Available online on 15.11.2015 at http://jddtonline.info
Journal of Drug Delivery and Therapeutics
Open access to Pharmaceutical and Medical research

RESEARCH ARTICLE

FORMULATION AND EVALUATION OF EFFERVECENT FLOATING TABLETS OF ANTIDIABETIC DRUG

***Anshuman Keshari, Dr. Pushpendra Kumar Tripathi, Arjita Srivashtava, Ratan Vishwas**

Department of Pharmaceutics, Rameshwaram Institute of Technology& Management Lucknow (Uttarpradesh), India

Received 01 Sep 2015; Review Completed 29 Sep 2015; Accepted 07 Oct 2015, Available online 15 Nov 2015

ABSTRACT

The aim present investigation is Formulation and Evaluation of Effervescent Floating Tablets of antidiabetic drug. Gastric retention are such systems, which increase the gastric retention time of the dosage forms at the stomach and upper part of the small intestine and suitable for the drug having site-specific absorption from the above sites. The Metformin HCl an orally administered biguanide of BCS class-3 High solubility and low permeability, which is widely use in the management of and the type-II diabetes, is an oral anti- hyperglycemic agent, shows incomplete absorption from the gastrointestinal tract and from the gastrointestinal track and absolute bioavailability is 50-60%with relatively short plasma half-life of 1.5-4.5 hours. It was using different polymers studying of deferent factors affecting the floating behavior of the prepare tablets was of our goals and important target in this part. Gastro-retentive tablets of Metformin HCl were prepared by wet granulation method using HPMC K200M (Hydroxylpropyl methyl cellulose) micro crystalline cellulose PH 101, sodium bicarbonate, HPMC K100 (LV), Magnesium stearate, colloidal silicon dioxide. In this formulation HPMC K 200 M was using different concentration. The Gastro-retentive tablet of Metformin HCl was evaluation of compression blend Angle of repose, Bulk density, tapped density, Drug compressibility study, Drug release rate, floating lag time etc. Result of our present study suggests that gastro-retentive tablets of Metformin HCl can be successfully designed to develop sustained release drug delivery which can reduce dosing frequency

Keywords: Effervescent system, gas generating system, gastro retentive drug delivery system, sustained drug release, Metformin hydrochloride

INTRODUCTION:

The oral route is considered as the most promising route of drug delivery. Effective oral drug delivery may depend upon the factors such as gastric several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying leading to non-uniform absorption profiles, incomplete drug release and shorter residence time of the dosage form in the stomach. This leads to incomplete absorption of drug shaving absorption window especially in the upper part of the small intestine, as once the drug passes down the absorption site, the remaining quantity goes unabsorbed. The Gastric emptying of dosage forms in humans factors because of which wide inter and are affected by several intra-subject variations are observed[1]. Since many drugs are well absorbed in the upper part of the gastrointestinal tract, such high vari-ability may lead to non-uniform absorption and makes the bioavailability unpredictable. Hence a beneficial delivery system would be one which possesses the ability to control and prolong the gastric emptying time and can deliver drugs in higher concentrations to the absorption site (i.e. upper part of the small intestine). Metformin HCl is an orally administered biguanide derivative widely used in the treatment of non-insulin dependent diabetes mellitus. It improves the glycemic control by enhancing insulin sensitivity in liver and muscles. Metformin also has beneficial effect on several cardiovascular risk factors such as dyslipidemia, elevated plasma-plasminogen activator inhibitor, other fibrinolytic abnormalities, and hyper insulenimia, and insulin resisance[2.] Oral administration is the most convenient and preferred means of any drug delivery to the systematic circulation. Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the systemic circulation. Frequent dosing of these drugs is required to achieve suitable therapeutic activity. To avoid this limitation, the development of oral sustained-controlled release formulations is an attempt to release the drug slowly into the gastrointestinal tract (GIT) and maintain an effective drug concentration in the systemic circulation for a long time.

Address for correspondence:
Anshuman Keshari
Department of Pharmaceutics,
Rameshwaram Institute of Technology & Management
Lucknow (Uttarpradesh), India
E-mail: anashuman k59@gmail.com

After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the gastrointestinal tract (GIT)[3]. These drug delivery systems suffer from mainly two adversities: the short gastric retention time (GRT) and unpredictable short gastric emptying time (GET), which can result in incomplete drug release from the dosage form in the absorption zone (stomach or upper part of small intestine) leading to diminished efficacy of administered dose[4].

MATERIAL AND METHODS

Table 1: List of various chemical/regents used in project work

Sr.No	Ingredient	Source
1	Metformin HCl	Biocon limited
2	Microcrystalline cellulose (Avicel PH 101)	FMC Biopolymer
3	Methocel K 200 M(HPMC)	Colorcon
4	Cabopol 971 P	Colorcon
5	Povidone K-30	BASF
6	Methocel K 100 LV(HPMC)	Colorcon
7	Methocel K 100 M (HPMC)	Colorcon
8	Sodium bicarbonate	Merck
9	Synpro Magnesium stearate	Ferro Industries
10	Colloidal silicon dioxide (Aerosil 200 Pharma)	Evonik industries AG
11	Eudragit® RL/PO	Evonik
12	Eudragit® RL/PO	Evonik
13	Tri ethyl citrate	Vertellus
14	Talc	Signet
15	Isopropyl alcohol	Sri tirumala Chemical
16	Acetone	Avantor
17	Acetonitrile	Avantor
18	HCL	Sigma-Aldrich

Table 2: List of Equipment used for the study

Sr.No	Equipment's	Manufacturer	Model No
1	Weighing balance	Sartorius	GPA5202
2	Mechanical stirrer	Remi Motors	5MHL PLU
3	V-cone blender	Chamunda	CPM VB-50
4	Mini Tablet Compression machine	Kambert	KMP-D8-08
5	Portable Hardness tester	Electrolab	EH-01
6	Automated Tablet Friabilator	Electrolab	EF-2W
7	Vernier Caliper	Mitutoyo	CD-8"CSX
8	Moisture analyser	Sartorius	MA150
9	Tap density tester	Electrolab	ETD-1020
10	Electromagnetic sieve shaker	Electoral	ENS-8 PLUS
11	Rapid Mixer granulator	Kevin	HSMG-10
12	Dissolution test apparatus	Electrolab	EDT-08LX
13	Differential scanning calorimetry	Tzero® DSC	Q2000 (TA Instruments,
14	Quadra-Co-Mill	Gansons Quadr	U-5
15	High performance liquid Chromatography (HPLC)	Waters and Agilent	Alliance and 1260
16	FTIR Spectrophotometer	Perkin Elmer	-------
17	Nuclear Magnetic Resonance	Bruker	AV300
18	Powder X-ray diffraction	Rigaku Ultima	--------
19	Oven	Thermolab	T00001000S
20	Stability Chamber	Newtronic	DCM-30

Procedure of pre-optimization study

Preparation of tablets by wet granulation technique

Floating matrix tablets containing of Metformin HCl were prepared using wet granulation method using HPMC K 100 M, K 200 M and carbopol 971 P as polymer. All ingredients and d drug weight individually passed through sieve no 30, mixed and granulated with 10% solution of PVP K 30 in water. The wet mass was passed through the sieve no 16 and dried rapid dryer at 30°C for 25min at 30cfm to control a final LOD of about NMT 2.0% w/w. Dried granules were passed through the sieves no 40G using Ganson's Co-Mill and were mixed with weight quantity of sodium bicarbonate, lubricated with magnesium stearate and glidant colloidal silicon dioxide.

Compression force was kept constant throughout the study. Compression was carried out for final blend by using CADMAC 16 x 9.5 mm oval shaped with logo deposed on upper punch (D tooling).

Table 3: Parameters in the RMG-(HSMG)

Sr.no	Parameters	Time (Min)	Impeller (rpm)	Chopper (rpm)
1	Dry Mix	10	500	NR
2	Binder Addition	1	500	NR
3	Kneading	1	500	1000

Table 4: Composition of floating tablets of Metformin HCl

Sr.No	Ingredients	Formula (mg/tab)				
1	**Metformin HCl**	**F_1**	**F_2***	**F_3**	**F_4**	**F_5**
		500	500	500	500	500
2	HPMC K 100 M	100	100	100	---	---
3	HPMC K 200 CR	---	---	---	130	180
4	Corbopol 941 P	32	32	22	---	---
5	Micro crystalline cellulose pH 101	37	24	34	46	44
	Binder					
6	PVP-30K	10	10	10	10	---
7	HPMC K 100 LV	---	---	---	---	10
Extra granular Ingredients						
8	Sodium bi carbonate	7	20	50	50	50
9	Colloidal silicon dioxide	7	7	7	7	8
10	Magnesium Stearate NF	7	7	7	7	8
Tablet Weight:		**700**	**700**	**730**	**750**	**800**

*** Coating formulation no F2 (10%)**

Table 5: Coating composition (10%) formulation no F2

S.NO.	INGREDIENT	WEIGHT (gm)
1	Eudragit RL/PO	11.84
2	Eudragit RS/PO	30.33
3	TEC	4.04
4	Talc	20.22
5	IPA	201.64
6	Acetone	146.65
7	Water	18.33

Coating procedure:

All ingredients were accurately weighted, Mixed manually desired quantity of Acetone and water, further added weighed quantity of TEC, stirrer for about 45 minutes by using mechanical stirrer and mixed weighed quantity of Talc in to above prepared solution stir for about 20 minutes by using mechanical stirrer **(Coating solution-1).** Mixed weighed quantity of Eudragit RL/PO and Eudragit RS/PO in to Isopropyl alcohol, stir for about 30 minutes by using mechanical stirrer **(Coating solution-2).** Mixed slowly coating solution-1 to coating solution-2 to prepare final coating solution and coating of formulation (F2) was done by using fully automatic pan coater ACG Coating QUEST-TC.

 ISSN: 2250-1177 CODEN (USA): JDDTAO

Procedure of Optimization Studies

Doe optimization by 3^2 central composite designs:

The project leads to a method for preparing an extended release tablet formulation of 500mg Metformin HCl. A unique blend of matrix system was used as a base for retarded release of drug. Two different grades of hydroxypropylmethyl cellulose (HPMC **K100 LV** and HPMC **K 200 M)** were mixed in different ratio to obtain a suitable matrix system for achieving the extended release profile of the said Metformin HCl. There are two independent variables and three responses in the formulation designing process. A 3^2 central composite design was employed for the purpose. Table 6: depicts the detailed composition of formulations prepared as per the optimization design.

Table 6: Independent Variables and Different Levels Selected for 3^2 Central Composite Design

Std	RUN	Factor 1 A: HPMC K 100 LV (mg)	Factor 2 B: HPMC K 200 LV (mg)	Response 1 Q1 %	Response 2 Q4 %	Response 3 Q10 %
12	1	12.50	150.00	32	69	100
9	2	12.50	150.00	32	69	100
6	3	20.00	150.00	31	64	100
1	4	5.00	80.00	34	68	92
2	5	20.00	80.00	33	66	93
5	6	5.00	150.00	31	64	92
8	7	12.50	220.00	28	62	89
13	8	12.50	150.00	28	69	100
11	9	12.50	150.00	28	69	100
10	10	12.50	150.00	28	69	100
4	11	20.00	220.00	27	50	90
7	12	12.50	80.00	31	67	100
3	13	5.00	220.00	31	66	98

Table 7: Composition of floating tablets of Metformin HCl

Sr.No	Ingredient	Formulation Code (mg/tab)								
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
1	Metformin HCl	500	500	500	500	500	500	500	500	500
2	HPMC K 200 M	80	150	220	80	150	220	80	150	220
3	MCC PH 100	169	99	29	161.5	91.5	21.5	154	84	14
	Binder									
4	HPMC K 100 LV	5	5	5	12.5	12.5	12.5	20	20	20
	Extra granular ingredients									
5	Sodium bicarbonate	50	50	50	50	50	50	50	50	50
6	Colloidal silicon dioxide	8	8	8	8	8	8	8	8	8
7	Magnesium sterate NF	8	8	8	8	8	8	8	8	8
	Table Wight:	820	820	820	820	820	820	820	820	820

Pre-Compression Evaluation

Evaluation of Powder Blends

1. Bulk density:

2. Tapped Density:

Tapped density was calculated from the formula below.

$$\text{Tapped density (g/ml)} = \frac{\text{Weight of the blend}}{\text{Tapped volume of the blend}}$$

3. Measures of Powder Compressibility:

For poorer flowing materials, there are frequently greater inter-particle interactions, and a greater difference between the bulk and tapped densities were observed. These differences are reflected in the compressibility index and Hausner's ratio.

Bulk density was calculated from the formula given below.

$$\text{Bulk density (g /ml)} = \frac{\text{Weight of the blend}}{\text{Bulk volume of the blend}}$$

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

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

Post-Compression Evaluation

1. Weight variation test: [5]

The USP weight variation test is run by weighing 20 tablets individually, calculating the average weight & comparing the individuals tablet weight to the average.

2. Thickness and Diameter:[6]

The thickness and diameter of the tablets were determined using a thickness gauge Vernier calipers model CD-8" CSX (Mitutoyo, New Delhi, India). Five tablets from each batch were used, and average values were calculated.

3. Hardness:[7]

Three tablets of each of the formulations were measured in the hardness test. The hardness was examined using a Hardness tester model EH-01 (Electrolab). The hardness was measured in kg/cm^2.

4. Friability: [8]

Then percentage friability was then calculated.

$$\%\mathbf{F} = \frac{(\mathbf{W1} - \mathbf{W2})}{\mathbf{W1}} \times 100$$

%F= Percentage friability

W_1= Initial weight of tablets

W2= Final weight of tablets.

5. Floating lag time and duration of floating:[9]

Floating characteristics of the prepared formulations were determined using USP XXII paddle apparatus under sink conditions. 900ml of hydrochloric acid buffer pH 1.2 was used as medium and the temperature was maintained to 37±0.5ºC thought the study. The time between the introduction of tablet and its buoyancy on the gastric fluid required for the tablet to float on the gastric fluid (**floating lag time**) and the time during which dosages for measurement buoyant (**duration of floating**) were measured. The integrity of the test tablets was observed visually during study.

6. Effect of Hardness on Buoyancy Lag Time[10]

Formulation F1 to F5 was selected to study the effect of hardness on buoyancy lag time. The tablets of batch 6 were compressed at different compression pressures to get the hardness of 5kg/cm2, 6kg/cm2, 7kg/cm2, 8kg/cm2 and 9kg/cm2. The tablets were evaluated for buoyancy lag time. The method was same as mentioned in determination of lag time.

7. In-vitro swelling study[11]

Tablets were weighed individually and placed separately in basket of dissolution medium containing hydrochloric acid buffer (pH 1.2) solutions 900 ml at 37±0.5°C. At 12 hours, the tablets were withdrawn from the basket and blotted with tissue paper to removed excess surface water and the swollen tablets were reweighed on analytical balance. Swelling index (SI) of tablets was calculated using the following formula:

$$\%\ \text{Swelling Index} = \frac{\text{Wet weight} - \text{Dry weight}}{\text{Wet weight}} \times 100$$

***In – Vitro* Drug Release Studies**

In-vitro dissolution studies were carried out in USP type-I (Basket) tablet dissolution apparatus using 900ml hydrochloric acid buffer pH 1.2 as dissolution media. The basket was rotated at 100 rpm and the temperature was maintained at 37±0.5°C throughout the study. Atprede termined time intervals 10 mL of the samples were withdrawn by means of an auto sampler machine with a pre filter. The volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium maintained at 37±0.5°C. The samples were analyzed for drug releases by measuring the absorbance at 255 nm using HPLC method.

RESULTS AND DISCUSSION:

Particle Size Analysis of Metformin HCl:

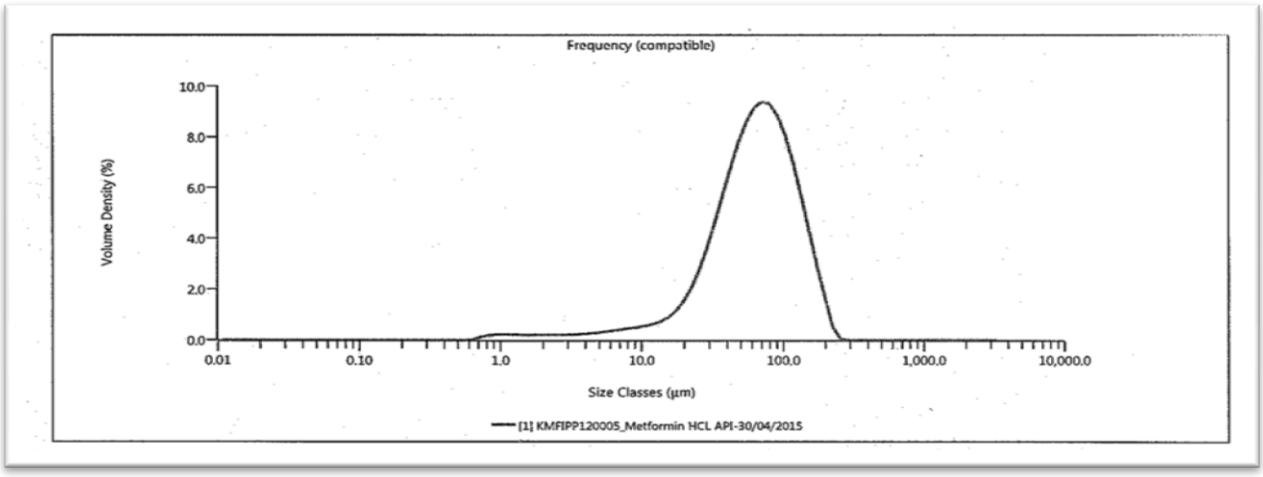


Figure 1: Particle size distribution

The flow properties of powders are dependent upon the particle size distribution as well as particle shape. Asymmetric particles have poor flow characteristics and hence granulation techniques are used to convert blends of drug and other additives into particles of uniform size having good flow properties.

 ISSN: 2250-1177 CODEN (USA): JDDTAO

PREPARATION OF STANDARD CURVE OF Metformin HCl

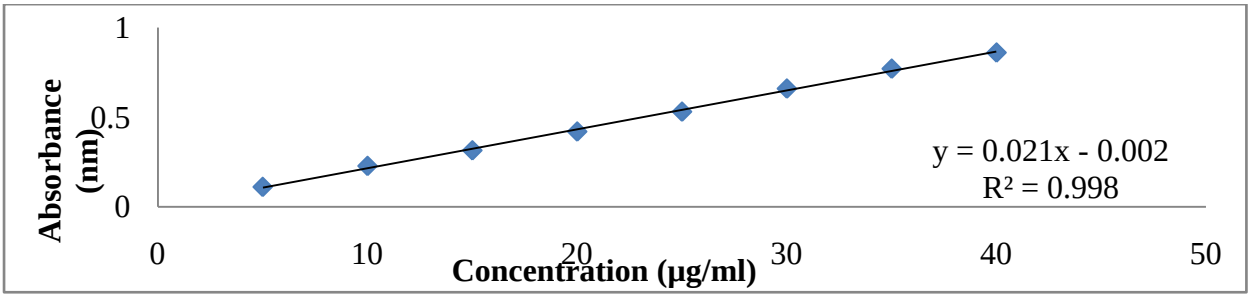


Figure 2: Preparation of Standard Curve of Metformin HCl

Linearity plot of Metformin HCl in the concentration range of 5-40 µg/ml were evaluated. Linear absorbance versus concentration gives regression equation; Y=0.0217x-0.002, with a correlation coefficient (r^2) of more than 0.99 in 0.1N HCl.

Fourier transform infrared spectroscopy:

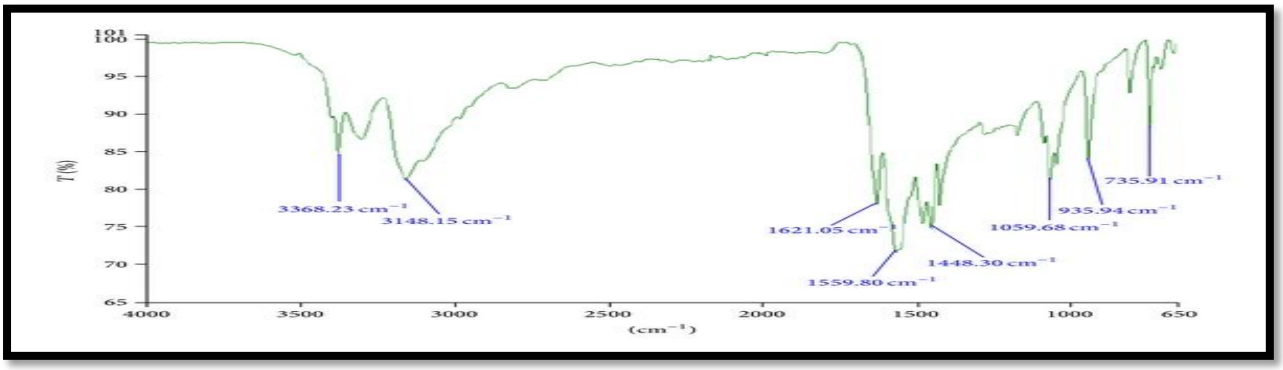


Figure 3: FT-IR spectrum standard of Metformin HCl

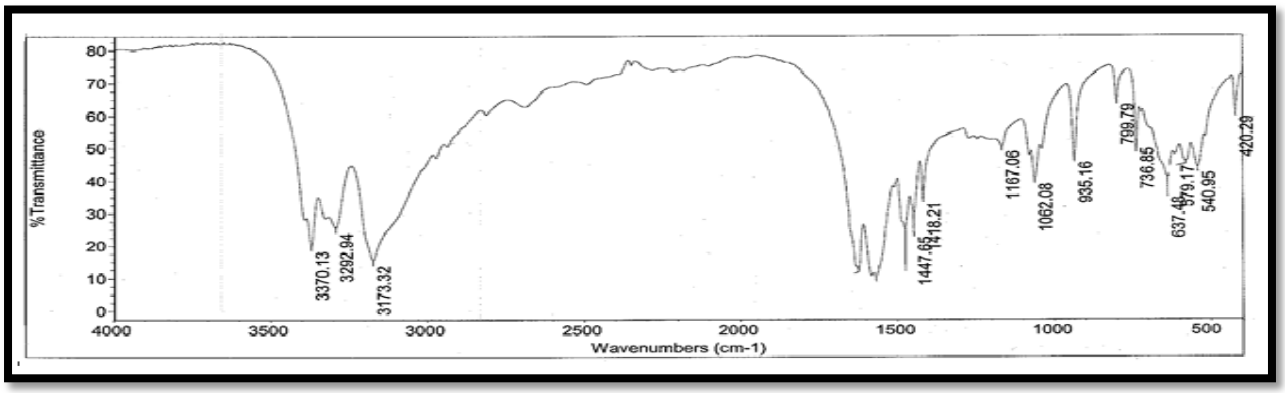


Figure 4: FT-IR spectrum of Metformin HCl

Nuclear magnetic resonance spectroscopy:

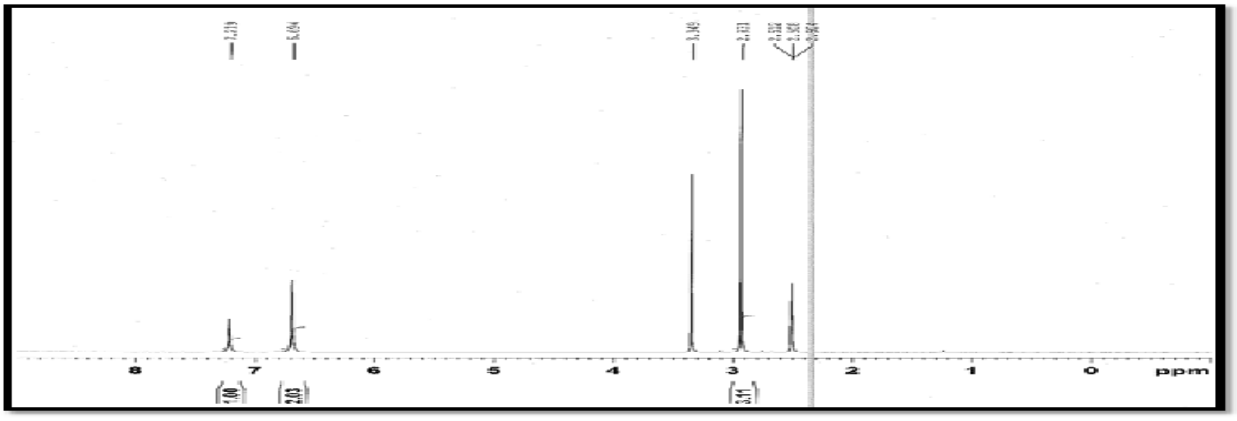


Figure 5: Nuclear magnetic resonance spectroscopy Ref. STD Metformin HCl

 ISSN: 2250-1177 CODEN (USA): JDDTAO

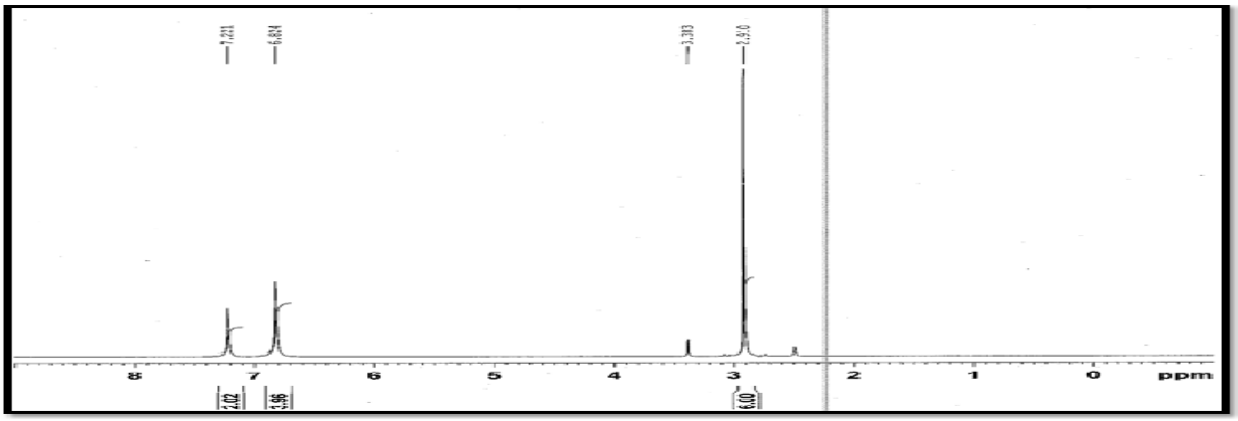


Figure 6: Nuclear magnetic resonance spectroscopy Ref. STD Metformin HClMASS

Mass Spectroscopy of Metformin HCl

Because of their low stabilities in the ion trap detector, these product ions (m/z=60.4 for Metformin HCl) are unsuitable for Quantitation of Metformin HCl. Therefore, the isolated precursorions (m/z=130.2 for Metformin HCl are selected for quantitative analysis without any fragmentation.

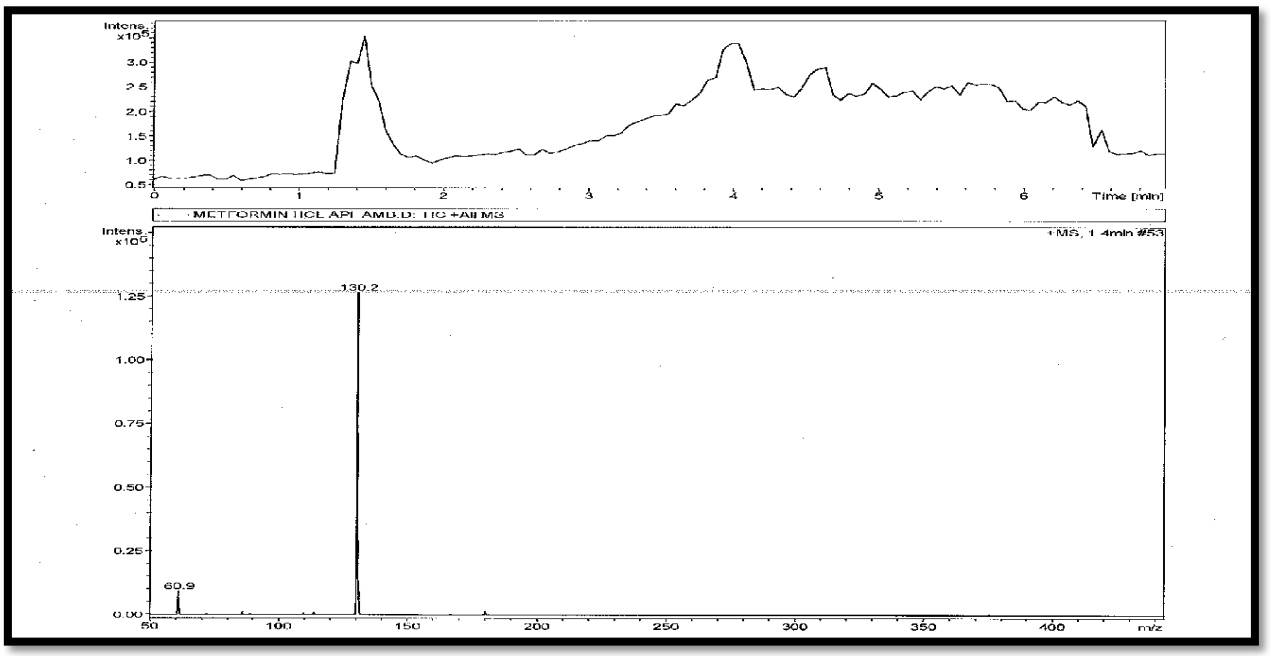


Figure 7: Mass Spectroscopy of Metformin HCl

POWDER X-RAY DIFFRACTOMETRY

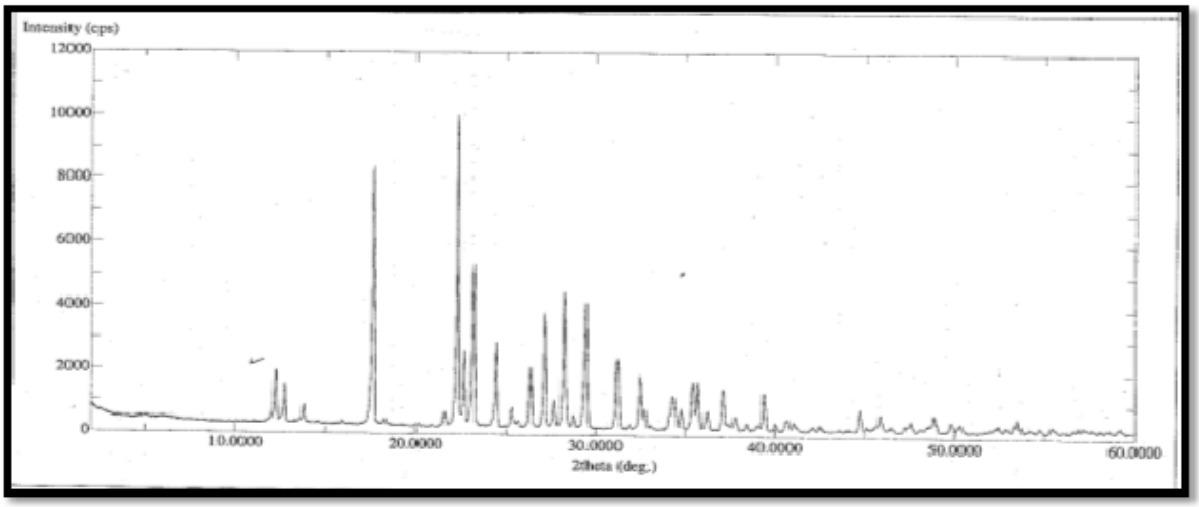


Figure 8: X- ray Diffraction graph of Ref. Std Metformin HCl

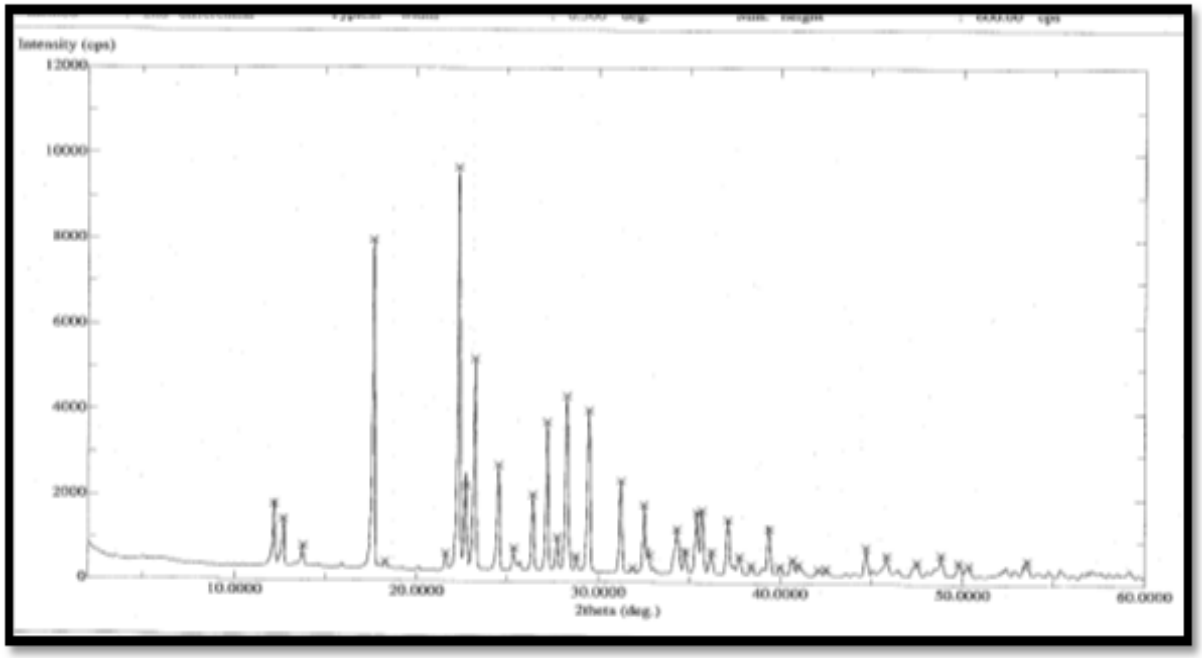


Figure 9: X- ray Diffraction graph of Metformin HCl

X-ray diffraction study of pure drug was carried out and its high intensity diffraction peaks at 2θshowed sharp peaks as similar to standard Metformin HCl , both

Pre-Optimization Studies

Evaluation of the Metformin HCl: Physical evaluation of the Drug

The API of were tested by various studies including bulk density 0.45gm/ml), tapped density 0.56 gm/ml, Hausner's ratio 1.24 and Carr's index 19.64 %). All the results showed very-very poor flow property.

PXRD pattern showing crystalline nature as showed in figure (8,9).

Table 8: Metformin HCl Characterization

Sr.No	Characteristics	Results
1	Physical Appearance	Off-White Powder
2	Bulk Density	0.45 gm/ml
3	Tap Density	0.74gm/ml
4	Carr's Compressibility Index	38.64
5	Hausner's Ratio	1.24
6	Melting Point	222 to226°C

Pre-Compression Evaluation

Table 9: Pre-compression parameters for formulations F1-F5

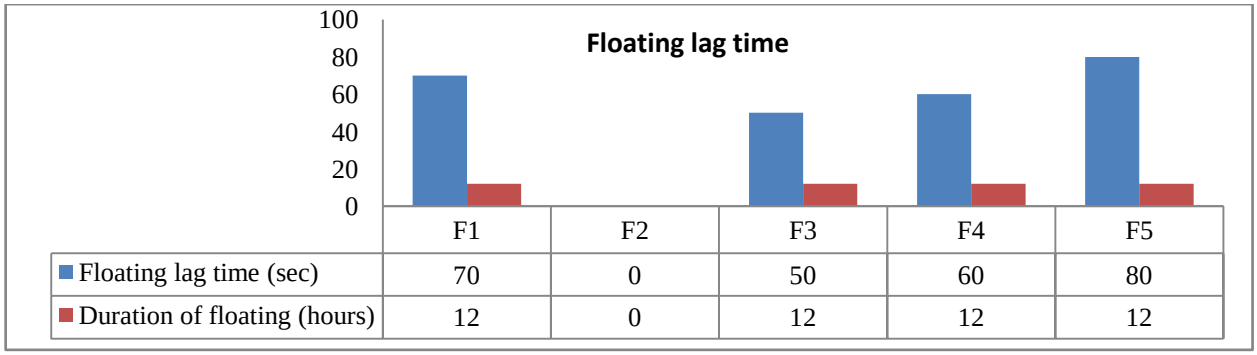
Sr.No	Batch No	Bulk Density (g/ml)	Tapped Density (g/ml)	Carr's Index	Hausner's Ratio
1	F1	0.519	0.65	20	1.25
2	F2	0.64	0.74	13.51	1.1
3	F3	0.59	0.71	16.90	1.22
4	F4	0.25	0.64	19.93	1.24
5	F5	0.56	0.66	15.06	1.17

Post-Compression Evaluation

Table 10: Post compression parameters for formulations F1-F5

Sr.no	Formulation code	F1	F2	F3	F4	F5
1	Thickness (mm)	6.45	6.42	6.82	5.12	5.75
2	Hardness (Kg/cm^2)	13.5	15.5	14.6	13.9	13.5
3	Friability (%)	0.742	0.234	0.342	0.782	0.740
4	Weight Variation (mg)	0.12	0.34	0.56	0.54	0.67

Floating Lag Time and Duration Of Floating



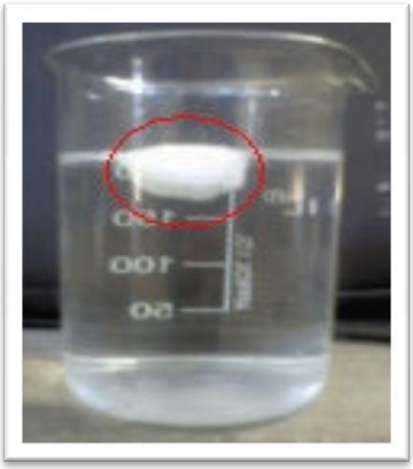
	F1	F2	F3	F4	F5
Floating lag time (sec)	70	0	50	60	80
Duration of floating (hours)	12	0	12	12	12

Figure 10: Floating lag time of various formulations

(a) At Initial Time

(b) After 50 Seconds

(c) After 70 Seconds



(d) After 12 hours

Figure 11: (a, b, c, d): Determination of Floating Time and Floating Lag Time

Studies to determine the Floating lag time and duration of floating of various formulations were carried out and the result indicated that floating lag time for all the tablets was within 0-4 minute after immersion into gastric media and duration of floating was greater than 12 hours for all batches. The effect of hardness on buoyancy lag time was studied and results indicated that with increasing the hardness, lag time also increased.

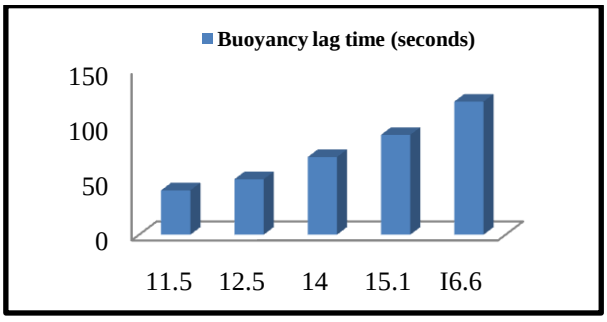


Figure 12: Effects of hardness on buoyancy lag time

IN VITRO DISSOLUTION TEST

The dissolution profile of all batches (F1 to F5) Prepared by High Shear Mixer Granulator and Marketed formulation in hydrochloric acid (1.2 pH) and results are reported in following tables:

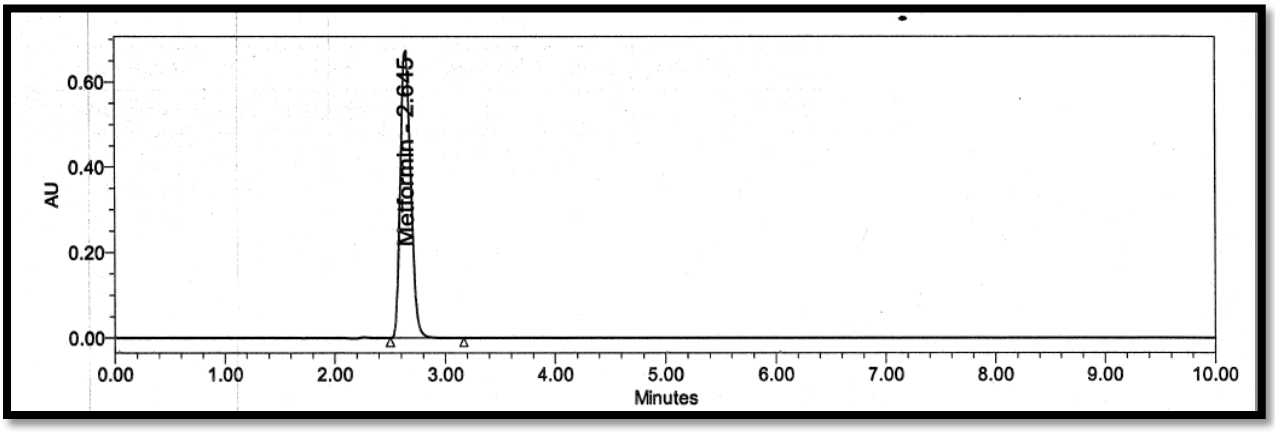


Figure 13: Specimen Chromatogram of Metformin HCl Standard

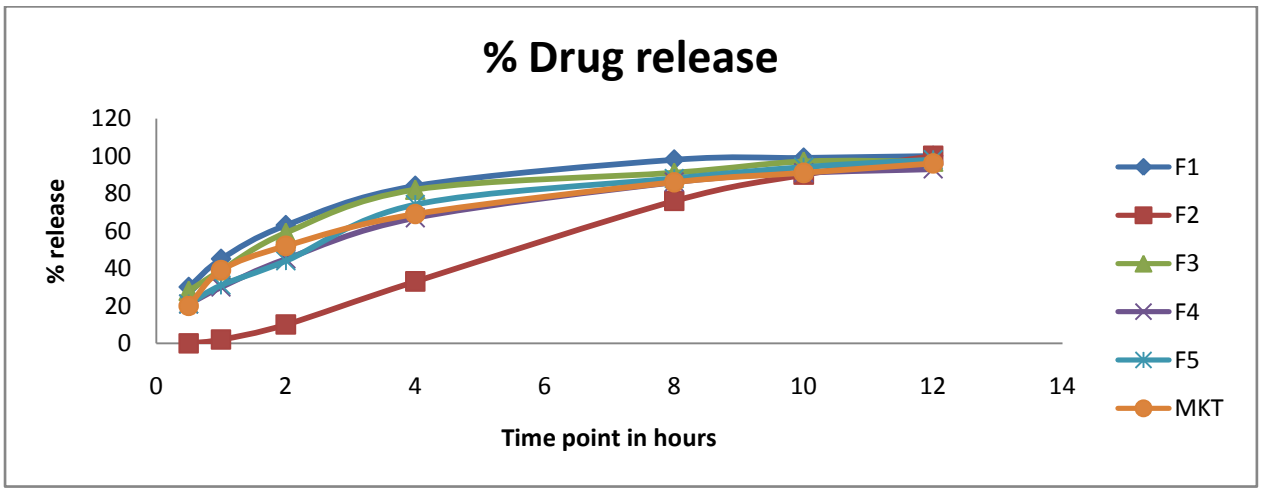


Figure 14: *In-vitro* drug release profiles graph

Prototype gastroretentive formulation Prepared by High Shear Mixer Granulator and Marketed extended release formulation in hydrochloric acid (1.2 pH) compared and it was realized that formulation F5 shown similar release profile as compared to others. Coated F2 formulation profile was much slower at initial time point therefore coating technique was discouraged further optimization.

DOE OPTIMIZATION BY 3^2 CENTRAL COMPOSITE DESIGN

PRE-COMPRESSION EVALUATION

Table 11: Pre-compression parameters for formulations F1-F9

Sr.No	Batch No	Bulk Density (g/ml)	Tapped Density (g/ml)	Carr's Index	Hausner's Ratio
1	F1	0.473	0.602	21	1.27
2	F2	0.551	0.674	18.24	1.22
3	F3	0.483	0.59	18.13	1.22
4	F4	0.491	0.619	20.67	1.26
5	F5	0.49	0.61	19.67	1.24
6	F6	0.514	0.593	13.32	1.15
7	F7	0532	0.633	15.48	1.18
8	F8	0.56	0.627	10.68	1.11
9	F9	0.457	0.549	16.45	1.20

 ISSN: 2250-1177 CODEN (USA): JDDTAO

Floating Lag Time and Duration Of Floating

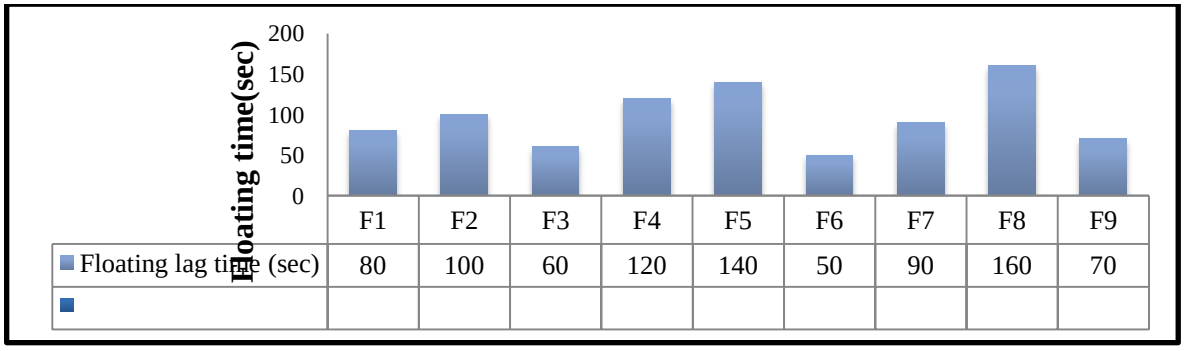


Figure 15: Determination of Floating Time and Floating Lag Time

Studies to determine the Floating lag time and duration of floating of various formulations were carried out and the results indicated that floating lag time which was observed for all the tablets was within 0-4 minute after immersion into gastric media and duration of floating was greater than 12 hours for all batches.

***In Vitro* Dissolution Test:** The dissolution profile of all batches (F1 to F9) Prepared for DOE optimization and Marketed formulation **in hydrochloric acid (1.2 pH) and results are reported in f**ollowing tables.

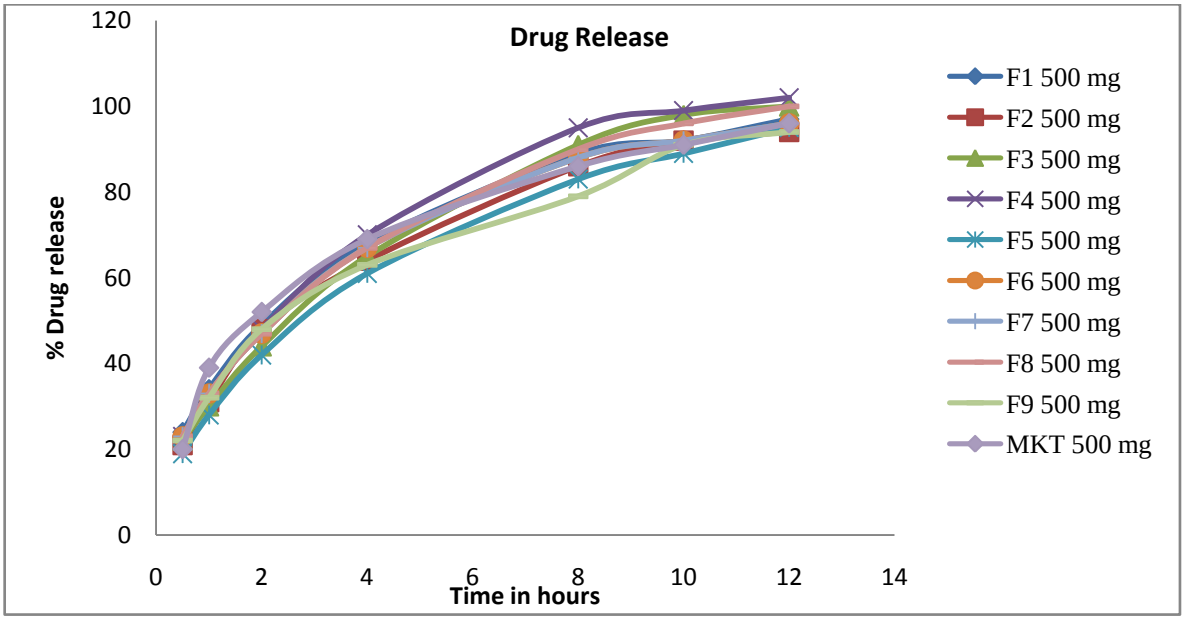


Figure 16: *In-vitro* drug release profiles of various formulations (F1 to F9 and MKT formulation)

Dissolution profile of DOE optimized gastroretentive formulation (F1-F9) and Marketed extended release formulation in hydrochloric acid (1.2 pH) compared and it was realized that all formulation (F1-F9) shown similar release profile as compared with Marketed extended release formulation, hence out of all formulation composition any of formulation can be chosen for further commercial scalability and production. From DOE optimization it also proves robustness range of process.

Assay (BY HPLC) OF Metformin HCl Tablets

Table 12: Assay (By HPLC) of Metformin HCl Tablets

Sr.no	Formulation	Area	% Assay
1	F1	2045019	99.10
2	F2	1966006	95.27
3	F3	1970934	95.51
4	F4	1982262	96.06
5	F5	2063604	100.00
6	F6	1862677	90.26
7	F7	1918276	92.96
8	F8	1953795	94.64
9	F9	2072338	100.42

 ISSN: 2250-1177 CODEN (USA): JDDTAO

Average standard – 2063511.6

Assay result of all formulation were observed in between (90 to 110%) of range.

SELECTION OF THE OPTIMIZED FORMULATION

The optimized formulation was selected by trading off the various responses. Fig.17

Depicts the overlay plot showing the location of the optimized formulation.

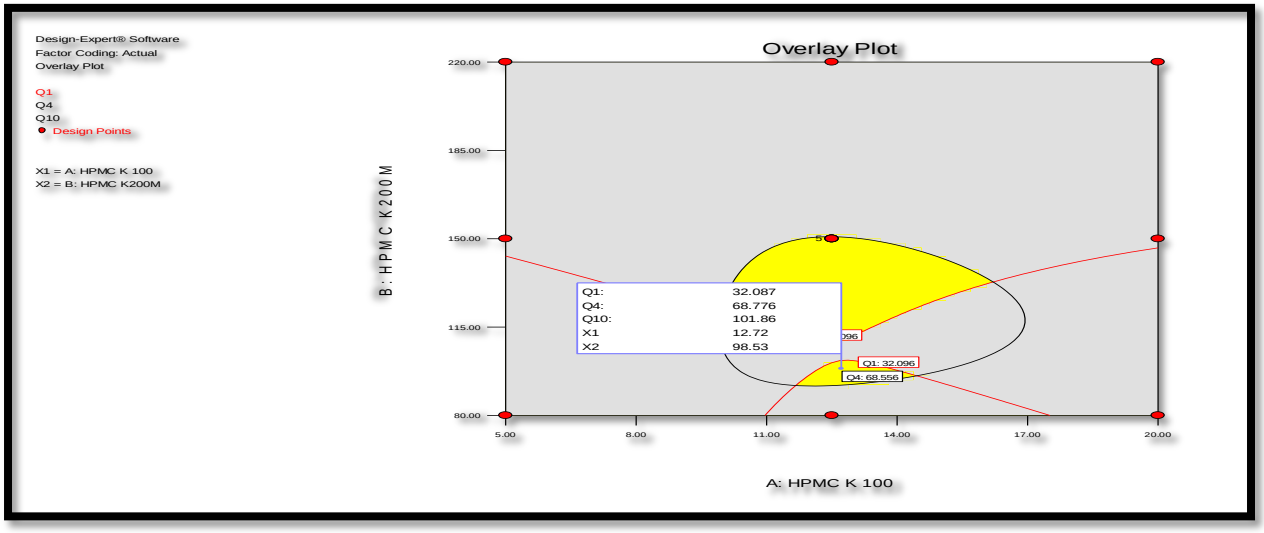


Figure 17: Selection of the optimized formulation

***In vitro* dissolution test of final formulation:**

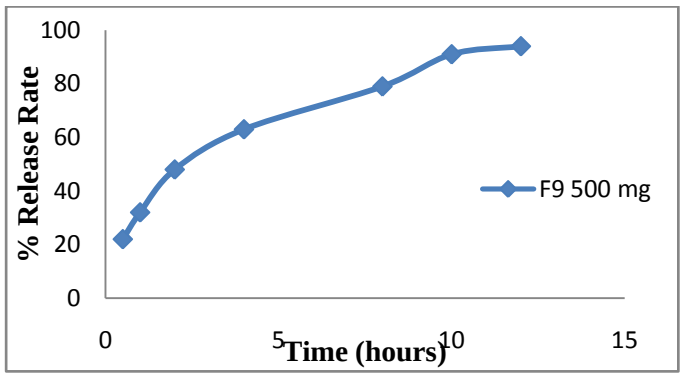


Figure 18: *In-vitro* drug release profiles of final formulation

Accelerated stability study of optimization formulation batch

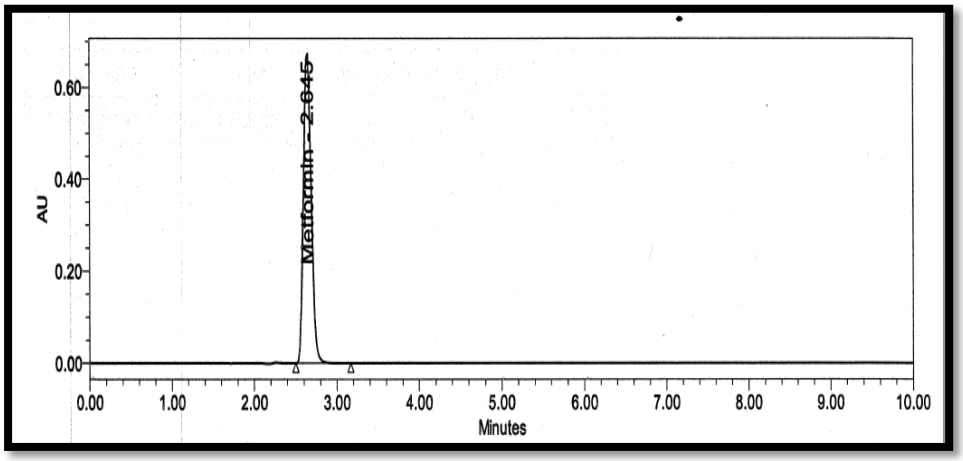


Figure 19: Specimen Chromatogram of Metformin HCl Standard

 ISSN: 2250-1177 CODEN (USA): JDDTAO

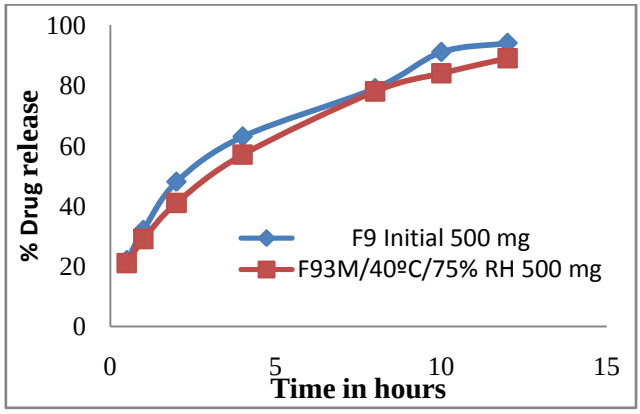


Figure 20: *In-Vitro* Drug release Stability studies

There is no significant fall observed in drug release profile of formulation F9 compared in initial and 3 month accelerated stability condition.

CONCLUSION

The main aim of the present dissertation was to develop novel Floating extended release formulation of Metformin HCl which is targeted to release drug till 12 hours at gastric region and compared the in-vitro similarity of novel formulation with already existing Marketed extended release formulation of Metformin HCl, which releases drug in intestinal region. Thus from the data obtained, it can be concluded that:

Gastroretentive dosage form of an antidiabetic drug of Metformin HCl formulated as an approach to increase gastric residence time and thereby minimizing hepatic extraction ratio followed by dangerous side effects. It was an effort to introduced sodium bicarbonate as effervescent agent in matrix based tablet, which tends to create buoyancy in formulation at gastric site, results tablet start floating in gastric region for sustained time period, thus release of drug at site of gastric mucosa in sustained way. Among the polymers used to improve the gastric residence, cellulose Polymers HPMC K100M, HPMC K200CR, showed better control over drug release than Carbopol 941P. Gastroretentive dosage form (Novel extended release formulation) are claiming to advantage to reduce dosing frequency over conventionally available IR formulation of 500 mg , 850 mg and 1000 mg recommended to two to three times daily leads to multiple dosing and patient incompliance as well as Potential side effects. Gastroretentive dosage form (Novel extended release formulation) is claiming to enhanced bioavailability and absorption of drug at site of gastric region.

ACKNOWLEDGEMENTS

I take it privilege sincerely express my deep sense of gratitude and thanks to guide **Dr. Pushpendra Kumar Tripathi(Director of Pharmacy),** Department of pharmaceutical, Rameshwaram Institute of Technology, whose meticulous guidance, valuable suggestion and constant motivation enabled me to complete this dissertation. The authors are thankful to **Biocon Research Limited (Bangalore)** for providing reference standards for permission as well as providing all facilities to complete this research work.

REFERENCES:

1. Rouge, N., Buri. P., Doelker, E., "Drug absorption sites in the gastrointestinal tract and dosage forms for site-specific delivery", Int. J. Pharm., 1996, 136, 117-139
2. Dunn, C. J.; Peters D. H. Metformin. A review of its pharmacological properties and therapeutic use in non insulindependant diabetes mellitus. Drugs 1995, 49 (5), 721-749.
3. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery system. Expert Opin Drug Deliv 2006; 3(2): 217- 33.
4. Iannucelli V, Coppi G, Bernabei MT, Camerorni R. Air compertment multiple-unit system for prolonged gastric residence. Part-I. Formulation study. Int J Pharm 1998; 174: 47-54.
5. The United States pharmacopoeia XX/National formulary XV. U.S. Pharmacopoeial convention, Rock-ville, MD, 1980; pg 958,990.
6. Lachman, L.; Lieberman, H.A.; Lachman, kaling, J.L. The theory and practice of industrial pharmacy, 3rded., Varghese Publishing House, Bombay, 1987; pg 296.
7. Lachman, L.; Lieberman, H.A.; Lachman, kaling, J.L. The theory and practice of industrial pharmacy, 3rd ed., Varghese Publishing House, Bombay, 1987; pg 297-98.
8. Indian pharmacopoeia, 5th ed., Published by the Indian pharmacopoeia commission,Ghaziabad, 2007; Vol. 1, pg 183.
9. The United States pharmacopoeia XX/National formulary XV. U.S. Pharmacopoeial convention, Rock-ville, MD, 1980; pg 958,990. Page 68
10. Srivastava, A. K.; Wadhwa, S.; Ridhurkar, D.; Mishra, B. Oral sustained delivery of atenolol from floating matrix tablets formulation and *in-vitro* evaluation. Drug Dev. Ind. Pharm., 2005; Vol. 31: pg 367–374.
11. Margret, C.; Bhavesh.; Venkateshwarlu, B.S.; Jayakar, B.; Bhowmik, D.; Sampath, K.P. Studies on formulations and evaluation of floating tablets containing anti-ulcer drugs, scholar research library, 2009; pg 102-114.

