

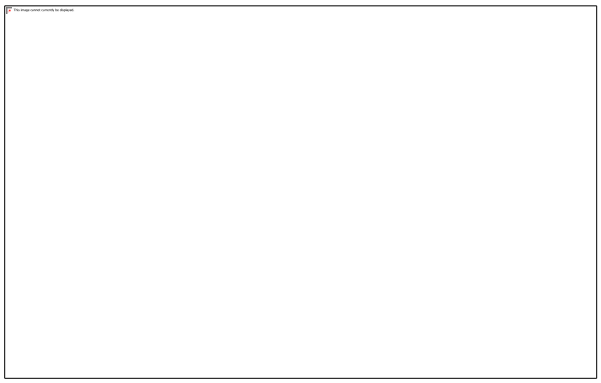

Figure N0:11-Hixson and Crowell Kinetic Model

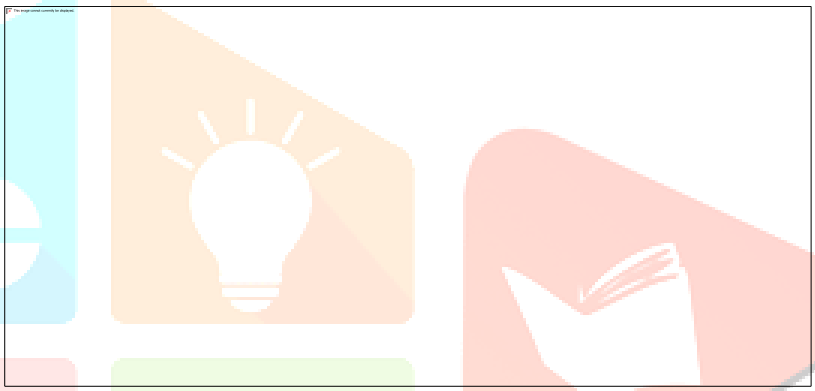

Figure N0:12-Kors-peppas Kinetic Model

CONCLUSION:

The Wet Granulation Method and Top Spray Granulation Methods are used to create the Metformin HCL Floating Tablet, which has a density below 1. The tablet has both an effervescent and a non-effervescent mechanism and is gastroretentive floating sustained releasing. The Floating (Non-Effervescent System) is caused by the HPMC K 100 Swellable Polymer, and the Effervescent System is caused by Sodium Bicarbonate. The outcome of the optimized batch is up to satisfactory and exhibits good free-flowing characteristics. The pharmacopoeia limit is met by the hardness, weight variation, and friability values. The in vitro dissolution studies demonstrate the drug's highest percentage of release.

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