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FORMULATION AND *IN VITRO* STUDIES OF METFORMIN HCL FLOATING TABLETS IN AN APPROACH TO IMPROVE DIABETES II THERAPY

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ABSTRACT
The objective of the present investigation was to design and develop gastroretentive drug delivery system of Metformin Hydrochloride. Floating tablets of Metformin Hydrochloride was developed using gas forming agents, like sodium bicarbonate, citric acid and polymers like Acacia gum and Xanthan gum. Tablets were prepared by wet granulation method. The prepared tablets were evaluated in terms of their pre-compression parameters, physical characteristics, estimate of drug content, total buoyancy time, buoyancy lag time and *in vitro* drug release amount. The results of the *in vitro* drug release studies showed that formulation one (FM-1) and formulation three (FM-3) had better control over release of drug. Formulation one resulted in sustained drug release of 76.3% over a period of 18hrs and formulation three resulted in sustained drug release of 77.27% over a period of 13hrs. It was concluded that these formulation could be given one dose per day. Formulation two (FM-2) might not have had good results as other two formulation but it produced sustained release of 96.79% over a period of 12hrs. And it was conclude that it can be given two doses per day. The drug release of all formulations improves uniform drug availability and helps increase adherence.

KEY WORDS
Metformin Hydrochloride, Acacia gum, Xanthan gum, Gas forming agents, Wet granulation method and *In vitro* studies.

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INTRODUCTION

Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. One of such difficulties is the ability to confine the dosage form in the desired area of the gastrointestinal tract[1]. To overcome this physiological problem, several drug

delivery systems with prolonged gastric retention time have been investigated. Attempts are being made to develop a controlled drug delivery system that can provide therapeutically effective plasma drug concentration levels for longer durations, thereby reducing the dosing frequency and minimizing fluctuations in plasma drug concentration at steady state by delivering drug in a controlled and reproducible manner[2]. Gastroretentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility of drugs that are less soluble in high pH environment. Gastric retention will provide new therapeutic possibilities and substantial benefits for patients.

The controlled gastric retention of solid dosage forms may be achieved by the mechanism of mucoadhesion[3,4], sedimentation[5,6], floatation[7], expansion[7,8], modified shape systems[9,10] or by the administration of pharmacological agents[11,12], that delaying gastric emptying. Based on these approaches, floating drug delivery systems seems to be the promising delivery systems for controlled release of drugs.

MATERIALS AND METHOD

MATERIALS

Metformin Hydrochloride, Xanthangum, Acacia gum, Polyvinyl pyrrolidine K_{30}, Magnesium stearate, Talc, and Isopropyl alcohol were used. All other chemicals and ingredients were used for study are of Analytical grade.

METHOD[13, 14]

Preformulation studies

Preformulation testing is an investigation of physical and chemical properties of drug substances alone and when combined with pharmaceutical excipients. It is the first step in the rational development of dosage form.

Compatibility studies

One of the requirement for the selection of suitable excipients or carrier for the pharmaceutical formulation is its compatibility. Therefore in the present work, a study was carried out by using FT-IR spectrophotometer to find out if there is any possible chemical interaction between Metformin HCL with Acacia gum and Xanthan gum.

Procedure

To study the compatibility of various formulation excipients with Metformin HCL, solid admixtures were prepared by mixing the drug with each formulation excipients separately in the ratio of 1:1 and stored in airtight containers at 30 ± 2^0C/65+5%RH. The solid admixtures were characterized using Fourier Transform Infrared Spectroscopy (FT-IR).

Method of Preparation and Formulation[15]

Preparation of Metformin Hydrochloride Floating tablets

Tablets were prepared by wet granulation method. Metformin Hydrochloride (500 mg) was mixed with required amount of polymers and other excipients (Table No.1). All the excipients were passed through sieve No.40, mixed and granulated with 10% solution of PVP K-30 in isopropyl alcohol. The wet mass was passed through sieve No.16 and dried at 45^{o}C for 2h. Dried granules were passed through sieve No.20 and mixed with magnesium stearate and talc.

EVALUATION PARAMETERS[13-15]

Pre-compression studies of floating tablet granules

Bulk density

5gm of Metformin HCL granules were weighed separately and transferred into 100ml measuring cylinder, initial volume was measured and calculated according to the formula

Formula

Bulk density = Mass / Volume

Tapped density

Tapped density is determined by placing a graduated cylinder containing a known mass of granules and mechanical tapper apparatus, which is

operated for a fixed number of taps until the powder bed volume has reached a minimum volume. Using the weight of the granules in the cylinder and this minimum volume, the tapped density may be computed.

Formula

Tapped density = Weight of granules / Tapped volume of granules

Angle of Repose

The manner in which stresses are transmitted through a bead and the beads response to applied stress are reflected in the various angles of friction and response. The most commonly used process of finding flowability is angle of repose, which may be determined experimentally by number of methods. The method used to find the angle of repose is to pour the powder a conical on a level, flat surface and measure the included angle with the horizontal.

Formula

$$\theta = \text{Tan}^{-1}(h/r)$$

Where,

θ **= Angle of repose,**

h = Height of the powder cone,

r = Radius of the powder cone.

Compressibility Index or Carr's Index

Carr's Index is measured using the values of bulk density and tapped density.

The following equation is used to find the Carr's Index,

$$CI = \frac{(TD-BD)}{TD} \times 100$$

Where, TD = Tapped density, BD = Bulk density.

Hausner's Ratio

It indicates the flow properties of the powder and ratio of Tapped density to the Bulk density of the powder or granules.

Formula:

Hausner's Ratio = Tapped density/Bulk density

Post-compression studies of floating tablet

Hardness or Crushing strength Test

Hardness of the tablet was determined using the Monsanto hardness tester (The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force.

The force required to break the tablet is measured in kilograms and a crushing strength of 4Kg is usually considered to be the minimum for satisfactory tablets. Oral tablets normally have a hardness of 4 to 10kg[16].

Thickness Test

The thickness of the tablet is mostly related to the tablet hardness can be uses as initial control parameter. Ten tablets were randomly selected from each tablet thickness was determined using a Vernier calliper and the reading was recorded in millimeters.

Friability Test

The pre-weighed tablets were placed in the friabilator, which was then operated for 100rpm, then dusted and reweighed. The Conventional compressed tablets that lose less than 0.5-1.0% of their weight are generally considered acceptable.

$$\text{Friability index} = \frac{I - F}{I} \times 100$$

Where,

I - Initial weight **F** - Final weight.

Weight variation test

Weights of 20 individual tablets were noted and their mean weight also calculated. The percentage deviation was calculated by using the following formula,

$$\text{Percentage deviation} = [X - X^{*}/ X] \times 100$$

X - Actual weight of the tablet

X* - Average weight of the tablet

Estimation of Drug Content

Ten tablets of each formulation were weighed and powdered. The quantity of powder equivalent to 100 mg of drug was transferred into 250 ml volumetric flask, it was shaken with 150 of distilled water and volume was adjusted to 250ml with water. The solution was filtered, suitable dilutions were made and absorbance was recorded by using U.V. spectrophotometer at 233nm. The experiment was repeated three times.

Calculation:

The amount of Metformin present in tablet can be calculated using the formula

$$A_t/As \times S_w/100 \times 100$$

Where, A_t = Absorbance of sample preparation

A_s = Absorbance of Standard preparation

S_w = weight at Metformin working standard (mg).

Floating or Buoyancy Test

The time taken for tablet to emerge on the surface of the medium is called the floating lag time (FLT) or buoyancy lag time (BLT) and duration of time the dosage form constantly remains on the surface of the medium is called the total floating time (TFT). The buoyancy of the tablets was studied in USP type II dissolution apparatus at 37±0.5^{o}C in 900ml of simulated gastric fluid at pH 1.2.The time of duration of floatation was observed visually.

***In Vitro* Drug Release Study**

In vitro drug release studies were carried out by using USP paddle dissolution test apparatus. 900ml of 0.1 N HCl (pH1.2) was taken in the dissolution vessel and the temperature of the medium were maintained at 37±0.5^{o}C. 100rpm was maintained, 1ml of sample was withdrawn at predetermined time intervals for 12 hours and the same volume of the fresh medium was replaced. The samples were analyzed at 233nm by using a UV spectrophotometer. The dissolution data obtained were plotted as percentage drug release versus time.

RESULTS AND DISCUSSION

RESULTS

PRE FORMULATION STUDIES

Compatibility studies (Fourier Transform Infrared Spectroscopic studies)

The Fourier transform Infra-red analysis was conducted for the surface structure characterization. FTIR spectrum of the formulated floating tablets, pure drug and polymers was recorded. Floating tablets were taken in a KBr pellet in FTIR Instrument. The Fourier Transform Infrared Spectroscopy study reveals that there is no interaction between the polymer and drug. Then all the functional groups found in the IR spectrum of pure drug, polymers and floating tablets. The functional groups found such as -NH_2, -NH, C-N, C-H (Figure No.1-6).

EVALUATION PARAMETERS

Pre-compression studies of floating tablet granules

Bulk density

The packing properties of the drugs and their formulations widely depend upon bulk density. It has been stated that bulk density values less than 1.2gm/cm^3 indicate good flow and values greater than 1.5g/cm^3 indicate poor flow.

From the result it can be seen that the bulk density values of the floating tablet granules are less than 1.2gm/cm^3, i.e. between 0.470 and 0.655 (Table No.2). This indicates good flow characteristics of the floating tablet granules.

Tapped density

From the result it can be seen that the Tapped density values of the floating tablet granules are less than 1.2gm/cm^3, i.e. between 0.430 and 0.578. This indicates good flow characteristics of the floating tablet granules (Table No.2).

Angle of Repose

Angle of repose less than 40° indicates free flowing properties of the floating tablets. However angle of repose greater than 40° indicates poor flow of material.

It can be observed, that the angle of repose for various batches of the granules is found to be less than 40°, falling between 26.97^0 and 28.84^0, indicating good flow property of the granules of floating tablet (Table No.2).

Compressibility Index or Carr's Index

Carr's Index less than 25 indicates free flowing properties of the floating tablet granules. However Carr's Index greater than 25 indicates poor flow of material.

It was observed, that the Carr's Index for various batches of the granules were found to be less than 25 and falling between 8.56 and 11.63; it indicates excellent flow properties of the floating tablet granules (Table No.2).

Hausner's Ratio

Hausner's Ratio less than or equal to 1.34 indicates free flowing properties of the floating tablet granules. However Hausner's Ratio greater than 1.34 indicates poor flow of material.

It was observed, that the Hausner's Ratio for various batches of the granules of the formulations were found to be less than 1.35 falling between 1.094 and 1.132; it indicates good flow properties of the floating tablets granules (Table No.2).

Post-Compression Studies of Floating Tablet

Hardness Test

The hardness of the floating tablet various batches were determined. The various batches of the floating tablets of hardness values are found within the limits. There were found to be in the range of 4.04-4.58 kg and it indicates good strength of the floating tablets (Table No.3).

Thickness Test

The floating tablets mean thicknesses were almost uniform in the all formulations and were found to be in the range of 0.46 - 0.56mm (Table No.3).

Friability Test

The floating tablets Friability values are found to be less than 1% in all cases and were found to be in the range of 0.673 - 0.90% (Table No.3).

Weight variation test

All this floating tablets passed weight variation test as the %weight variation was within the pharmacopoeia limits. The weight of the all tablets was found to be uniform with low standard deviation values (Table No. 4, 5 and 6).

Floating or Buoyancy Test

Total Floating Time (hrs)

The tablets are also studied for how long they stay floating in the stomach in the solution that resembles the stomach solution and measured as total floating time (Table No.7).

DISCUSSION

Floating tablets of Metformin HCl were prepared by wet compression method. The prepared floating tablets are round in shape. The Fourier transform infra-red analysis was conducted for the surface structure characterization. FTIR spectrum of the formulated floating tablets pure drug and polymers was recorded (Figure No.1-6). The Fourier Transform Infrared Spectroscopy study reveals that there is no interaction between the polymer and drug. The active ingredient Metformin was pure and its graph matches with the graph listed on the British pharmacopeia. The study of the mixture of active ingredient and polymers (Metformin with Xanthan gum, Metformin with Acacia gum and Metformin and Xanthan gum with acacia gum) showed that there were no changes in the peaks yet slight intensity differences were seen in relation to the pure Metformin graph. So the result revealed that there was no reaction that affected the active parts or functional groups of Metformin HCl. Then all the functional groups found in the IR spectrum of pure drug, polymers and floating tablets. The functional groups found in Metformin HCl are -NH2, -NH, C-N, and C-H. Standard calibration curve of Metformin HCL obeys the Beer's law in the range between 5-30µg/ml.

Bulk density (0.470 and 0.655gm/cm3) and Tapped density (0.430 to 0.578gm/cm3) values are within the limits, indicating that the granules have the required flow property for compression. The values obtained for angle of repose for all formulations are tabulated in table the values were found to be in the range 26.970 to 28.840. This indicates good flow property of the granules. Compressibility index (9.17 to 11.63) and Hausner's ratio (1.094 to 1.132) values are within the limits, indicating that the granules have the required flow property for wet compression.

The hardness of the floating tablet of all the formulations was determined and the hardness results (4.04 to 4.58 kg) were found to be within the accepted limits and this indicates good strength of the floating tablets. Tablet mean thicknesses were different among formulations but they were almost uniform within a formulation. The thickness results per formulation were FM-1: 0.46cm, FM-2: 0.51cm and FM-3: 0.56cm. Friability values are found to be less than 1% in all trials and they are considered satisfactory. Weight variation test was performed for all the tablets and it was found to be within the

pharmacopoeia limits. The weight of tablets of formulation 1 and 2 was found a very small amount lower than the desired amount (800mg) and the weight for formulation 3 was found to be a little bit higher. And the result proved weight of tablets within a formulation was uniform with low standard deviation values.

The drug content of the three batches of formulation was measured and found to be almost equal to the desired active ingredient in a tablet (500mg). The formulations 1, 2 and 3 resulted 98.38%, 99.01% and 100.39% respectively. The little fluctuation of drug content was due to the small differences of each formulation from the required weight of tablet (800mg). Formulation 1 and 2 tablets were having weight lower than the desired, which resulted in decreased amount of drug content. Formulation 3 tablets were having weight higher than desired, which resulted in higher drug content. Because the fluctuation in drug content was little and due to minor errors in compression process, it can be said there was proper mixing of the drug with the excipients.

The Metformin HCL floating tablets provide good floating behavior in the solution medium resembling the stomach content. So all the formulation batches showed density below than that of gastric fluid (1.004gr/cm^3). When the tablets contacts the test medium, the tablet expanded (because of the swellable polymers) and there was liberation of CO_2 gas (because of effervescent agents such as citric acid and sodium bicarbonate), the density decreased due to this expansion and upward force of CO_2 gas generation. This plays an important role in ensuring the floating capability of the dosage form. The difference in floating time and buoyancy time was due to the formulations degree of liberating CO_2 and swelling ability that is related to the polymers used in each formulation. Formulation FM-2 took 21min to float and stayed buoyant for 12hrs but formulation FM-1 and 3 floated with in 1:55min and 2:05min and it stayed buoyant for over 24hrs. This shows better floating and buoyancy behavior when Xanthan gum or combination of Xanthan gum and Acacia gum is used as a polymer than using only Acacia gum.

The floating time increased and decreased depending upon the integrity of the polymers. The formulation (FM-1) that used the polymer Xanthan gum and the combination formulation (FM-3) that used Xanthan gum and Acacia gum was found to have floating characters for a long period of time (up to 24hrs). But the formulation (FM-2) that used only Acacia as its polymer had shorter floating time (up to 12hrs) (Figure No.7-10).

The *in vitro* drug release profile of tablets from each batch (FM-1 to FM-3) was carried in 0.1N HCl for d/t period of time by using paddle type dissolution apparatus. From the in vitro dissolution data, FM-1 (formulation containing Xanthan gum) was found to have the best drug release and the cumulative % of drug release was found to be 76.3% in 18hrs of study. FM-3 (formulation containing Xanthan gum and Acacia gum) had cumulative % of drug release result of 77.27% in 13hr of study and the result was in better compared to FM-2 with cumulative % of drug release 96.79% in12hrs of study (Table No.8-10 and Figure No.11).

The formulation FM-1 drug release was sustained and that is because it had Xanthan gum as its polymer. The Xanthan gum had swelling and floating behavior that produced controlled release of CO_2 and active ingredients in the formulation. Based on the in vitro drug release profile of the formulation FM-2 containing Acacia gum didn't not have sufficient duration of floating that resulted in lower retention time of the drug. It might be due to the polymer Acacia gum not effectively influencing the retention time of the drug. And this could have been due to the high polymerization of Acacia gum, which was unable to swell and remain intact for a longer time instead of disintegrating. The formulation FM-3 drug release was sustained but not as quit good as FM-1. The reason for that is the combination of polymers Xanthan gum and Acacia gum used in the formulation, which made the formulation to have lower retention of the active ingredients than FM-2.

Table No.1: Formulation of different batches of Metformin Hydrochloride Floating Tablets (mg/tab)

S.No	Formulations	Drug (Metformin HCL)	Polymers		Citric acid	Sodium Bicarbonate	PV K_{30}	Magnesium stearate	Talc
			Xanthan gum	Acacia gum					
1	FM-1	500	200	-	15	50	Qs	25	10
2	FM-2	500	-	200	15	50	Qs	25	10
3	FM-3	500	100	100	15	50	Qs	25	10
Wt of tab= 800mg									

Table No.2: Precompression studies of powders

S.No	Formulations	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Angle of Repose (θ)	Carr's Index (%)	Hausner's Ratio
1	FM-1	0.655	0.578	27.76	11.63	1.132
2	FM-2	0.518	0.470	28.84	9.17	1.103
3	FM-3	0.470	0.430	26.97	8.56	1.094

Table No.3: Postcompression studies of Metformin Hydrochloride Floating Tablets

S.No	Formulations	Hardness Test (kg/cm)	Thickness Test (cm)	Friability Test (%)	Estimation of Drug Content
1	FM-1	4.58	0.46	0.673	98.38
2	FM-2	4.16	0.51	0.85	99.01
3	FM-3	4.04	0.56	0.90	100.39

Table No.4: FM-1 Weight variation test results

Trial	Wt of Tablet	Avg. Wt of Tablet	Deviation	% of Deviation
1	780	789.5	-0.0121795	-1.2179487
2	780	789.5	-0.0121795	-1.2179487
3	785	789.5	-0.0057325	-0.5732484
4	789.6	789.5	0.00012665	0.01266464
5	814	789.5	0.03009828	3.00982801
6	814	789.5	0.03009828	3.00982801
7	786.7	789.5	-0.0035592	-0.3559171
8	793.1	789.5	0.00453915	0.45391502
9	782.6	789.5	-0.0088168	-0.8816765
10	817.5	789.5	0.03425076	3.42507645
11	786	789.5	-0.0044529	-0.4452926
12	783.5	789.5	-0.0076579	-0.7657945
13	780.6	789.5	-0.0114015	-1.1401486
14	784	789.5	-0.0070153	-0.7015306
15	784	789.5	-0.0070153	-0.7015306
16	781.2	789.5	-0.0106247	-1.062468
17	781.2	789.5	-0.0106247	-1.062468
18	782	789.5	-0.0095908	-0.9590793
19	782	789.5	-0.0095908	-0.9590793
20	803	789.5	0.01681196	1.68119552

Table No.5: FM-2 Weight variation test results

Trial	Wt of Tablet	Avg. Wt of tablet	Deviation	% of Deviation
1	782	773.95	0.01029412	1.02941176
2	795	773.95	0.02647799	2.64779874
3	785	773.95	0.01407643	1.40764331
4	785	773.95	0.01407643	1.40764331
5	766	773.95	-0.0103786	-1.037859
6	766	773.95	-0.0103786	-1.037859
7	771	773.95	-0.0038262	-0.38262
8	762	773.95	-0.0156824	-1.5682415
9	762	773.95	-0.0156824	-1.5682415
10	770	773.95	-0.0051299	-0.512987
11	770	773.95	-0.0051299	-0.512987
12	770	773.95	-0.0051299	-0.512987
13	777	773.95	0.00392535	0.39253539
14	777	773.95	0.00392535	0.39253539
15	773	773.95	-0.001229	-0.1228978
16	773	773.95	-0.001229	-0.1228978
17	775	773.95	0.00135484	0.13548387
18	775	773.95	0.00135484	0.13548387
19	776	773.95	0.00264175	0.26417526
20	769	773.95	-0.0064369	-0.6436931

Table No.6: FM-3Weight variation test results

Trial	Wt of tablet	Avg. Wt of tablet	Deviation	% of wt deviation
1	815	811.1	0.00478528	0.478527607
2	815	811.1	0.00478528	0.478527607
3	810	811.1	-0.001358	-0.135802469
4	814	811.1	0.00356265	0.356265356
5	809	811.1	-0.0025958	-0.259579728
6	812	811.1	0.00110837	0.110837438
7	812	811.1	0.00110837	0.110837438
8	807	811.1	-0.0050805	-0.508054523
9	815	811.1	0.00478528	0.478527607
10	809	811.1	-0.0025958	-0.259579728
11	814	811.1	0.00356265	0.356265356
12	811	811.1	-0.0001233	-0.012330456
13	810	811.1	-0.001358	-0.135802469
14	808	811.1	-0.0038366	-0.383663366
15	805	811.1	-0.0075776	-0.757763975
16	805	811.1	-0.0075776	-0.757763975
17	815	811.1	0.00478528	0.478527607
18	810	811.1	-0.001358	-0.135802469
19	813	811.1	0.00233702	0.233702337
20	813	811.1	0.00233702	0.233702337

Table No.7: Floating or Buoyancy Test results

S.No	Formulations	Buoyancy Lag Time (min)	Total Floating Time(hrs)
1	FM-1	1.55	24
2	FM-2	21	12
3	FM-3	2.05	24

Table No.8: *In vitro* drug release study results (FM-1)

S.No	Hour	Absorbance	Concentration	Amount of drug release (900ML)	Percentage of Drug Release
1	0	0	0	0	0
2	1	0.0955	1.364286	122.7857	24.55714
3	2	0.1308	1.868571	168.1714	33.63429
4	3	0.1376	1.965714	176.9143	35.38286
5	4	0.1425	2.035714	183.2143	36.64286
6	5	0.1527	2.181429	196.3286	39.26571
7	6	0.1718	2.454286	220.8857	44.17714
8	7	0.1876	2.68	241.2	48.24
9	8	0.2034	2.90571	261.514	52.3029
10	9	0.2197	3.138571	282.4714	56.49429
11	10	0.2213	3.161429	284.5286	56.90571
12	11	0.2234	3.191429	287.2286	57.44571
13	12	0.2365	3.378571	304.0714	60.81429
14	13	0.2472	3.531429	317.8286	63.56571
15	14	0.2531	3.615714	325.4143	65.08286
16	15	0.2649	3.784286	340.5857	68.11714
17	16	0.2747	3.924286	353.1857	70.63714
18	17	0.2824	4.034286	363.0857	72.61714
19	18	0.2967	4.238571	381.4714	76.29429

Table No.9: *In vitro* drug release study results (FM-2)

S.No	Hour	Absorbance	Concentration	Amount of Drug Release (900ML)	Percentage of Drug Release
1	0	0	0	0	0
2	1	0.1446	2.065714	185.9143	37.18286
3	2	0.2135	3.05	274.5	54.9
4	3	0.2372	3.388571	304.9714	60.99429
5	4	0.2541	3.63	326.7	65.34
6	5	0.2666	3.808571	342.7714	68.55429
7	6	0.2741	3.915714	352.4143	70.48286
8	7	0.2852	4.074286	366.6857	73.33714
9	8	0.2986	4.265714	383.9143	76.78286
10	9	0.3145	4.492857	404.3571	80.87143
11	10	0.3312	4.731429	425.8286	85.16571
12	11	0.3475	4.964286	446.7857	89.35714
13	12	0.3764	5.377143	483.9429	96.78857

Table No.10: *In vitro* drug release study results (FM-3)

S.No	Hour	Absorbance	Concentration	Amount of Drug Release (900ML)	Percentage of Drug Release
1	0	0	0	0	0
2	1	0.1105	1.57857	142.071	28.4143
3	2	0.1206	1.72286	155.057	31.0114
4	3	0.1392	1.98857	178.971	35.7943
5	4	0.1734	2.47714	222.943	44.5886
6	5	0.1817	2.59571	233.614	46.7229
7	6	0.2106	3.00857	270.771	54.1543
8	7	0.2268	3.24	291.6	58.32
9	8	0.24	3.42857	308.571	61.7143
10	9	0.2507	3.58143	322.329	64.4657
11	10	0.2721	3.88714	349.843	69.9686
12	11	0.2844	4.06286	365.657	73.1314
13	12	0.2956	4.22286	380.057	76.0114
14	13	0.3005	4.29286	386.357	77.2714

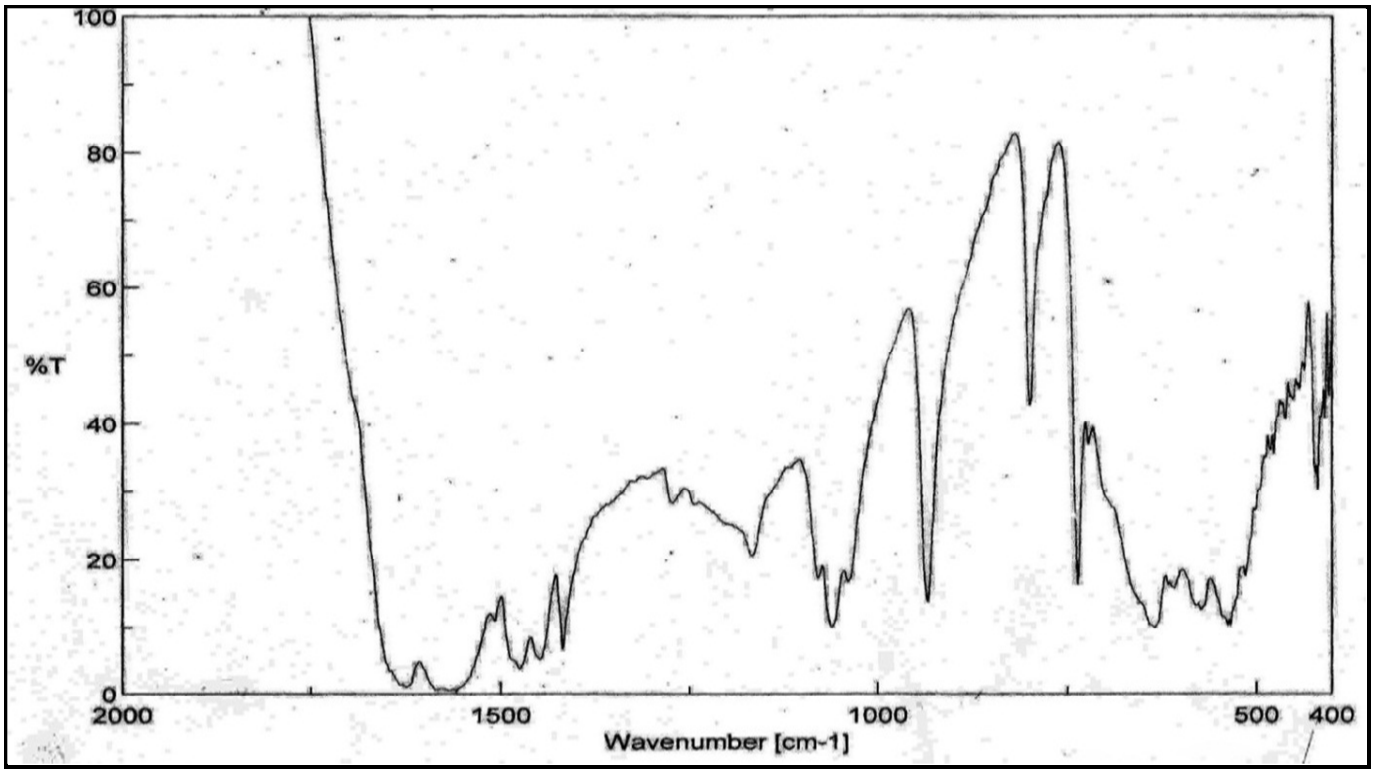


Figure No.1: FTIR spectrum of pure drug (Metformin HCL)

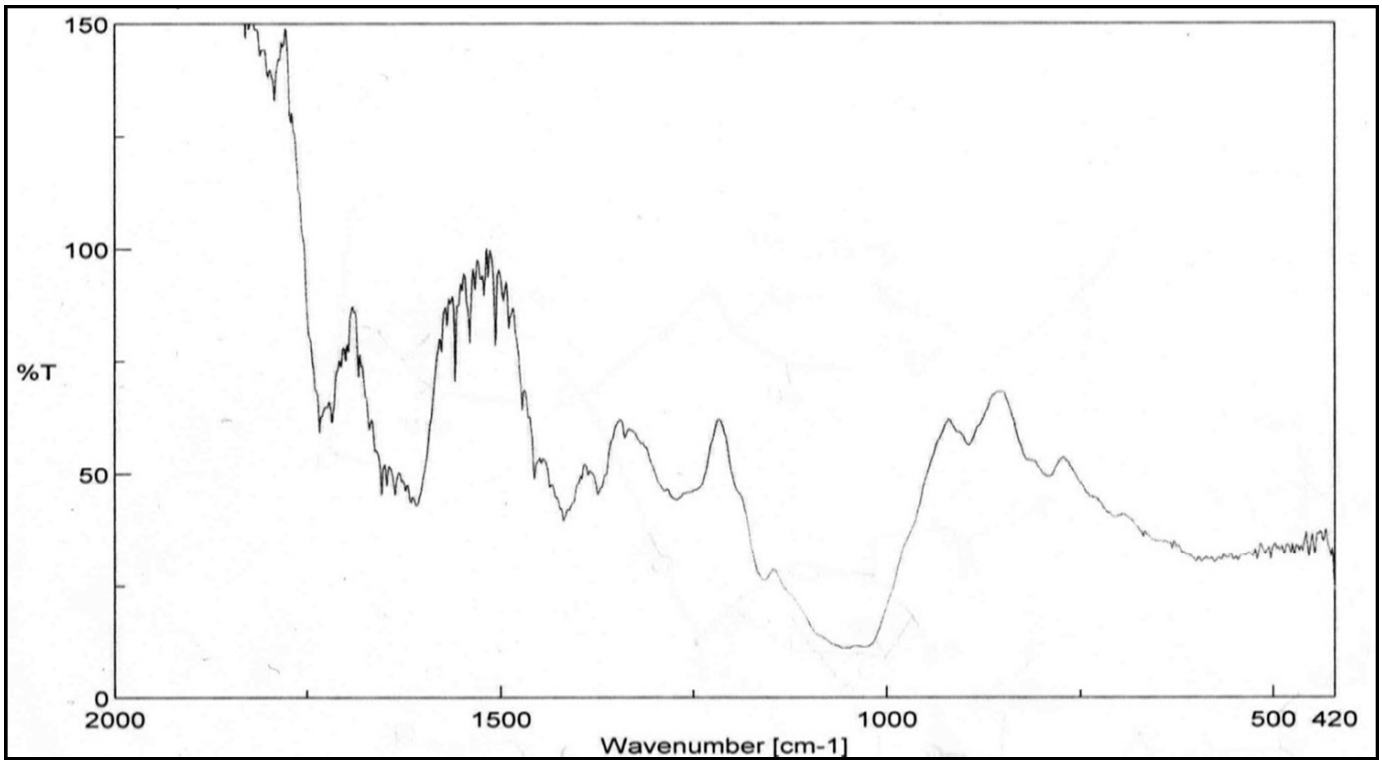


Figure No.2: FTIR spectrum of Xanthan gum

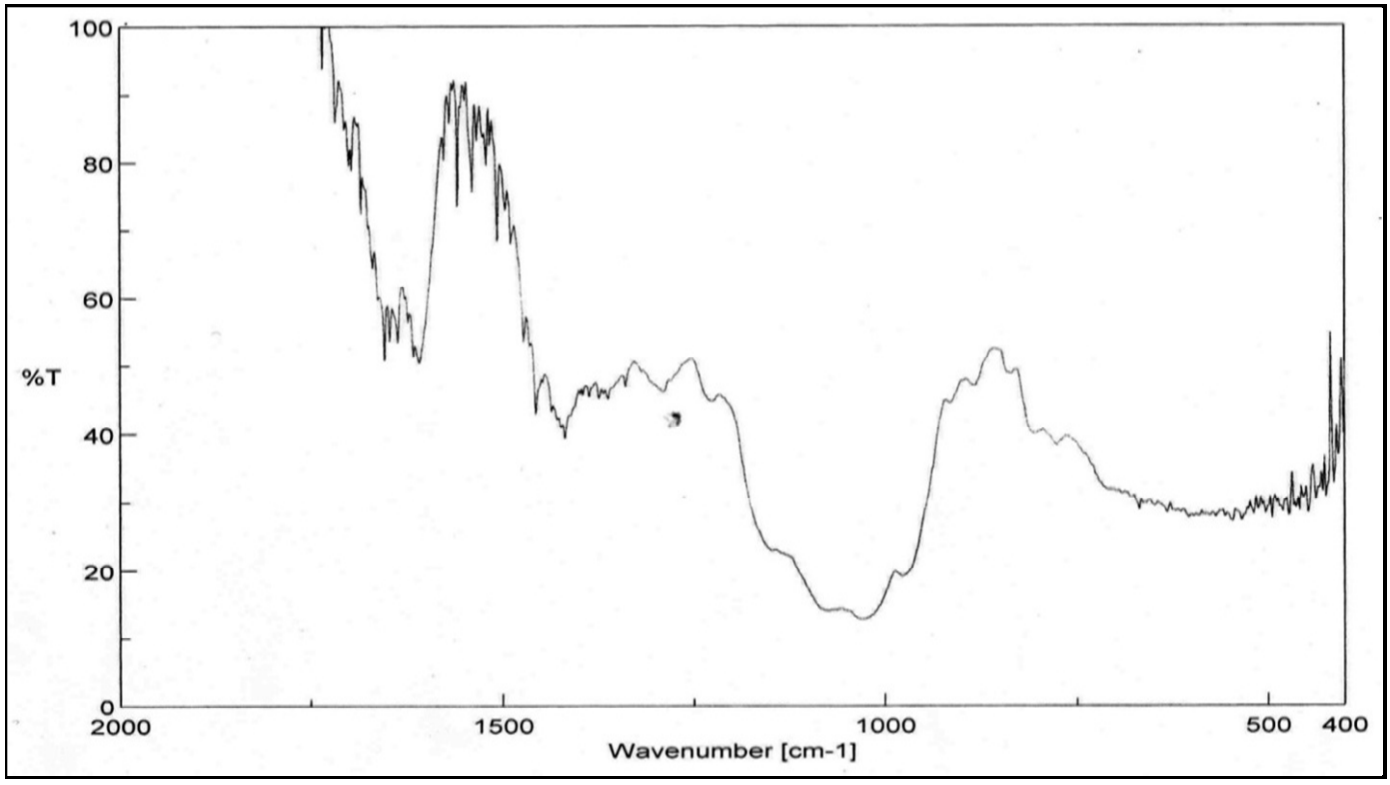


Figure No.3: FTIR spectrum of Acacia gum

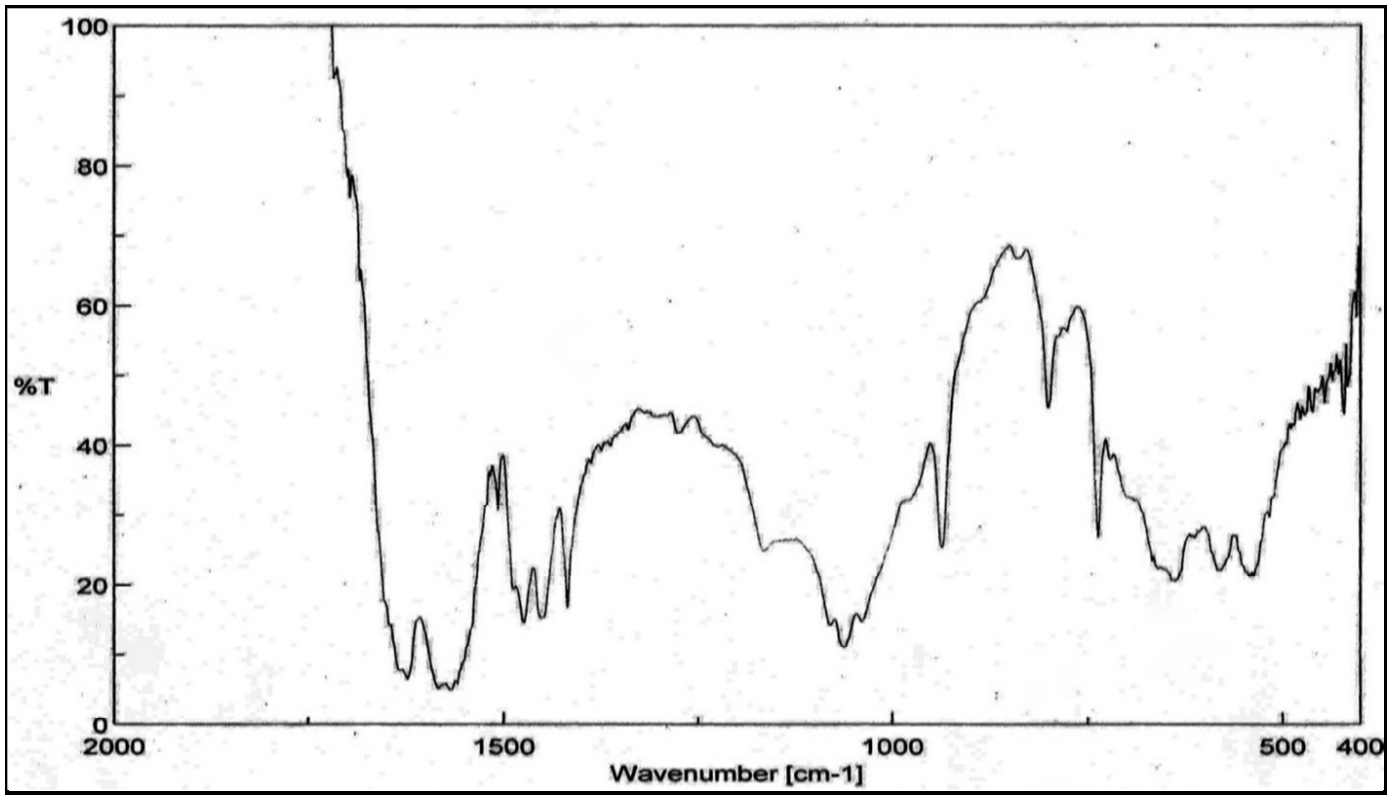


Figure No.4: FTIR spectrum of Metformin HCL + Acacia

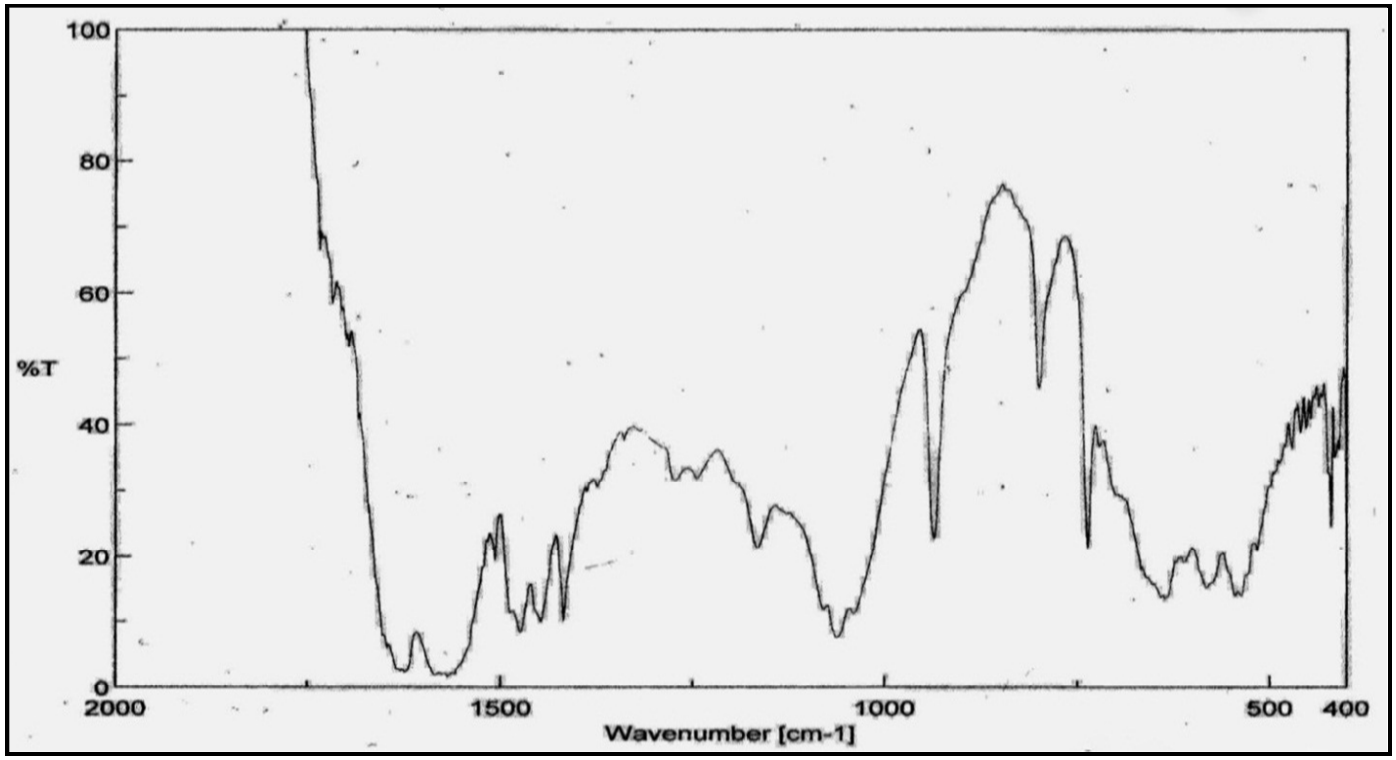


Figure No.5: FTIR spectrum of Metformin HCL + Xanthan Gum

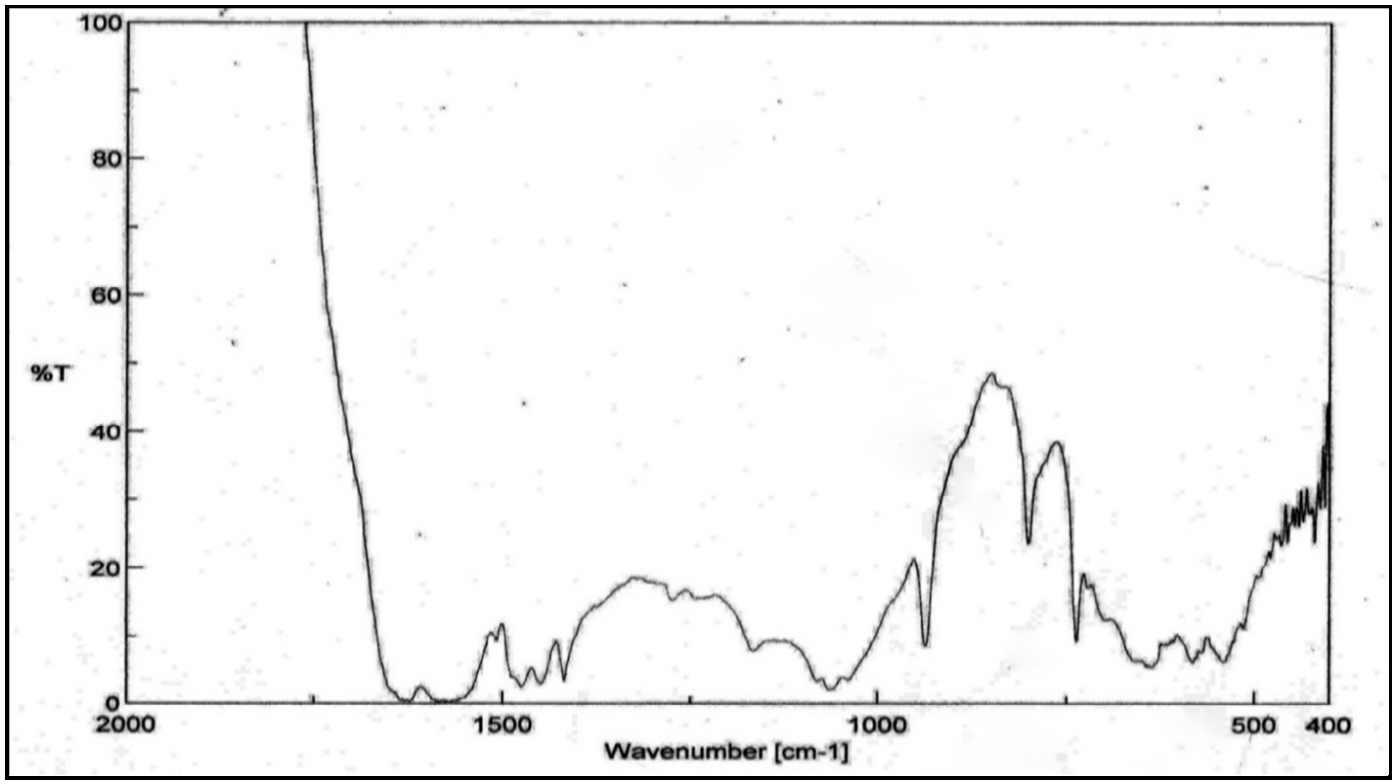
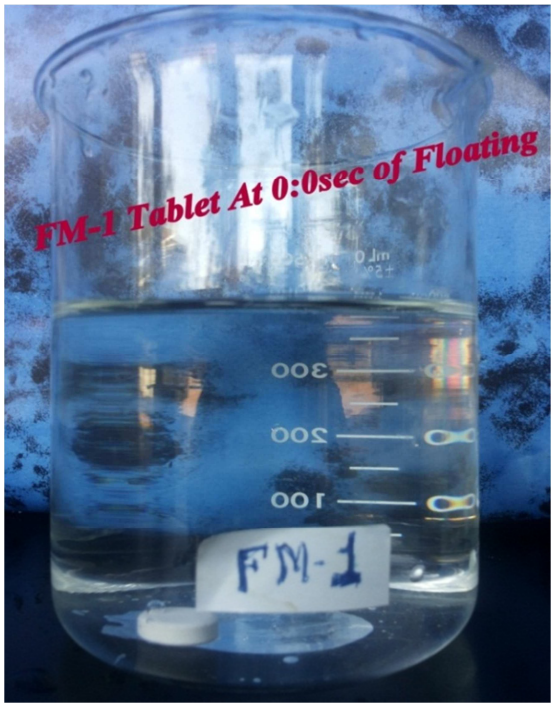


Figure No.6: FTIR spectrum of Metformin HCL + Xanthan gum + Acacia gum



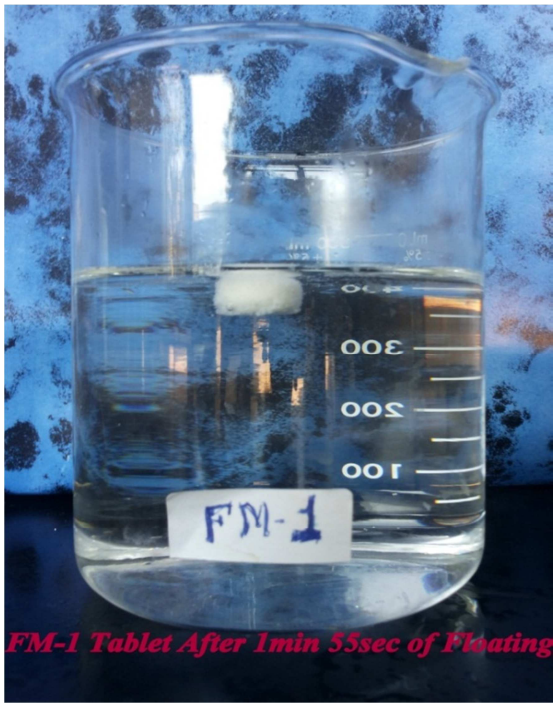
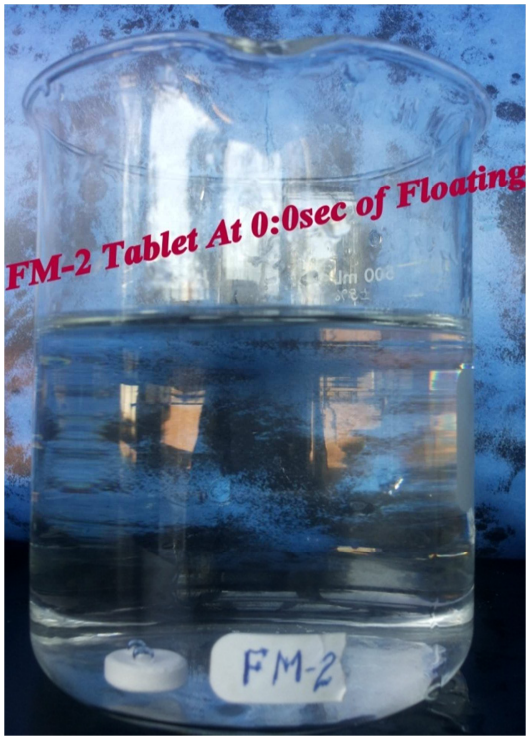


Figure No.7(a): FM-1 At Floating Time:0sec Figure No.7(b): FM-1 At Floating Time:1min 55sec



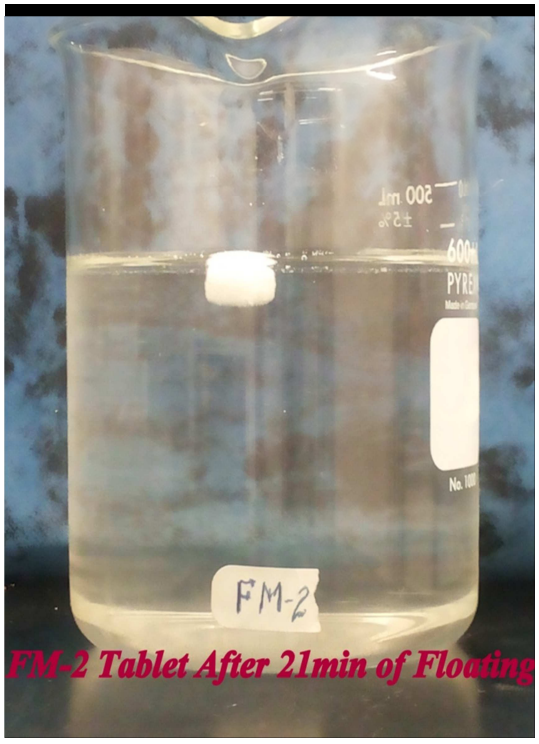
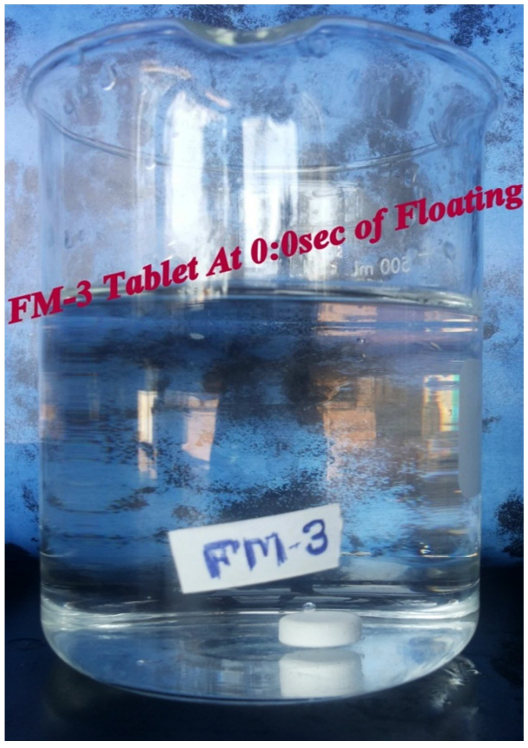


Figure No.8(a):FM-2 At Floating Time:0 sec Figure No.8(b): FM-2 At Floating Time: 21mins



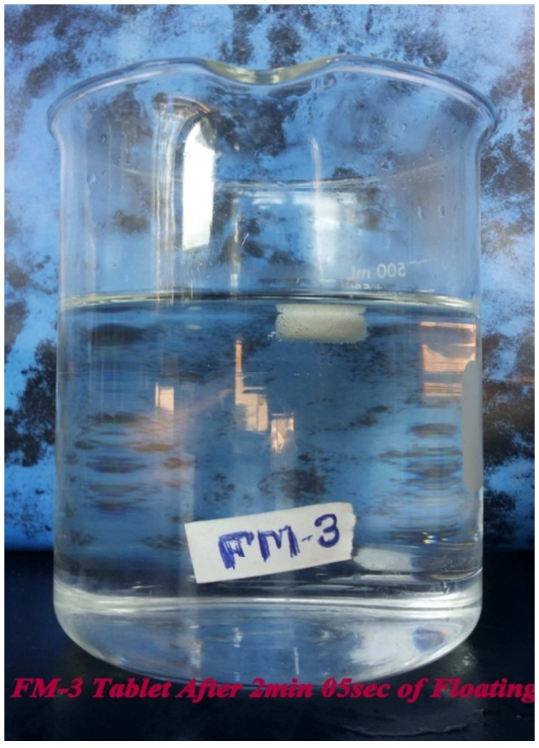


Figure No.9(a): FM-3 At Floating Time: 0:0sec **Figure No.9(b): FM-3 At Floating Time 2min 05sec**

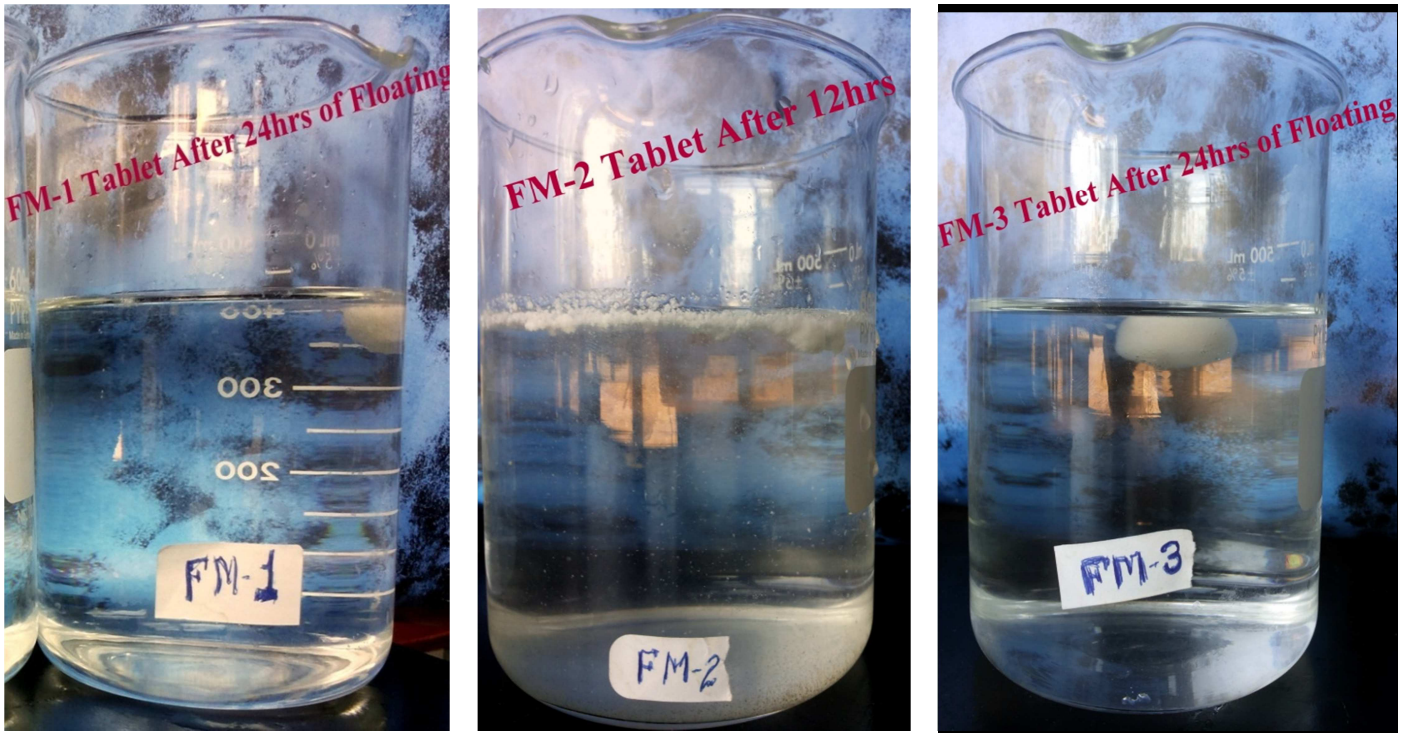


Figure No.10: FM-1, FM-3 after 24hrs and FM-2 after 12hrs

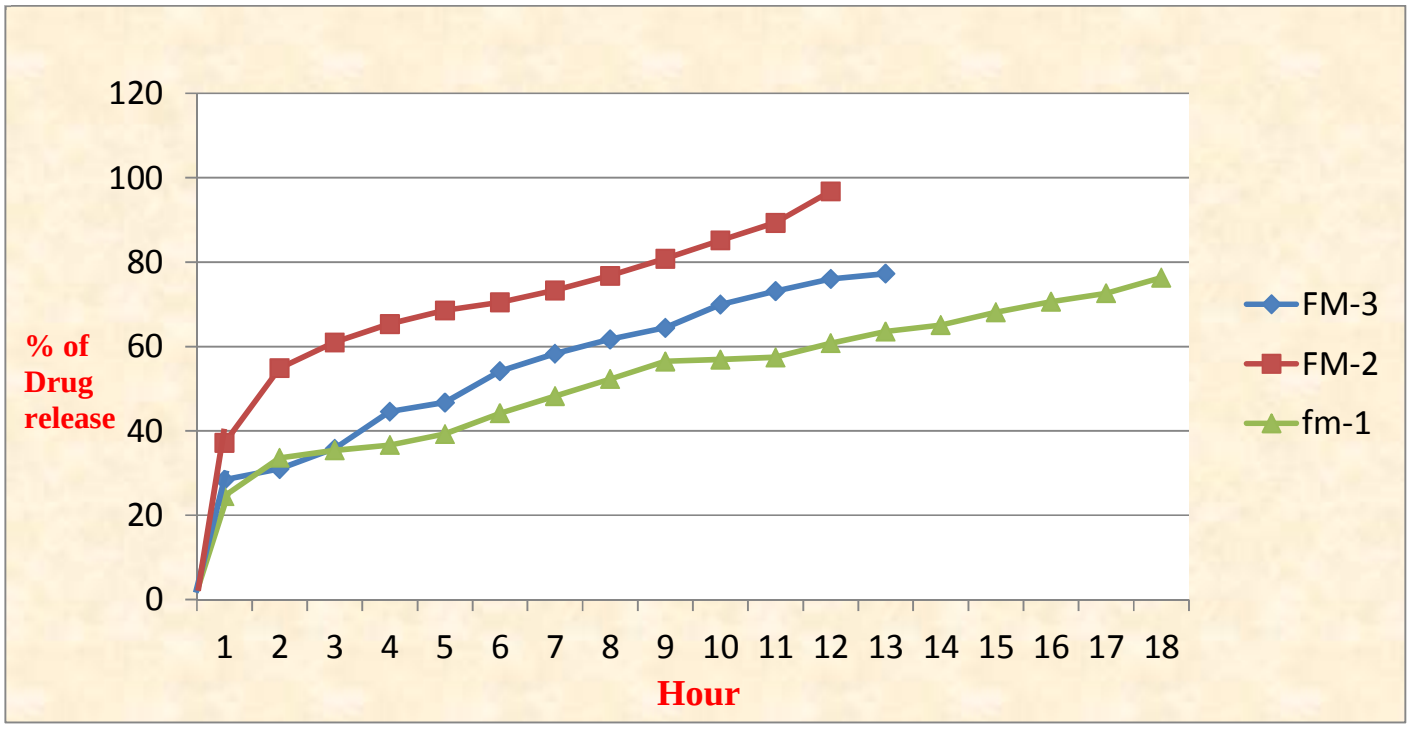


Figure No.11: *In vitro* drug release of FM-1, FM-2 & FM-3

CONCLUSION

The Floating tablets of Metformin HCL were successfully formulated by wet granulation technique. The Floating tablets of Metformin HCL containing Xanthan gum (FM-1 and FM-3) showed satisfactory results with short buoyancy lag time, total buoyancy time more than 24 hrs. The formulations could decrease dosing frequency and make it once a day. Yet this formulations dosing could be decreased to a much lower frequency. Formulation-2(FM-2) had lower controlling ability of the drug release, yet it showed a sustained release and can be used as two doses per three days.

As a result, frequent dosing and possible incomplete absorption of the drug can be avoided. Therefore, it was concluded that the drug (Metformin HCl) was suitable for floating drug delivery system, which is a new choice of an economically effective, safe and more bioavailable formulation in the management of type II diabetes mellitus. It could also help decrease the frequency of occurrence of adverse drug reaction caused by patient or health professional (E.g. Dose missing).

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Yie W. Chein. “Novel Drug Delivery System”, *Marcel jekker Inc, New York,* 2nd edition, 1992, 1-3.
2. Jose Gutierrz Rocca, Hosen Omidian and Khalid Shah. “Progresses in Gastroretentive drug delivery systems”, *Pharmatech,* 1, 2003, 152-156.
3. Ponchel G, Irache J M. Specific and non-specific bioadhesive particulate system for oral delivery to the gastrointestinal tract, *Adv Drug Del Rev,* 34, 1998, 191-219.
4. Lenaerts V M, Gurny R. Gastrointestinal Tract-Physiological variables affecting the performance of oral sustained release dosage forms, *Bioadhesive Drug Delivery System. Boca Raton, FL CRC Press*, 1990.
5. Rednick A B, Tucker S J. Sustained release bolus for animal husbandry, *US patent 3 507,* 952, April 22, 1970.
6. Davis S S, Stock well A F, Taylor M J, *et al.* The effect of density on the gastric emptying of single and multiple unit dosage forms, *Pharm Res,* 3, 1986, 208-213.
7. Urguhart J, Theeuwes F. Drug delivery system comprising a reservoir containing a plurality of tiny pills, *US patent 4 434 153,* February 28, 1, 1994.
8. Mamajek R C, Moyer E S. Drug dispensing device and method, *US Patent 4 207 890,* June 17, 1, 1980.
9. Fix J A, Cargill R, Engle K. Controlled gastric emptying. III. Gastric residence time of a non-disintegrating geometric shape in human volunteers, *Pharm Res,* 10, 1993, 1087-1089.
10. Kedzierewicz F, Thouvenot P, Lemut J, Etienne A, Hoffman M, Maincent P. Evaluation of peroral silicone dosage forms in humans by gamma-scintigraphy, *J Control Release,* 58, 1999, 195-205.
11. Groning R, Heun G. Oral dosage forms with controlled gastrointestinal transit, *Drug Dev Ind Pharm,* 10, 1984, 527-539.
12. Groning R, Heun G. Dosage forms with controlled gastrointestinal passage-studies on the absorption of nitrofurantion, *Int J Pharm, 56,* 1989, 111 -116.
13. Mohamed Raffick M, Muthu Mohamed J, Vetriselvan S. Preparation and Evaluation of *in-vitro* release Kinetics of novel bilayer metoprolol succinate as sustained release and amlodipine besylate as immediate release

tablets, *International Journal of Biological and Pharmaceutical Research,* 3(2), 2012, 285-297.

14. Lachman L, Lieberman H, Kanig J. The theory and practice of industrial pharmacy, *Varghese publication house,* 3rd edition, 2009, 297-303.
15. Raju D B, Sreenivas R and Varma M M. Formulation and evaluation of floating drug delivery system of Metformin Hydrochloride, *J. Chem. Res.*, 2(2), 2010, 274-278.
16. The Anonymous. Hardness or Crushing strength, *Pharmainfo.net,* 2008.

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