FORMULATION AND EVALUATION OF METFORMIN FLOATING TABLETS BY USING NATURAL GUMS

Krishnapillai mathusoothanan1,2*, Gudanagaram Ramamoorthy Vijayasankar1, Bendi Sri Venkateswarlu1, Rajappa Margret Chandira1.
1Department of Pharmaceutics, Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation (Deemed to be University), Salem 636308, Tamil Nadu, India,
2Department of Pharmaceutics, Grace College of Pharmacy, Palakkad 678004, Kerala, India

ABSTRACT

The current research was aimed to formulate, evaluate and optimize gastro retentive formulations for antidiabetic drugs. The drugs chosen for the study were metforminHCL (MH), which are benefited by preparing stomach specific drug delivery systems in the form of floating matrix tablet. Identification of drugs was done by DSC Study. The analytical methods on UV spectrophotometer were developed for the *in-vitro* analysis of drug. The Metformin HCL floating matrix tablet was prepared for using Natural gum like almond gum and Neem gum.Both gums acting as a release retarding agents. First perform pre formulation studies. Solubility, Melting point, Standard calibration curve, Compatibility study done by FTIR Study. The floating tablet prepared by direct compression method.Absorbtion maxima getting 234 nm. The results of the study indicates FT-IR spectrum of drug and excipients did not differed with major peaks of drug. Precompression study indicates that the powder blend shows good flow property. Evaluation study Perform by Weight variation test, Thickness, Floating lag time, Total floating time Drug Content, Swelling index, *In-vitro* release study should be done. The 2^2 factorial design optimization of metformin HCL floating matrix tablet was done. Radiological study was performed on healthy albino rabbits for checking the gastro retention for optimized floating tablets. The *in-vivo* X-ray imaging study clearly indicated that the optimized formulations remained afloat in gastric fluid up to 12 h in the stomach of rabbit. Pharmacokinetic studies of optimized Metformin tablets were performed on healthy Albino rabbits. The optimization of gastro retentive tablet was successfully done by applying statistical design. It can be concluded that oral antidiabetic treatment may be achieved efficiently by preparing floating

tablets, which could results in increase in bioavailability along with Sustained release of action resulting in possible reduction in dose and side effects of drug.

Keywords: floating tablets, Natural polymers, Microspheres, Sustained release formulations

INTRODUCTION

As the Parenteral administration can cause pain, anxiety from multiple injections, and risk of infection, non-invasive forms of drug administration are encouraged to promote carriage. The oral controlled-release drug delivery system is considered a type of controlled-release drug delivery because of its advantages of easy administration, flexible formulation, and low sterility.

Type 2 diabetes mellitus is a disease that occurs due to problems in the way the body regulates and uses sugar as fuel. This sugar is also called glucose. This prolonged pain can cause too much sugar in the blood. Finally, high blood sugar can cause complications in the blood vessels, nervous system, and immune system. Type 2 diabetes has two main complications. The pancreas does not produce enough insulin, the hormone that controls the entry of glucose into cells. And cells respond less to insulin and eat less sugar. Type 2 diabetes cannot be cured. Weight loss, healthy eating and exercise can help control this disease. If diet and exercise are not enough to control blood sugar, diabetes medication or insulin may be recommended.

Gastric Retention Floating Matrix Tablets can be designed to increase the residence time of drugs in the stomach and improve bioavailability. Floating matrix tablets are a great strategy for developing controlled-release drugs and provide a simple and effective way to achieve prolonged drug release. Gastric-retaining floating matrix tablets are a good way to deliver certain anti-diabetic drugs into the gastrointestinal tract. Metformin hydrochloride is a hypoglycemic drug commonly used in the treatment of NIDDM. Due to specific absorption limitations, the oral bioavailability of metformin hydrochloride is 50-60%. It is a safe drug with a half-life of 2 hours. It is not completely absorbed and creates a low bioavailability problem. Usually 80-100% of the drug is eliminated unchanged. The total daily requirement of metformin hydrochloride is 1.5-3 g/day. Which allows the drug to stay in the stomach longer regardless of the amount of bowel movement. In effervescent flotation systems, a hydrophilic polymer is combined with a gaseous material such as sodium bicarbonate. While sodium bicarbonate is used to increase the body's energy by releasing carbon dioxide when it comes into contact with gastric fluid, the hydrophilic polymer provides control of drug release. In this study, swellable hydrophilic

polymers based on a combination of natural polysaccharides [gum, neem gum, xanthan gum] and semi-synthetic hydrogel [HPMC K100M] were used. The advantage of these connections is to ensure maximum gel formation, swelling and maintenance of buoyancy at the rate of release in gastric juice

MATERIALS AND METHODS

The chemicals used in the research work were pure drugs like MetforminHCL (Yarrow Chem Products), and the excipients like Neem Gum, Almond Gum, Magnesium stearate (Prowess lab chemicals). Software's that is used in the study includes Microsoft exce, Mini tab.

METHODS

Compatibility study (FTIR)

The Fourier transform infrared (FTIR) spectra of samples were obtained using FTIR Spectrophotometer. Pure drug, polymers and their mixtures were subjected to FTIR Study. About 2–3 mg of sample was taken with dried potassium bromide of equal weight and Compressed to form a KBr disk. The samples were scanned from 400 to 4000 cm−1.

Preparation of Absorption maxima for Metformin HCL using pH 1.2 stimulated gastric fluid.

Accurately weighed amount of Metformin hydrochloride (100 mg) was dissolved in small quantity of stimulated gastric fluid pH 1.2 and then diluted to 100 ml with the same solvent. Each ml of the stock solution contains 1 mg of Metformin hydrochloride. From this stock solution different standard of working standard solutions i.e., 2, 4, 6,8,10 µg/ml were made up with stimulated gastric fluid pH 1.2 and the absorbance was measured at 234nm using stimulated gastric fluid as blank by UV spectroscopic method. A graph was plotted by using concentration at X-axis and absorbance at Y-axis.

Formulation of Metformin HCL Floating Tablets.

The tablets containing 250 mg of the drug were prepared by direct compression method and the various formulas used in the study are shown in Table 1. The drug, diluents were passed through sieve No 40. All the above ingredients were properly mixed together. Talc was passed through sieve No 80, mixed and blended with initial mix. The powder blend was compressed into tablets on a ten station rotary punch tablet machine using 9 mm convex punch.

COMPOSITION OF FLOATING TABLETS OF METFORMIN HCL

Batch/INGRDEIENTS	F1	**F2**	**F3**	F4	F5	F6
MET FORMIN HCL	250	250	250	250	250	250
NEEM GUM	40	60	80	---	---	---
ALMOND GUM	---	---	---	40	60	80
SODIUM BI CARBONATE	70	70	70	70	70	70
MCC	200	180	160	200	180	160
LACTOSE	75	75	75	75	75	75
MAGNESSIUM STERATE	10	10	10	10	10	10
TALC	5	5	5	5	5	5
TOTAL	650	650	650	650	650	650

EVALUATION OF METFORMIN FLOATING TABLETS

An evaluation was performed to access the pre-compression properties of the powder blend and post-compression properties of developed gastric floating tablet formulations.

Precompression parameters

Angle of repose

Fixed funnel position and free standing cone method is used to determine the static angle of repose "Θ". It is the maximum angle possible between the surface of a pile of powder and the horizontal plane. A paper was placed on a flat horizontal surface and above which the funnel was clamped with its tip 2 cm height. The powder blend of Metformin HCL was poured separately through the funnel until the apex of the cone thus formed just reached the tip of the funnel. The mean diameters of the base of the powder cones were determined and the tangent of the angle of repose calculated using the equation,

$$\tan \Theta = h/r$$

h = height of granule pile

r = radius of tablet granules

Angle of repose (Θ) = $\tan^{-1}(h/r)$.

Bulk density

Bulk density is ratio of total mass of powder to the bulk volume of the powder. Bulk density is expressed as g/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and tendency of particles to adhere together. Required quantity of powder sample was in a measuring cylinder and the volume, V_b, occupied by each of the samples without tapping the measuring cylinder was noted and this gives you the bulk density. The bulk density was calculated using the following equation;

Bulk density = Weight of sample/ Bulk volume (V_b)

Tapped density

It is defined as the ratio of total mass of the powder to the tapped volume of the powder. The tapped density can be measured by pouring a specified quantity of powder sample through a glass funnel into a 50ml graduated cylinder. The cylinder is tapped from a height of 2cm until a constant weight is obtained. After 100 taps, the volume occupied by the powder is measured and this is called as the tapped volume and the tapped density was calculated using the formula;

Tapped density = Weight of sample/ Tapped volume (V_t)

Hausner's ratio

This is measured as the ratio of tapped density to the bulk density. This can be expressed using the equation;

Hausner's ratio = Tapped density/ Bulk density

Compressibility index

Compressibility is the ability of the powder to reduce its volume under pressure. This was calculated by using the equation;

Compressibility index = (Tapped density- bulk density)/ tapped density*100

Post compression parameters of tablets

Thickness test

The thickness in millimeters (mm) was measured individually for 10 pre weighed tablets by using Vernier Calipers. The average thickness and standard deviation were reported.

Hardness

Hardness is defined as the ability of the tablet to withstand the mechanical shocks during handling. Three tablets are randomly picked and hardness was determined. Hardness can be measured using the Monsanto Hardness tester and can be expressed in kg/cm^2.

Friability

Twenty (20) tablets were selected from each batch and weighed. Each group of tablets was rotated at 25 rpm for 4 minutes (100 rotations) in the Roche friabilator. The tablets were then dedusted and re-weighed to determine the loss in weight. Friability was then calculated as per weight loss from the original tablets.

$$\% \text{ friability (F)} = \frac{\text{(initial weight (Wi) – final weight (Wf))}}{\text{Initial weight (Wi)}} \times 100$$

Disintegration test

Disintegration test was performed using an altered disintegration method with six tablets (n=6). The USP disintegration test apparatus was maintained at a temperature 37±0.5°C. The test was performed for both using 0.1N HCl and phosphate buffer respectively.

Weight variation test

Twenty tablets were collected randomly and weighed individually. The individually weighed tablets compared with an average weight for the determination of weight variation. The uniformity of weight is determined according to I.P specification. As per USP specification not more than two of the individual weight should deviate from average weight by more than 5% and none deviate more than twice that percentage. The percentage of deviation was calculated using the equation;

$$\textbf{\% Deviation} = \frac{\textbf{Individual weight-Average weight}}{\textbf{Average weight}} \times \textbf{100}$$

Drug content

Twenty tablets were taken, powdered and the powder equivalent to one dose each was transferred to a 100 mL volumetric flask and 0.1N HCl was added. The volume was then made up to the mark with 0.1N HCl. The solution was filtered and diluted suitably and drug content in the samples was estimated using UV-Visible spectrophotometer at 234 nm.

***In vitro* buoyancy studies :(floating lag time & Floating Time)**

The *in vitro* buoyancy was determined by floating lag time. The tablets were placed in

a 100 mL beaker containing 0.1N hydrochloric acid. The time required for the tablet to rise to the surface and to float was determined as ***floating lag time***. The duration of time for which the dosage form constantly remained on the surface of medium was determined as the ***total floating time.***

Swelling Index

The swelling property of floating tablet was done by putting the tablet in a graduated glass vessel containing 250 ml of 0.1 N HCl acid maintained at 37 ± 0.5◦C.At regular time intervals, the tablet was collected and the liquid present on the surface of tablet was carefully removed. The swollen tablet was then reweighed and calculated swelling index.

$$\% \text{ of swelling} = \frac{W2-W1}{W1} \times 100$$

W2 = Weight of the swollen tablets
W1 = Initial weight of the tablets

In – Vitro **Drug Release Studies**

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900ml of 0.1N HCl was placed in the vessel and the USP apparatus –II (Paddle Method) was used. The medium was allowed to equilibrate to a temp of 37±0.5°C. Tablet was placed in the vessel and the vessel was covered, the apparatus was operated for 12 hours at 50 rpm. A definite time intervals, 5 ml of the fluid was withdrawn, filtered and again 5ml of the fresh buffer was replaced. Suitable dilutions were done with the dissolution fluid and the samples were analyzed spectrophotometrically at 234 nm.

In-vitro **drug release kinetics**

Kinetic model had described drug dissolution from solid dosage forms in which the dissolved amount of drug is a function of test time.In order to study the exact mechanism of drug release from the tablets,drug release data was analysed according tozero order,first order ,higuchi square root,Korsmeyer – Peppas model.The criteriafor selecting the most appropriate model were chosen on the basis of goodness of fit test.The data were processed for regression analysis using MS EXCEL statistical function.

Stability studies of selected formulation

After comparing the *in-vitro* drug release, selected tablet were taken for stability studies. The study was conducted according to the international conference on harmonization (ICH) guidelines. Best floating tablet of Metformin H◦CL separately were packed in HDPE bottles and loaded at accelerated conditions like 40◦C±2◦Cand 75% ±5% RH for 3 month. The samples were withdrawn at intervals of 0,15,30,60 & 90 days and analyzed for their physical appearance and drug content.

RESULTS AND DISCUSSION

Preformulation Studies

Physicochemical Evaluation of Drug Molecule

Physical Description of APIs

Metformin HCL was a white, odorless, non-hygroscopic, crystalline powder.

Solubility

It is freely soluble in water and slightly soluble in 95% alcohol and is practically insoluble in acetone, ether and chloroform. It is freely soluble as HCl salt.

S. No.	Solvents	Observation
1	Water	Freely soluble
2	Ether	Insoluble
3	Acetone	Insoluble
4	0.1N Hcl	Insoluble

Determination of λ_{max} of Metformin HCL in 0.1N HCl

The λ_{max} of the Metformin HCL was found to be 234 nm in 0.1N HCl. The tablet designed to release in stomach environment. Hence the λ_{max} obtained in 0.1N HCl was used for the calculations.

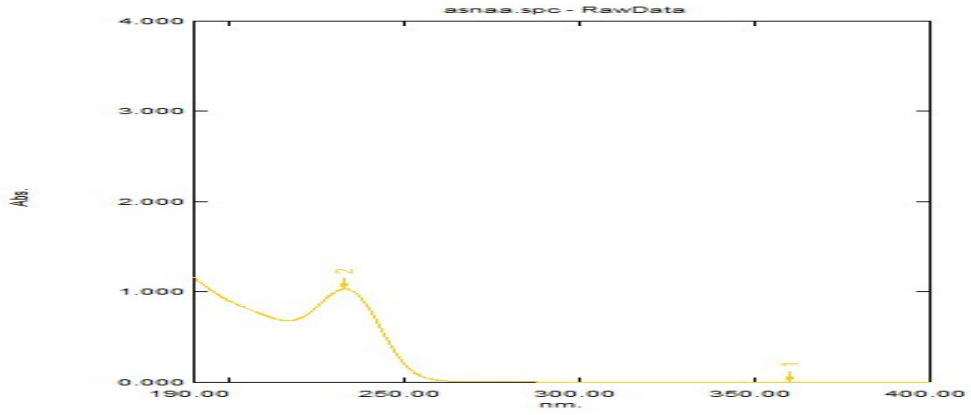


Fig: λmax of Metformin HCL in 0.1N HCl

Sl. No.	λ_{max} in 0.1N HCl
1.	234nm

Fig : λ_{max} of MetforminHCL in 0.1N HCl

Preparation of standard plot

a) Standard plot for Metformin HCL in 0.1N HCl

Table : Standard Plot for Metformin HCL in 0.1N HCl

S.NO	Concentration (µg/ml)	Absorbance(nm)
1	0	0
2	2	0.223
3	4	0.409
4	6	0.618
5	8	0.817
6	10	0.991

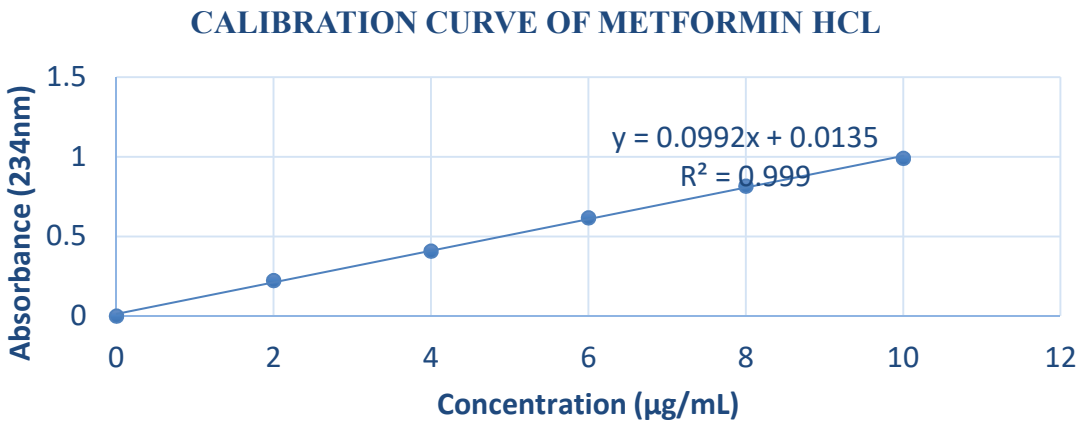


Fig : Calibration curve of MetforminHCL in 0.1N HCl

The calibration curve was plotted by taking concentration in X axis and the absorbance in the Y axis. The curve was increased in a linear manner and straight line was observed. The slope was found to be 0.038 and R^2 was 0.999

Compatibility Studies

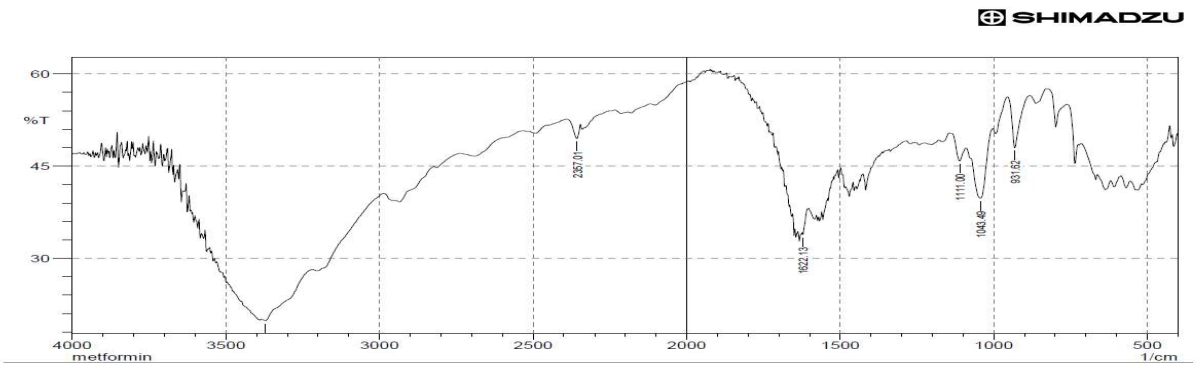


Fig : FTIR spectroscopy for Metformin HCL pure

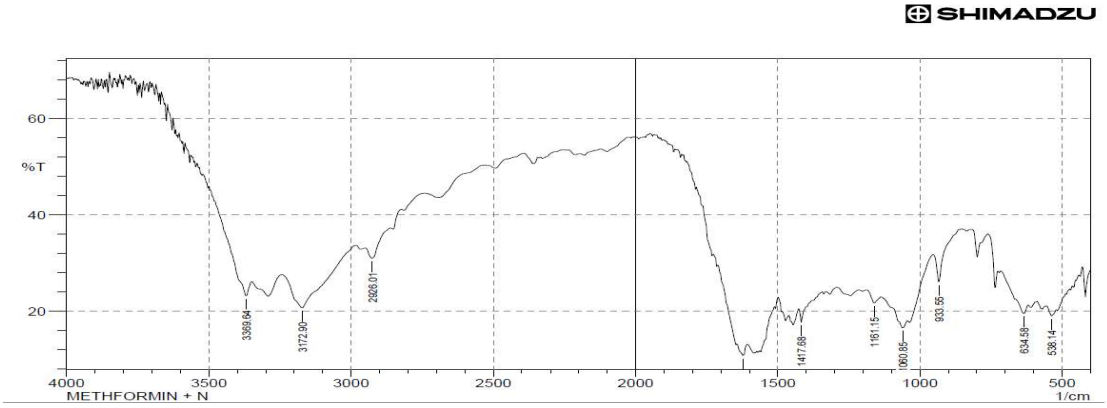


Fig : FTIR spectrum of pure drug of Metformin hydrochloride + Neem Gum

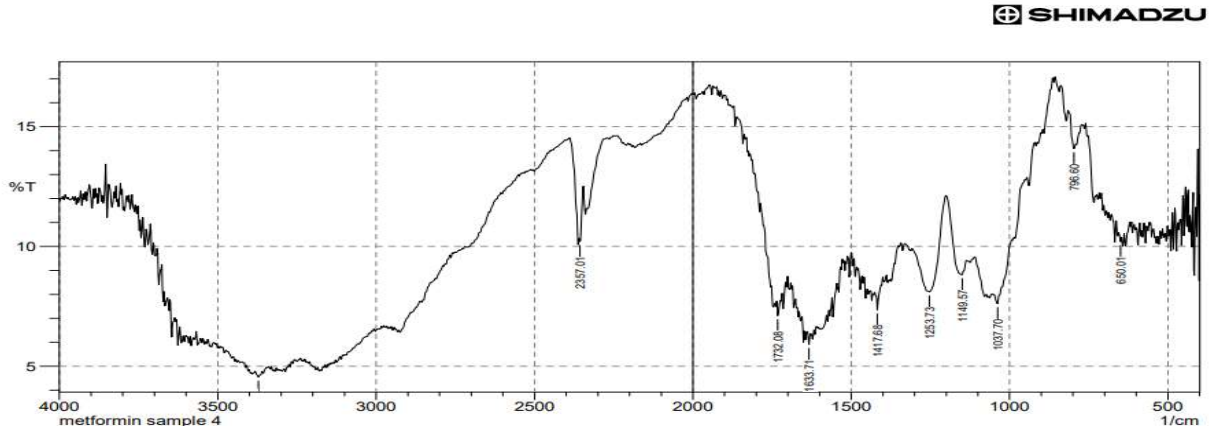


Figure : FTIR spectrum of pure drug of Metformin hydrochloride + Almond Gum

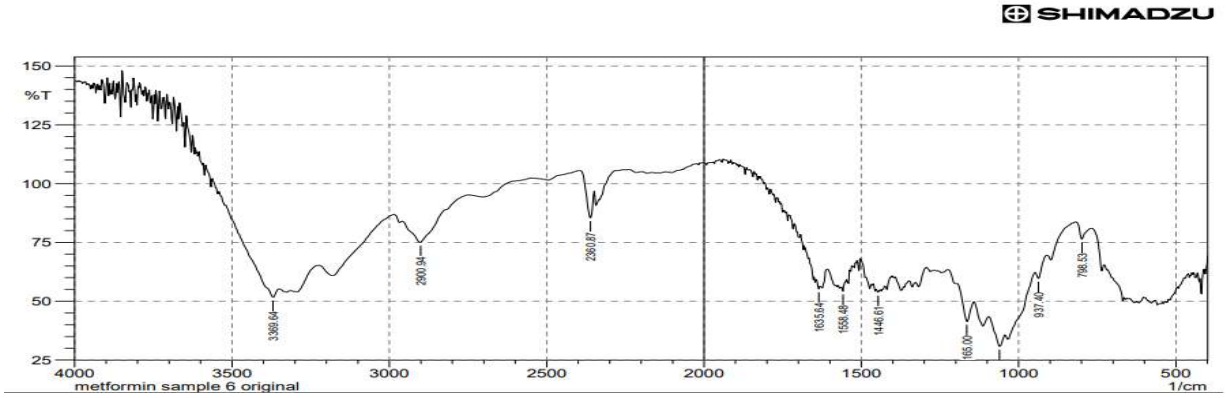


Figure: FTIR spectrum of pure drug of Metformin hydrochloride + Micro Crystalline Cellulose

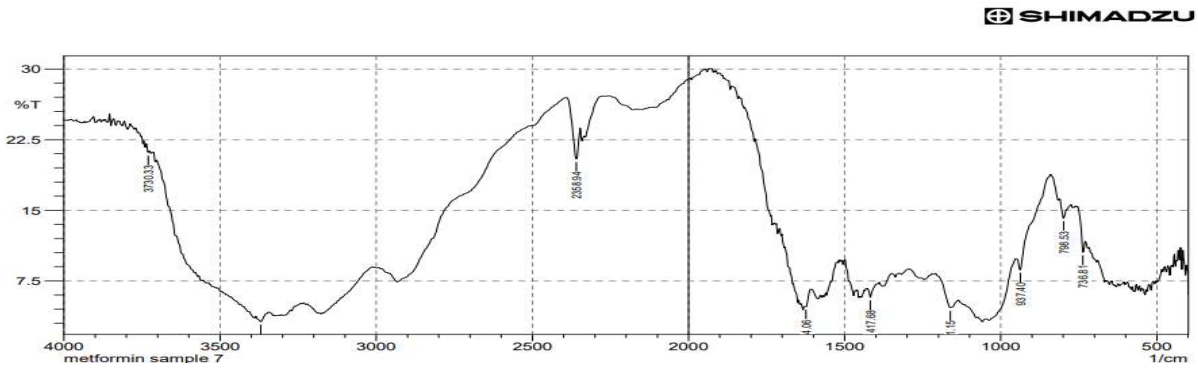


Figure : FTIR spectrum of pure drug of Metformin hydrochloride +Neem Gum+Alomod Gum+Micro Crystalline Cellulose

Table: Interpretation Table of Pure Drug of Metformin Hydrochloride +Neem Gum+Alomod Gum+Micro Crystalline Cellulose

SNo.	Interpretation	Standard value	Metformin HCL pure	MetforminHCL+Excipients
1	H Atom	780cm^{-1}	798cm^{-1}	796cm^{-1}
2	Sulphones	1160-1140cm^{-1}	1161cm^{-1}	1149cm^{-1}
3	C=N Stretching	1650-1550cm^{-1}	1624cm^{-1}	1622cm^{-1}

The results of the study indicate FTIR spectrum of Drug and excipients did not differ with major peaks of Metformin HCL.all the major peaks of the drug appeared on the blend indicate that there is no possible interaction between drug and Excipients.

Precompression parameters

Micromeritics properties

The properties like compressibility index, Angle of repose, Tapped density, Bulk density and Hausner ratio were calculated and all estimated parameters found within the limit

Physical properties of powders for batch

Batch	Angle of repose(Ɵ)	Bulk density (g/cm3)	Tapped density (g/cm3)	Carr's index (%)	Hausner's ratio
M1	25.224±0.32	0.61±0.02	0.72±0.02	10.33±0.28	1.12±0.02
M2	26.465±0.28	0.65±0.14	0.74±0.14	12.46±0.19	1.18±0.13
M3	25.308±0.34	0.64±0.18	0.71±0.08	14.76±0.22	1.16±0.24
M4	27.426±0.26	0.67±.0.12	0.78±.0.02	10.42±0.38	1.14±0.08
M5	25.228±0.22	0.66±0.14	0.82±0.04	12.84±0.72	1.13±0.10
M6	26.722±0.27	0.69±0.16	0.70±0.12	13.78±0.08	1.17±0.01

n = 3 observations ± SD

POST COMPRESSION PARAMETER

All formulations were tested for physical parameters like Hardness, Thickness, Weight variation, Friability and found to be within the pharmacopoeia limits. The results of the tests were tabulated. The drug content of all the formulations was determined and was found to be within the permissible limit. This study indicated that all the prepared formulations were good.

Batch	Tablet thickness (mm)	Weight variation (mg)	Hardness (kg/cm2)	Tablet friability (%)	Floating Lag Time (s)	Total floating duration (Hr)	Drug content
M1	4.13±0.15	650±2.25	5.6±0.16	0.76±0.16	42	>12	88.23
M2	4.54±0.10	655± 3.12	5.6±0.22	0.62±0.18	56	>12	92.84
M3	4.32±0.10	650±0.34	6.1±0.27	0.58±0.06	31	>12	90.52
M4	4.82±0.15	645±2.33	5.6±0.28	0.72±0.07	82	>12	86.72
M5	4.96±0.05	655±0.20	5.9±0.18	0.74±0.18	96	>12	98.48
M6	4.24±0.10	650±0.22	5.8±0.16	0.54±0.14	74	>12	94.22

n = 3 observations ± SD

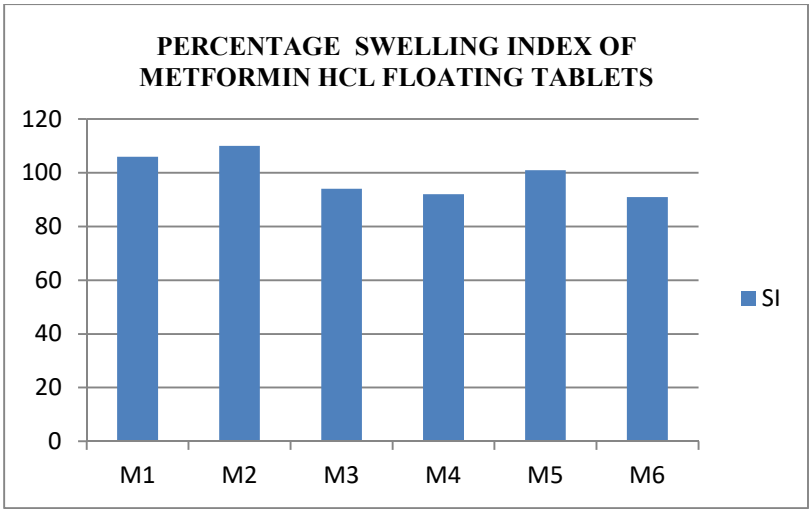
Digital photo image of Prepared Metformin HCL Floating Tablets

0 hrs	4 hrs	8 hrs	12 hrs
			

Swelling Index of tablet

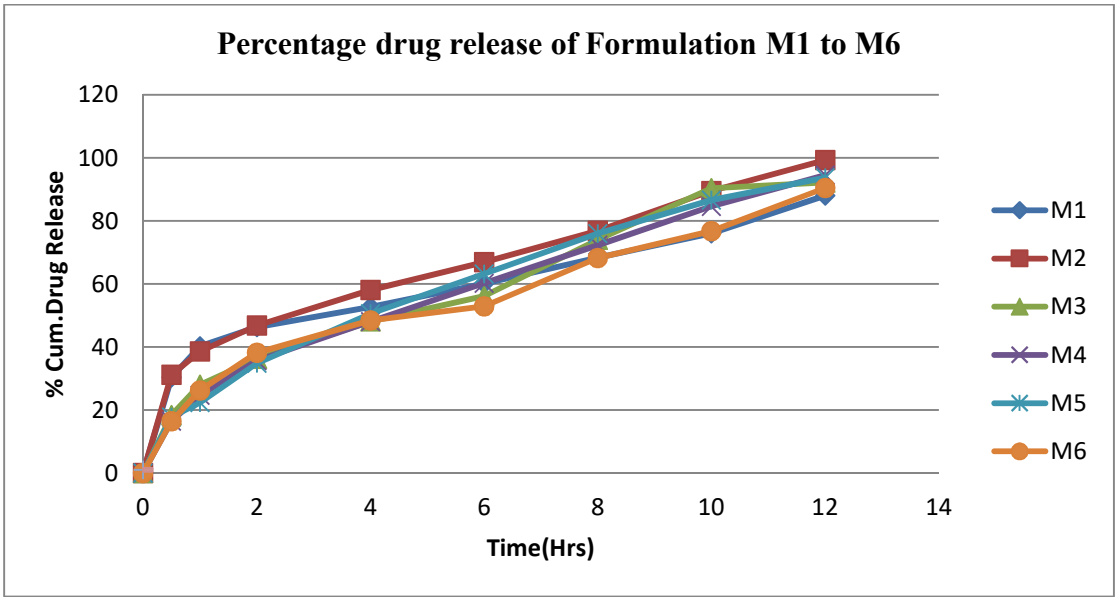
All the formulations of Metformin HCL floating tablets were evaluated for water uptake study. And it was concluded that as the viscosity of hydrophilic polymer concentration increase the water uptake increase which results in increasing of swelling index. At the same time concentration of Neem gum also having similar impact on the swelling property of the formulation.

Formulation Code	Swelling Index (%)
M1	106
M2	110
M3	94
M4	92
M5	101
M6	91



IN-VITRO DRUG RELEASE STUDY METFORMIN HCL FLOATING TABLETS

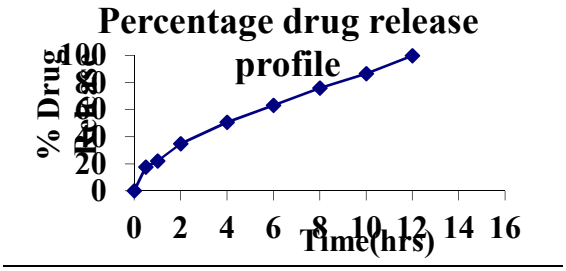
Time (hrs)	Formulation Code					
	M1	M2	M3	M4	M5	M6
0	0	0	0	0	0	0
0.5	30.38±1.6	31.17±2.2	18.35±1.4	16.45±2.4	17.78±1.8	16.44±1.3
1	40.26±1.8	38.62±1.8	28.05±1.2	24.72±1.6	22.36±1.5	26.26±2.2
2	46.32±1.4	46.86±1.7	36.28±2.6	35.66±2.3	34.86±1.7	38.21±2.5
4	52.68±1.7	58.08±1.8	48.16±2.4	48.01±2.5	50.62±1.2	48.46±2.2
6	60.12±1.6	66.92±1.5	56.18±2.1	60.22±2.1	63.12±1.8	52.92±2.1
8	68.36±1.9	76.82±1.6	74.06±1.9	72.32±1.6	75.93±2.1	68.24±2.1
10	76.10±1.5	89.44±1.2	90.34±1.6	84.56±1.8	86.62±3.8	76.72±3.6
12	88.02±1.7	99.28±1.7	92.16±2.4	94.52±2.4	93.74±1.4	90.43±1.8

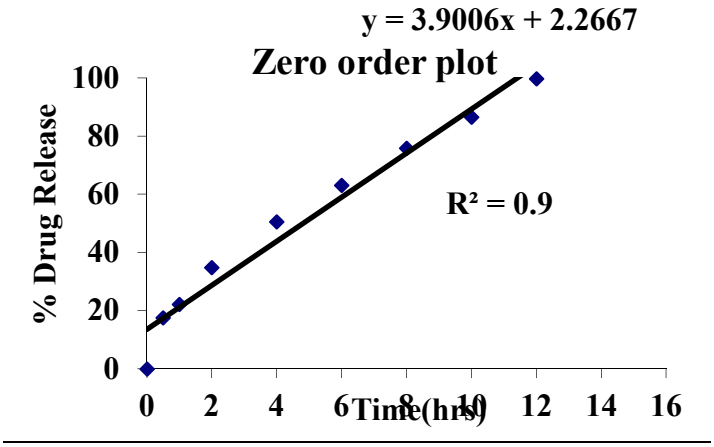


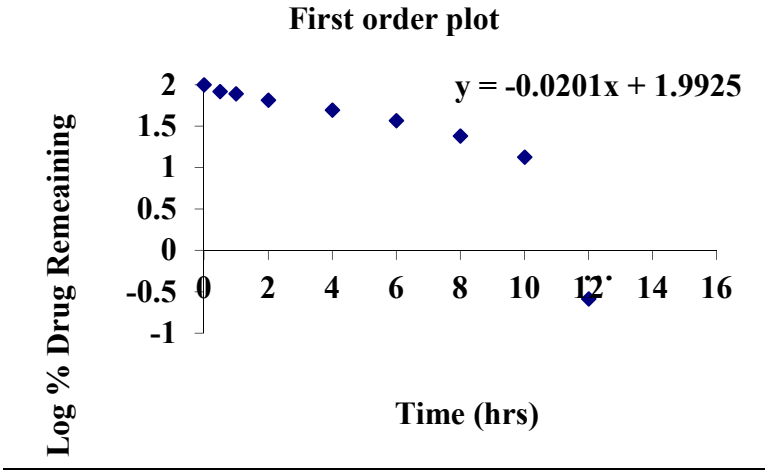
Result Analysis: M2 was found to be the best formulation which have 12 hrs of floating and 99.74 % drug release.

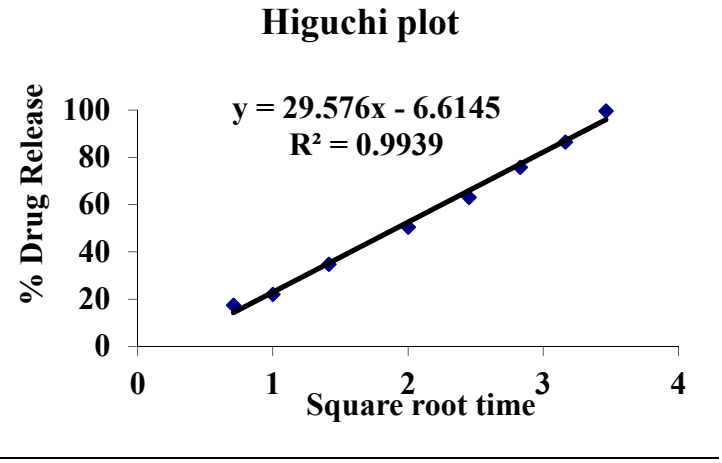
INVITRO RELEASE KINETICS STUDY METFORMIN HCL FLOATING TABLETS

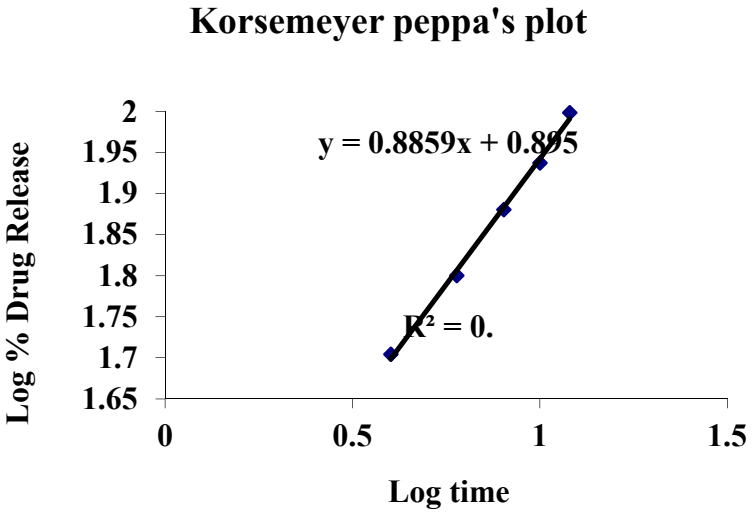
The cumulative amounts of metformin HCL released from the tablets at different intervals were fitted with various models,Zer order kinetic model,First order kinetic model,Higuchi model and Korsmeyar-peppas model .











Formulation code	Zero order		First order		Korsemeyer model		Higuchi's		Mechanism
	R^2	K	R^2	K	r^2	n	R^2	K	
A7	0.9	2.2	0.802	1.99	0.9	0.88	0.993	1.99	Anomalous transport- Non fickian equation

According to the data Kosmeyr-Peppas equation, the release exponent (n value) for all the formulation were ranged from(0.43 <n< 0.85) which indicated that the mechanism of drug release of formulationsA7 was anomalous transport(Non-Fickian) diffusion. This indicated that the release was dependent on both drug diffusion and polymer erosion.

Layout factorial design

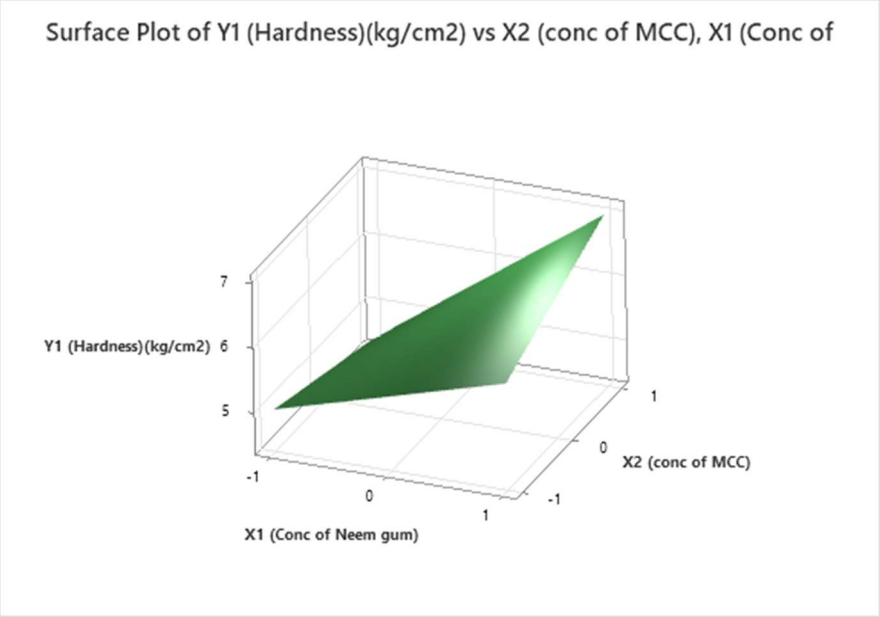
Independent variables of Optimization

Factors	Levels	
	-1	+1
X1(Neem Concentration)	55	65
X2(Con of Micro crystalline cellulose)	165	175

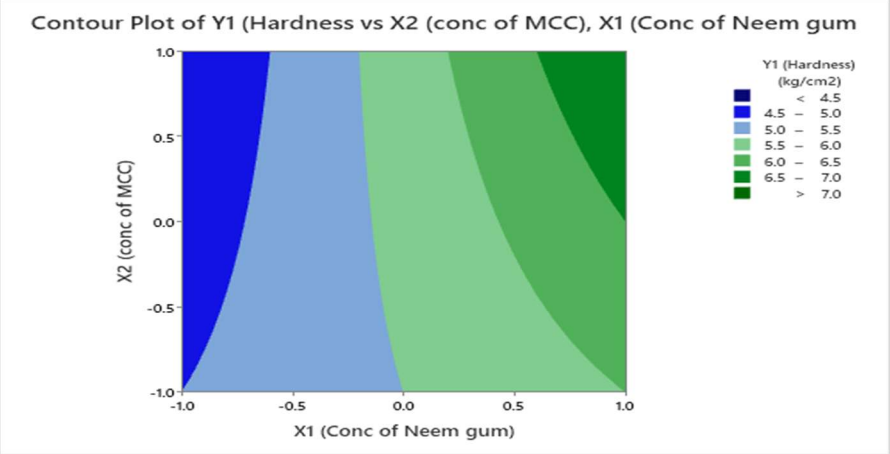
Dependence/Response variable optimization

Code	Dependent Variables
Y1	Friability
Y2	Hardness
Y3	*In-vitro* dissolution study

Surface Plot of Y1 (Hardness)(kg/cm2) vs X2 (conc of MCC), X1 (Conc of Neem gum)



Contour Plot of Y1 (Hardness vs X2 (conc of MCC), X1 (Conc of Neem gum)



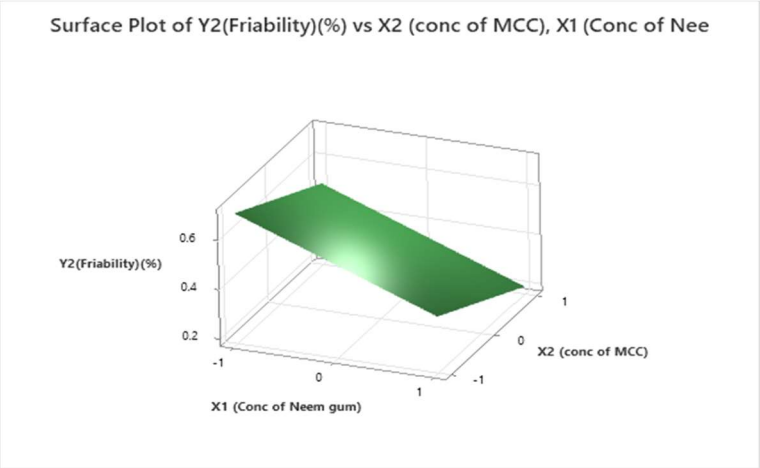
Effect of hardness

The values for hardness of the tablets Y1 ranges between 4 – 7 Kg/cm^2 and were significantly influenced (P = <0.05) by one study factor (X1).

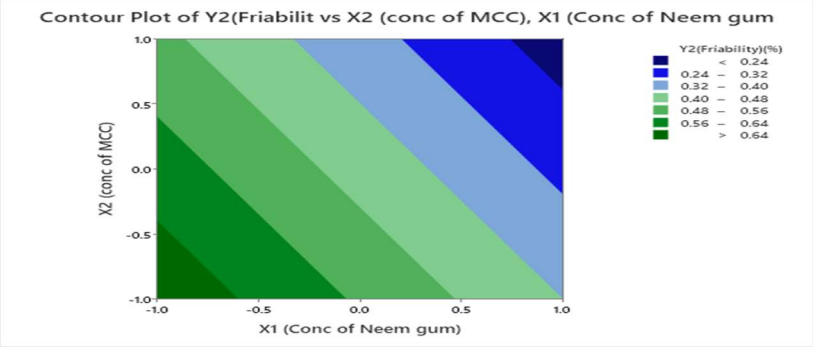
Hardness was found to an inverse function of X1 and X2. Hardness of the tablets slightly increased with increasing amount of Neem gum and MCC

Neem gum alone were more predominant than MCC on hardness of the tablet. It has indicated by the observed respective coefficient.

Surface Plot of Y2(Friability)(%) vs X2 (conc of MCC), X1 (Conc of Neem gum



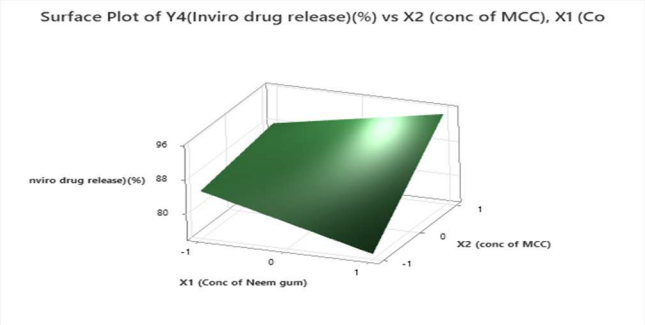
Contour Plot of Y2 (Friabilitvs X2 (conc of MCC), X1 (Conc of Neem gum)



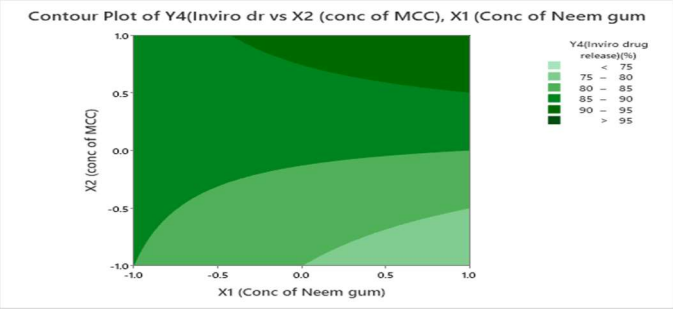
Effect of Friability

The value for friability of tablets Y2 ranges between 0.2-0.7% indicated all the formulation were successfully passed. Decreased value of friability. Combination of Neem gum and MCC favourable for the reduction of friability friability test. Optimum concentration of Neem gum significantly influences the friability values

Surface Plot of Y4(*In-vitro* drug release)(%) vs X2 (conc of MCC), X1 (Con Neem gum



Contour Plot of Y4*(In-vitrodrug release vs* X2 (conc of MCC), X1 (Conc of Neem gum



Effect of *In-vitro* Release Study

The values for drug release of the tablets Y1 ranges between 75-95% and were significantly influenced (P = <0.05) by (X1) and X2)

It was found to an inverse function of X1 and X2. *In-vitro* release of the tablets slightly increased with increasing amount of Neem gum and MCC .

Summary of Polynomial Equations for factorial fit

Regression Equation:A statistical model in co-operating interactive and polynomial terms was used to evaluate the responses.

$$Y= b0 +b\ 1X1 + b2\ X2 + b11\ X1X2 + b22\ X2X2 + b12\ X1X2$$

Y= Dependent variable

b0 = Arithmetic mean response of 4 runs

b_1,b_2, b12 = estimated coefficient factor

Where y is the dependent variables, b0 is the arithmetic mean response of the nine runs, and b1 is the estimated coefficient for the factors X1. The main effects (X1 and X2) represent the average result of changing one factor at a time from its low to high value.

On the basis of the preliminary trial a 2^2 full factorial design was employed to study the effects of independent variables on dependent variables. Response surface plots were generated using mini tab software.

STABILITY STUDIES

After comparing the *in-vitro* drug release, selected tablet were taken for stability studies. The study was conducted according to the international conference on harmonization (ICH) guidelines. Best floating tablet of Metformin HCL separately were packed in HDPE bottles and loaded at accelerated conditions like 40◦C±2◦Cand 75% ±5% RH for 3 month. The samples were withdrawn at intervals of 0,15,30,60 & 90 days and analyzed for their physical appearance and drug content.

Parameter	Initial	After 3 Month
Hardness(kg/cm^2)	5.92	5.34
Friability(%)	0.54	0.52
Floating Lag Time(Sec)	65	65
Total Floating Time(Minutes)	.>12	>12
In-vitro release study (%)	99.74	98.12

- 15 tablets were subjected to stability studies.
- The hardness and friability study of the tablets remained as same as that of the initial formulation. There was only a small difference in the *in-vitro dissolution* study.
- Stability study showed that there are no significant changes in the dissolution pattern.

SUMMARY

The investigations carried out in this present work so far have encouraged us to draw the conclusions: The λ max value of MetforminHCL obtained during this study matches with the literature value of 234 nm. The developed analytical method was found to be suitable for the quantitative estimation of drug in dissolution fluids and in tablets.

The FTIR studies indicated no interaction between MetforminHCL and excipients. The compressibility index was found to be less than 18 % indicating that the powder

bed is compressed into a compact tablet mass. The angle of repose (θ) for all the formulations after adding glidants was in the range of 25.224 to 27.426 indicating good flow property. Hardness of the floating tablets was in the range of 4.6 kg/cm2 to 5.8 kg/cm2 indicating tablets are of adequate strength.

The friability all the tablet formulations were found to less than 1% indicating prepared tablets have sufficient strength. Drug content was within ± 5% which ensures uniformity in drug content in all the tablet formulations. The buoyancy lag time & total floating time in the range of 46 sec to 84 sec. & 0.5 h to 12hrs.The total floating time increases as the proportion of polymer Neem Gum increases in the tablet formulation.

Among the various ratios of Neem gum and Almond gum, the formulation batch M2 floated for 12 hrs with a floating lag time of 46 sec and released 99% of the drug in 12h. Considered as best formulation.

The optimized formulations M2 stored for a period of 90 days shows no change in physical properties, drug content and *in-vitro* release pattern indicating developed formulation could provide a better shelf life. Thus, the study of pre-compression and compression characteristics, *in-vitro* release and stability studies concluded the objectives of the study.

CONCLUSION

Floating SR tablets of Anti-diabetic drug MetforminHCL can be formulated as an approach to increase gastric residence time there by improve its bioavailability and to overcome the limitations of conventional approaches of gastric retention. All the formulations gave better –Floating Sustained drug release. Systematic studies were conducted using different polymers in different concentrations prepare MetforminHCL floating tablets.

Tablet containing Neem Gum and sodium bi carbonate (M2) Showed satisfactory results with respect to floating lag time, total floating duration, swelling index and sustained drug release rates and M2 Formulation was found to have maximum release profile**.**

Higher R2 Values were obtained for Sustained release (Anomalous transport Non–fickan release) and found to be the best fit kinetic model. Formula M2 Showed better physical stability when stored at 40◦C under 75%RH for 3 months. From the studies, it was concluded that the gastro retentive floating tablets of MetforminHCL Batch M2 showed excellent buoyancy and sustained drug release more than 12 hrs and thus enhanced bio availability.

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