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Formulation and Evaluation of Bilayer Floating Tablets for the Treatment of Diabetes Mellitus

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Keywords: Bilayer tablets, floating drug delivery system, Metformin Hydrochloride, Glibenclamide.

ABSTRACT

The present research work was an attempt to design a formulation of Bilayer floating tablets with rapaglinide as sustained release layer and glipizide as immediate release layer for the treatment of type II diabetes mellitus. The extended release was prepared by wet granulation method using HPMC K 100M as sustained release polymer and sodium bicarbonate as gas generating agent to reduce floating lag time. Immediate release layer was prepared by direct compression using sodium starch glycolate as super disintegrant. Gastro retentive floating drug delivery systems have been designed to increase its residence time in the stomach. The granules were evaluated for bulk density, tapped density, Compressibility index, and hausner's ratio. The granules showed satisfactory flow properties. The tablets were subjected to weight variation test, hardness test, friability test, drug content test and swelling index. All the tablets were passed the tests. With the incorporation of a gas generating agent the floating lag time was 27 sec, and the duration of floating was >8hrs. The drug release from the prepared tablets was sufficiently sustained (more than 8hrs). The release kinetics of the Bilayer floating tablet was evaluated using regression coefficient analysis. The formulated tablets show a Zero order drug release and the mechanism is correlated well with Korsmeyer peppas mode with super case II transport mechanism. Stability studies did not show any changes in physical appearance, physicochemical properties, and drug release.

1. INTRODUCTION

Diabetes may be characterized by hyperglycaemia. These may help in insulin secretion defects and both insulin action. Due to development of insulin resistance the inadequate insulin secretion and tissues dimension may lead to abnormalities of fats, carbohydrate and metabolism of protein. [1,2] These may lead to change or may increases the concentration of blood glucose level. These may damage many systems of the body like blood vessels, nerves. According to the survey it was concluded that 0.5 to 3% of person was surfer from these diseases. Now a day's its reaches to more than 7 %. Around 200 to 300 million people are affected and it should be double or triple in next few years. [3,4]

It is a heterogenous disorder. These may arise from interactions of genetic and environment and a lifestyle factor. Insufficient insulin production and a genetic factor is causing the type 2 diabetes. [5,6] It may be resistance to the insulin target tissues. Erectile dysfunction, blindness, poor healing wound, failure of kidney and heart diseases may form during long term diabetes. Type 2 diabetes is more common than type 1. Statistical data of India shows that around 57 to 60 million of patients is been affected in year 2025. This will make the India in world largest diabetic population. [7,8,9]

Oral anti-hypertensive agents are use for the treatment of diabetes. Insulin and herbal treatment are used for this. Insulin is a hormone which may have 51 amino acids. It was first synthesis as a pro insulin precursor in the pancreas's cells of p-cells. It was converted by the action of enzymes to insulin. This was extracted from the bovine and porcine pancreases. Now a days human insulin is made of recombinant DNA technology. These are affected that previous insulin. Some other types of drugs is been categorized into this like, alpha-glucosidase inhibitors, sulfonylureas, thiazolidinediones. [10,11,12]

Now a days, some herbal formulation is been used for this treatment like pedes of ginseng: it was used for health promoting. Bitter Melon: these may give bitter taste. It was mainly used to treat diabetes. Fenugreek: this may used to treat the remedy of diabetes. G. sylvestre found in the Himalayas and in tropical forest of India. This may use to block the sugar. This may use oral hypoglycaemic drugs. [13,14,15]

2. MATERIAL AND METHODS

2.1 Preformulation Study

Confirmation of Drug: UV spectroscopy and DSC thermograph is use for the Confirmation of drugs. [16, 17]

Calibration Curve of repaglindine and glipizide in pH 1.2 HCl Buffer: Around 15mg of drug (repaglindine) were weigh and dissolve it into 1.2pH HCL. After that it was transfer into volumetric flask. 0.07 to 1.5ml of sample was withdrawn from the prepared solution. After dilution with 10ml (1.2pH HCl), different concentration of 0.6-1.5 µg/mL. Absorbance was taken at λ_{max} 241 nm.

DSC study: The mixture of drugs and polymers are filled in an ampoule and it was stored at 37.0°C ± 0.5°C. for the end of 28days the ampoules are removed and use for interaction study.

Determination of Solubility: Solubility is the most important parameter in pre-formulation study. Drug solubility at 37°C for 24h for both drugs was determined. It was put on a shaker and continually shaken. It was done up to 18 to 24 hrs. it was filter through Millipore filter and assayed by spectrophotometrically.

Determination of FTIR Study: Bulk drugs were identified by using FTIR Spectrophotometer. KBR pellet technique was used for sample analyses. hydraulic pressure is used for the preparation of Pellets of drug. Frequency range of 400-4000 cm^{-1} is used.

Drug–Excipient Interaction: DSC and FTIR technique are used for the study of drug-excipient interaction. In which the polymers may be heated 50 to 460 °C. ampules was washed with water and acetone. Sealed the ampoules with samples (Repaglindine, glipizide and mixture of Repaglindine and glipizide). Then these samples were kept for 28 days in stability chamber. Three sets of each mixture are prepared, from which 1 set is for initial analysis while two sets are kept @ 40ºC/80 % RH for 1 month. After 1 month the samples are observed visually for change of colour or its appearance in powder form. From these two sets of samples, one set is analysed using HPLC while one set is used for DSC and FTIR study that clarifies if any interaction is occurred between drug-excipient. DSC and FTIR study were done for the pure drug of Repaglindine, glipizide and their mixture. Then the samples were

weighed and these samples are put into an aluminium crucible and the sealed. These samples may be scanned at 50 to 400 °C at 20 °C. The thermograms were formed. [18, 19]

Table No. 1: Drug–excipient Interaction

Sr.no	Sample Composition	Weight per vial
1	Repaglindine	2g Repaglindine
2	Glipizide	2g Glipizide
3	Repaglindine + glipizide	1g repaglindine + 1g glipizide
4	Repaglindine + excipients	0.5g Repaglindine+ 0.5g HPMC+ 0.5g cross povidone+0.5g magnesium stearate
5	Glipizide + excipients	0.5g Glipizide +0.5g lactose+0.5g microcrystalline cellulose + 0.25g magnesium stearate + 0.25g sodium bicarbonate

2.2 Evaluation study of drug and excipients [20]

Angle of Repose (Ɵ): Combination of excipients and drugs are prepared and it was transfer into funnel. Funnel will only touch the apex of the heap of the drug.

$$\text{Angle of repose } (\theta) = \tan^{-1}\left(\frac{h}{r}\right)$$

Where, θ = angle of repose, h = height of heap, r = radius of base of heap circle.

Bulk density: It was determined by the following formula:

$$\rho \text{ bulk} = \frac{m}{V \text{ bulk}}$$

Tapped density: A weighed powder was introduced into the measuring cylinder. Tapped density was calculated from the following formula:

$$\rho \text{ tapped} = \frac{m}{V \text{ tapped}}$$

Carr's Index: Compressibility of a powder show the indication of Carr's Index. It gives following equation:

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

If the Carr's Index is below 15% the flowability is good and if it is greater than 25% the flow ability is poor.

Hausner's Ratio: It was calculated by the following formula:

Hausner's ratio = (Tapped density)/(Bulk density)

If the Hausner's Ratio is greater than 1.25 the flow ability is poor.

2.3 Immediate Release Tablets

Tablet preparation: The drug (repaglinide) is been mixed with disintegrant (Sodium starch glycolate) for 20 mins and pour into a porcelain mortar. After that it should be passes through the sieve (40). Direct compression process is used for the compressed the tablets. Rimek minipress-1 tablet machine is used for this process. [21]

Table No. 2: Compositions of immediate release layer tablet

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**
Repaglinide	2.73	2.73	2.73	2.73	2.73
Sodium starch glycolate	5	3.6	2.5	2.5	5
Sodium lauryl sulphate	1.2	1.2	1.2	1.2	1.2
MCC 102	41.36	43	44	44	41.36

2.4 Sustained Release Tablet Formulation

Tablet preparation: For the preparation of tablets glipizide and HPMC is mixed with other excipients. It should pour into porcelain mortar and stirrer about 10 mins. This preparation is used for the formation of mass by granulating fluid using isopropyl alcohol. Then these masses were passes through the sieve no 16 and put that into an oven with temperature 50 °C. [22]

Table No. 3. HPMC K4M for 100 mg

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Glipizide	13	13	13	13	13	13	13	13	13	13
HPMC K4M	25	25	25	15	11	11	15	15	11	11
Sodium Bicarbonate	11	10	15	15	10	15	10	11	11	10
Citric acid	3	3	3	3	3	3	3	3	3	3
PVP K30	12	12	12	12	12	12	12	12	12	12
SLS	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium Stearate	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
MCC 102	25.6	20.2	21.3	25.7	43.4	42.3	29.5	39.5	45.5	45.5

Table No. 4. Na CMC for 100mg

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Glipizide	13	13	13	13	13	13	13	13	13	13
Na CMC	25	25	25	15	11	11	15	15	11	25
Sodium Bicarbonate	11	10	15	15	10	15	10	11	11	11
Citric acid	3	3	3	3	3	3	3	3	3	3
PVP K30	12	12	12	12	12	12	12	12	12	12
SLS	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium Stearate	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
MCC 102	25.6	20.2	21.3	25.7	43.4	42.3	29.5	39.5	45.5	45.5

Table No. 5. HPMC K4M and Na CMC for100mg

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Glipizide	11	11	11	11	11	11	11	11	11	11
HPMC K4M	25	25	25	15	11	11	15	15	11	11
Na CMC	25	25	25	15	11	11	15	15	11	25
Sodium Bicarbonate	11	10	15	15	10	15	10	11	11	11
Citric acid	3	3	3	3	3	3	3	3	3	3
PVP K30	12	12	12	12	12	12	12	12	12	12
SLS	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium Stearate	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
MCC 102	25.6	20.2	21.3	25.7	43.4	42.3	29.5	39.5	45.5	45.5

2.5 Formulation of Bilayer Tablets:

This bilayer floating tablets contains repaglinide and glipizide. Around 50gm and 100gm of repaglinide and glipizide are weighed and taken. By using direct compression method bilayer tablets were prepared. [23]

Table No. 6. Bilayer tablet (150 mg)

Ingredients	F1	F2	F3	F4	F5
Immediate release layer (50mg)					
Repaglinide	2.73	2.73	2.73	2.73	2.73
Sodium Starch Glycolate	5	3.6	2.5	2.5	5
MCC 102	41.36	43	44	44	41.36
Sodium Lauryl Sulphate	1.7	1.7	1.7	1.7	1.7
Floating Bioadhesive Sustain layer (100 mg)					
Glipizide	12.1	12.1	12.1	12.1	12.1
HPMC K4M	25	25	25	15	11
Na CMC	25	25	25	15	11
Sodium Bicarbonate	11	10	15	15	10
Citric acid	3	3	3	3	3
PVP K30	12	12	12	12	12
SLS	1.5	1.5	1.5	1.5	1.5
Magnesium Stearate	1.5	1.5	1.5	1.5	1.5
MCC 102	25.6	20.2	21.3	25.7	43.4

2.6 Evaluation of Tablets [24, 25, 26, 27]

Weight Variation Test: Electron balance is use for the weight variation.

Hardness: From the formulation tablets are selected and put in between the tester and press until the tablet is break.

Friability test: For performing this evaluation parameter friabilator is use. It was use for 5min and at 25 to 30RPM. After completion of this process the tablets were weigh again.

Friability test = (Weight of tablets before test-weight after test)/(weight of tablets after test))/100

Thickness: If the thickness of tablet is ± 5% it passes the test.

Drug Content: Minimum quantity of tablets was taken for this test and crush them by the help of mortar pistal.After that it was dissolve in 0.1N HCl into 100ml of volumetric flask. Whatman filter paper is use for the filtration of the solution.

Disintegration Test: Disintegration test apparatus has basket rack with six glass tubes and the glass bottom contains mesh sieves. For around 30 to 40times per minutes this basket was raise up and down. Temperature (37 ± 2 °C) is maintained for this test.

Dissolution Test: By using USP dissolution apparatus type II are used for the preparation of different batches of the tablets. 0.1 N HCl is used for the dissolution medium for immediate release layer of tablets and other 0.01 N HCl with SLS of 0.5%w/v is used for the sustained release layer. Temperature (37 ± 0.5∘C) with 60ROM is maintained. After certain interval of time sample was taken and volume was filled with fresh water. For the filtration Whatman filter paper is use.

Wetting Time: Two tablets are taken and HCl buffer with pH 1.2 is use for the wetted of absorbent paper and remaining buffer was drain out from petri-dish. Stopwatch is use for the recording.

Swelling index: The test was performed in a 1l of beaker contains 0.1N HCl at a temperature (37 ± 0.5°C) at a RPM of 60 for 30min. after the completion of this process tablets were remove and weigh the excess amount of tablets.

$$\text{Swelling Index} = (\text{Weight of dry tablet} - \text{weight of swollen tablet}) \times 100 \,)/(\, \text{Weight})$$

Maximal Water Uptake Capacity: Formulated tablet was weighed and put it into a Desiccator for 4hours. Active silica is present in desiccator.

$$\text{Water content} = (\text{weight before drying} - \text{weight after drying} / (\text{weight before drying}))/100$$

2.7 Stability Studies of bilayer

This study was carryout for 6 months. Temperature, humidity and time are used in this process. Aluminium is used for the packing the tablets and it may stable in stability chamber. Evaluation test were done every month. Hardness test, drug content and floating characteristics were tested at every 23hours. [28]

Table No. 7. Stability study

Sr. NO	Condition	Duration(month)
1	40°C/76%RH (acceleration)	6month
2	30°C/66% RH (intermediate)	12month
3	25°C/65% RH (long term)	12month

3. RESULT AND OBSERVATION

3.1 Pre formulation Study

UV spectroscopy: The maximum of repaglidine and glipizide is at 241nm and 276nm.

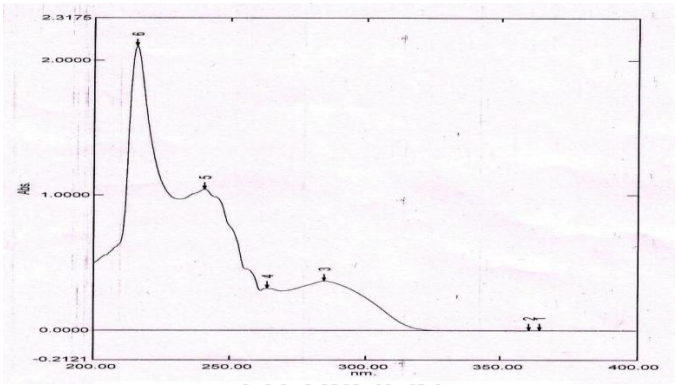

Figure No. 1. Repaglinide

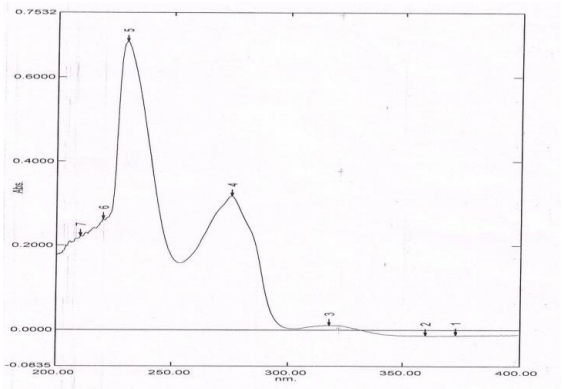

Figure No. 2. Glipizide

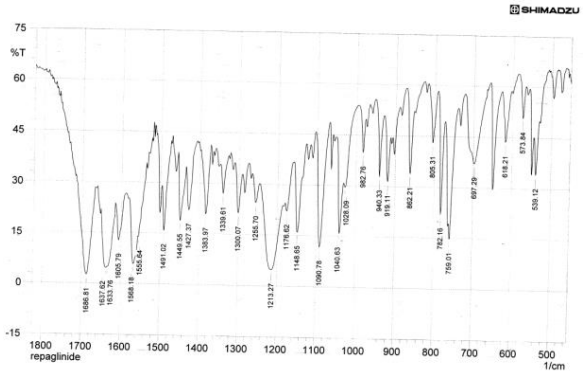

Figure No. 3: Repaglinide

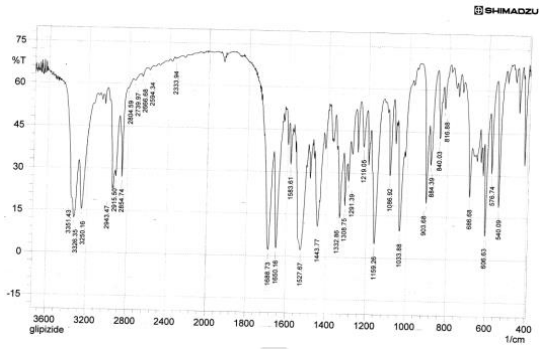

Figure No. 4. Glipizide

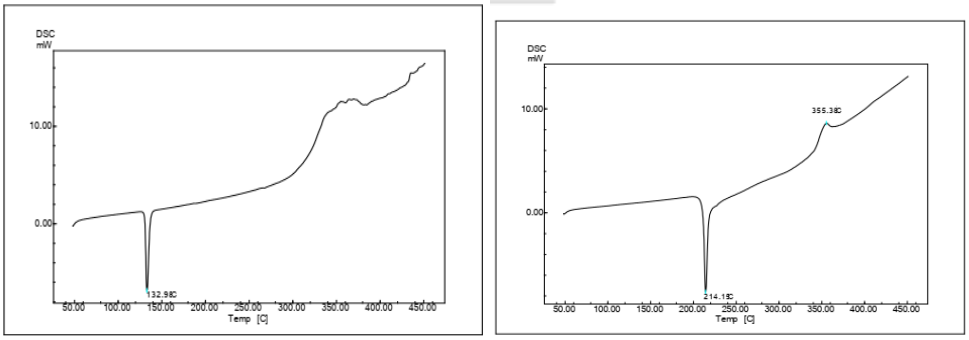

Figure No. 5. Pure Repaglinide and glipizide

The peak of repaglinide was confirmed by DSC study. The peak temperature is at 132.9 °C. from the graph it was confirmed that the melting point of repaglidine is at 131 °C -134 °C.

The peak of glipizide was confirmed by DSC study. The peak temperature is at 214.16 °C. The melting point of glipizide is at 210 °C -214 °C.

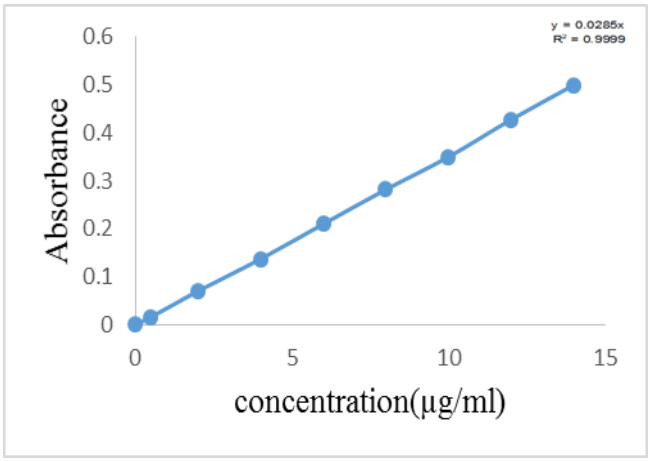

Figure No. 6. Repaglidine (pH 1.2)

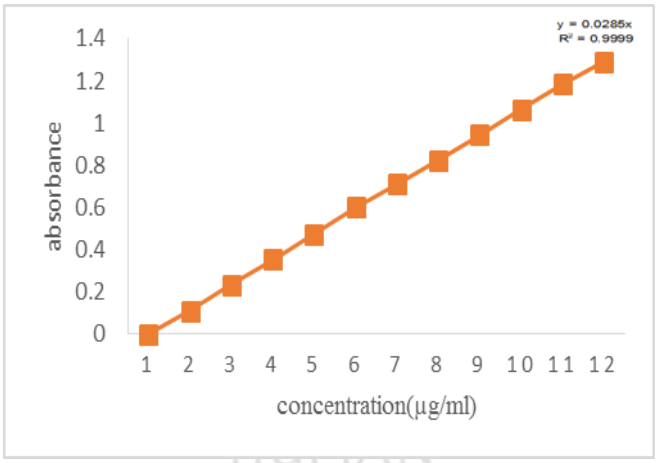

Figure No. 7. Glipizide (pH 1.2 HCl buffer)

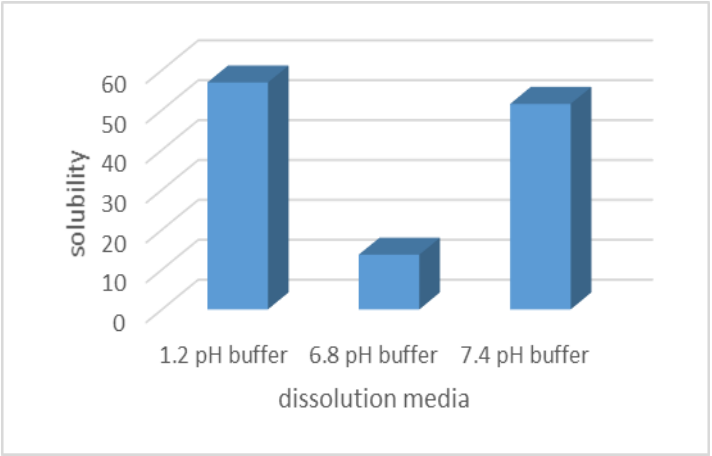

Figure No. 8. Repaglinide solubility

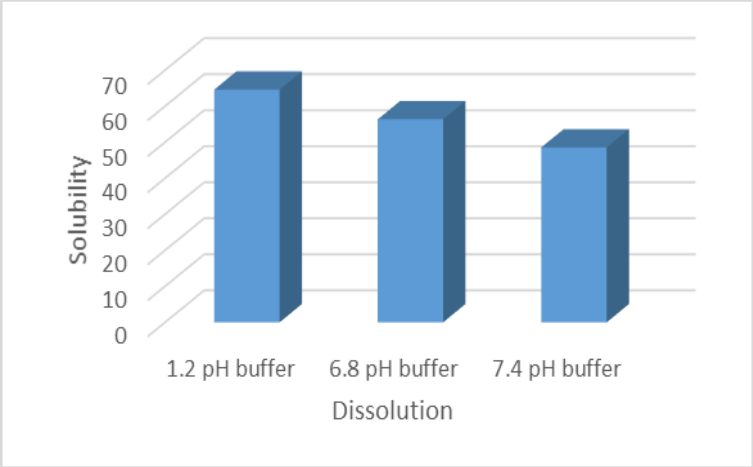

Figure No. 9. Glipizide solubility

3.2 Drug-Excipient Interactions

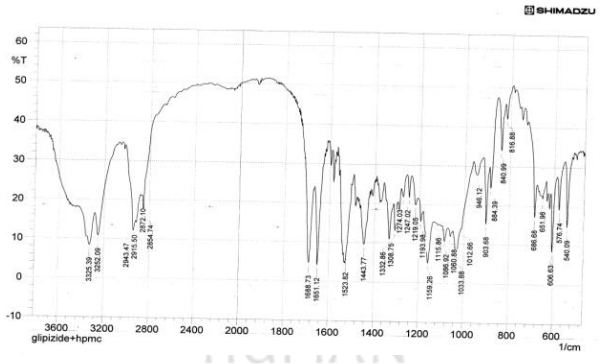

Figure No. 10. FTIR of repaglinide mixture

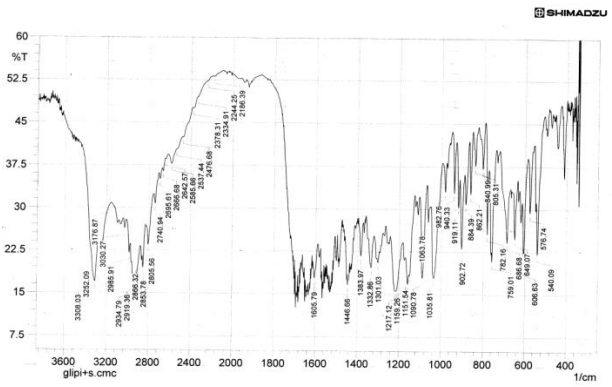

Figure No. 11.FTIR of Glipizide and Na CMC mixture

The drug and excipients interaction are done by FTIR study. This study shows that there is no interaction with functional groups.

3.3 Evaluation of Drugs, polymers and excipients

Table No. 8. Physical parameters of drug, polymers and excipients

Ingredients	Angle of Repose (θ)	Bulk Density gm/cm^3	Tapped Bulk Density gm/cm^3	Hausner's Ratio	Compressibility Index (%)
Repaglinide	29.64±0.31	0.26±0.09	0.40±0.21	1.78±0.25	34.52±1.25
Glipizide	28.56±0.42	0.28±0.15	0.31±0.14	1.15±0.42	25.40±1.52
HPMC K4M	32.56±0.52	0.25±0.05	0.42±0.15	1.19±0.25	24.52±1.25
Na CMC	34.59±0.41	0.26±0.02	0.80±0.16	1.34±0.15	35.63±1.45
SLS	32.15±0.45	0.35±0.06	1.53±0.17	1.49±0.25	38.25±1.63
Sodium Bicarbonate	36.59±0.85	0.65±0.04	1.48±0.06	1.70±0.63	38.25±1.45
Citric acid	29.21±0.75	0.67±0.12	0.93±0.04	1.52±0.75	35.25±1.29
SSG	28.25±0.79	0.70±0.16	1.28±0.35	1.49±0.48	32.35±1.45
Mg stearate	32.58±0.52	0.19±0.21	0.48±0.25	1.68±0.45	41.25±1.75
PVP K30	28.58±1.25	0.30±0.45	0.41±0.25	1.45±0.75	31.25±1.25
M.C.C.	34.85±0.25	0.25±0.75	0.51±0.56	1.35±0.74	34.32±1.05

3.4 Immediate release tablets

Table No. 9. Immediate release powder blend

Formulation	Angle of Repose (θ)	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Hausner's Ratio (HR)	Compr. Index (%)
F1	19.2±0.5	0.56±0.24	0.35±0.47	1.58±0.26	19.20±1.2
F2	25.15±0.6	0.78±0.23	0.55±0.59	1.65±0.29	31.25±1.3
F3	28.60±1.4	0.85±0.45	0.63±0.49	1.70±0.32	45.56±1.5
F4	31.19±1.1	0.86±0.55	0.78±0.65	1.79±0.40	55.69±1.6
F5	38.69±1.2	0.89±0.60	0.82±0.70	1.80±0.48	53.67±1.8

Table No. 10. Post compression parameters of immediate release tablets

Parameters	F1	F2	F3	F4	F5
Hardness (kg/cm^2)	2.6±0.5	2.6±0.5	2.8±0.7	2.9±0.8	3.0±0.9
Friability (%)	0.4±0.2	0.3±0.4	0.3±0.3	0.4±0.5	0.4±0.6
Disintegration time (sec)	45.5±1.6	51.25±1.6	55.25±1.8	58.36±2.8	57.25±2.9
Drug content (%)	99.58±1.4	97.58±1.5	96.58±1.2	95.6±1.2	94.26±1.5
% In vitro drug release	97.85±1.6	97.40±1.9	96.45±1.5	93.45±1.5	93.65±1.8
Weight variation (mg)	51.25±1.6	50.25±1.3	51.26±1.2	51.12±1.2	50.36±1.3
Wetting study (sec)	7.2±0.40	7.0±0.58	6.9±0.68	7.0±0.56	7.0±0.65
Thickness (mm)	1.0±0.011	1.1±0.016	1.1±0.010	1.2±0.019	1.2±0.025

Figure No. 12. Immediate release tablet

Different concentration shows that the formulation F1 having faster wetting ability as compared to different formulation.

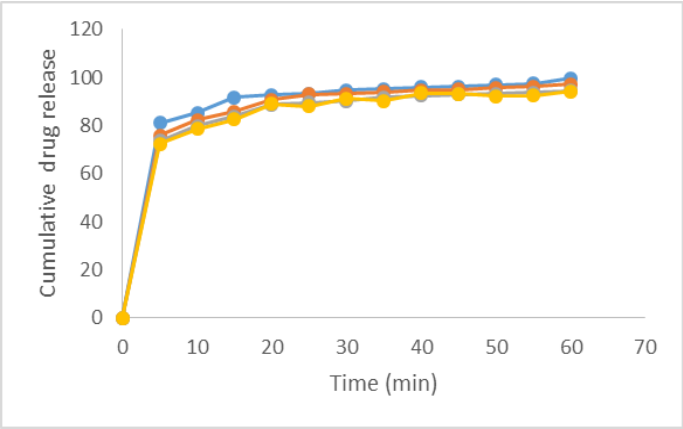

Figure No. 13. Immediate release layer tablet

3.5 Floating bio adhesive sustained release tablets

Table No. 11. Adhesive sustained release layer

Formulation	Angle of Repose (θ)	Bulk Density gm/cm^3	Tapped Density gm/cm^3	Hausner's Ratio (HR)	Compressibility Index (%)
F1	31.26±0.21	0.365±0.21	0.226±0.48	1.10±0.23	9.25±0.17
F2	32.22±0.20	0.300±0.22	0.236±0.35	1.15±0.15	13.59±0.16
F3	33.24±0.25	0.326±0.20	0.234±0.55	1.20±0.16	18.48±0.15
F4	35.23±0.23	0.320±0.19	0.245±0.45	1.21±0.17	9.45±0.12
F5	30.24±0.22	0.301±0.21	0.248±0.65	1.25±0.01	8.48±0.11
F6	32.22±0.21	0.310±0.21	0.196±0.36	1.09±0.03	8.49±0.11
F7	35.26±0.26	0.325±0.22	0.195±0.74	1.45±0.05	10.2±0.17
F8	34.24±0.21	0.356±0.23	0.185±0.36	1.25±0.13	10.3±0.16
F9	32.23±0.27	0.349±0.24	0.178±0.45	1.35±0.12	10.56±0.15
F10	33.23±0.22	0.369±0.29	0.167±0.45	1.46±0.12	8.48±0.14

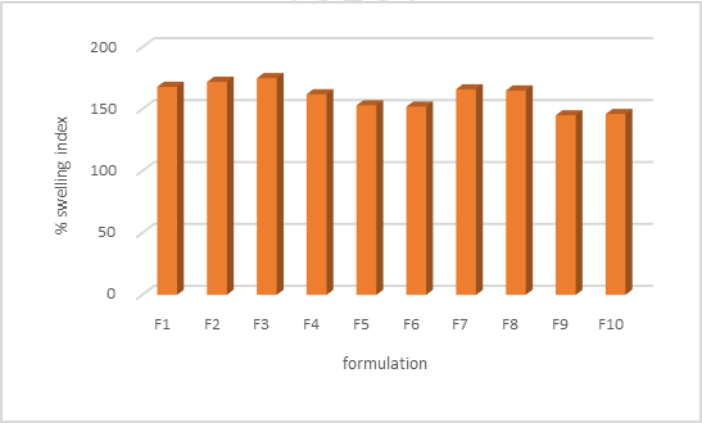

Figure No. 14. Swelling study (F1-F10)

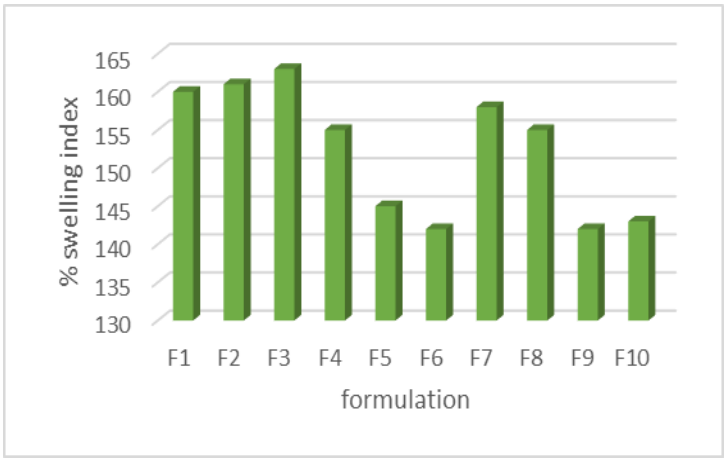

Figure No. 15. Swelling study (F1-F10)

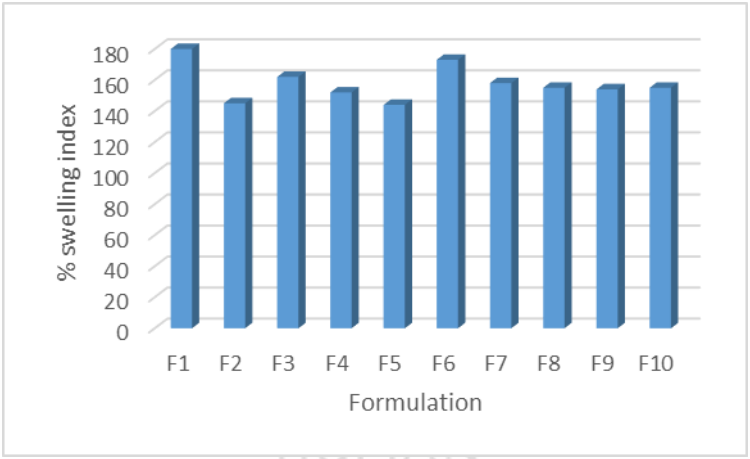

Figure No. 16. Swelling study (F1-F10)

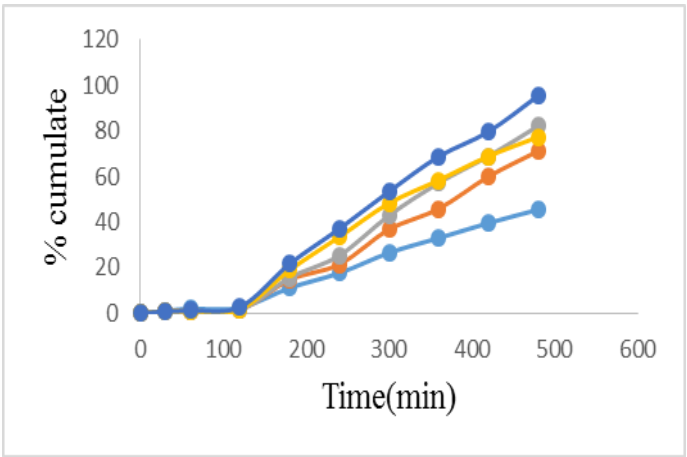

Figure No. 17. Sustained release layer tablets HPMC K4M (F1-F5)

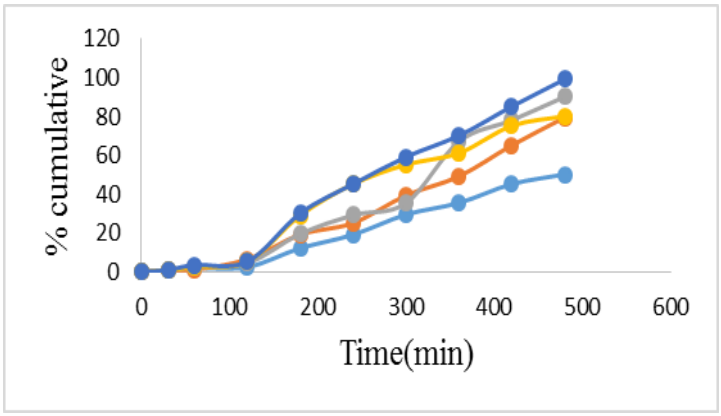

Figure No. 18. Sustained release layer tablets HPMC K4M (F6-F10)

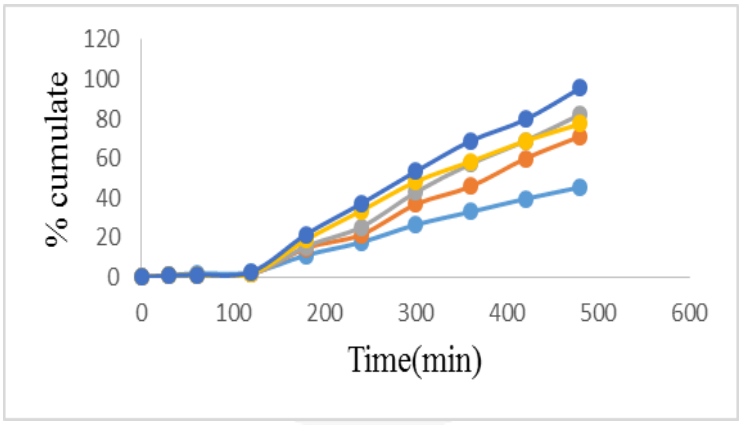

Figure No. 19. Sustained release layer tablets (Na CMC) (F1-F5)

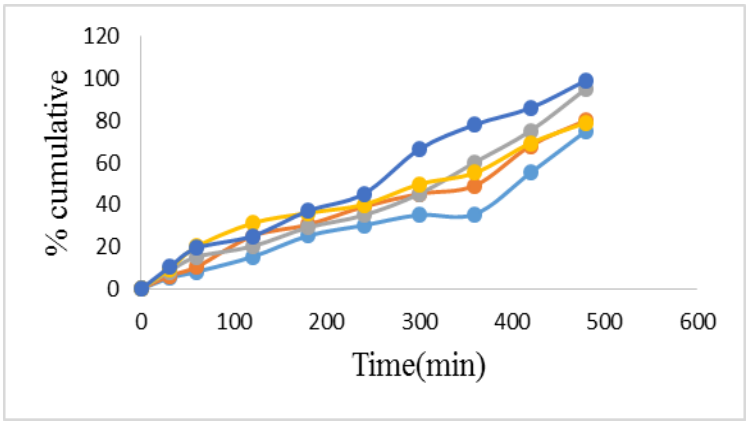

Figure No. 20. Sustained release layer tablet (Na CMC) (F6-F10)

3.6 Evaluation of Bilayer Floating Bio adhesive Tablets

Table No. 12. Evaluation parameter of bilayer floating bio adhesive tablets

Formulation	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	Weight (mg)	Disintegration Time (sec)
F1	6.96±0.08	4.2±0.36	0.4±0.2	150±1.8	39±1.2
F2	6.25±0.09	3.5±0.35	0.5±0.3	160±1.8	38±1.2
F3	6.29±0.05	2.2±0.11	0.6±0.2	155±1.2	38±1.9
F4	6.29±0.07	3.6±0.22	0.4±0.5	150±2.4	37±1.5
F5	6.29±0.06	4.5±0.32	0.3±0.6	150±1.7	41±1.2

For immediate release layer, thickness and drug content are in the range of 90-99% and for sustained release layer 95-99%. The weight variation and friability test were found within the range.

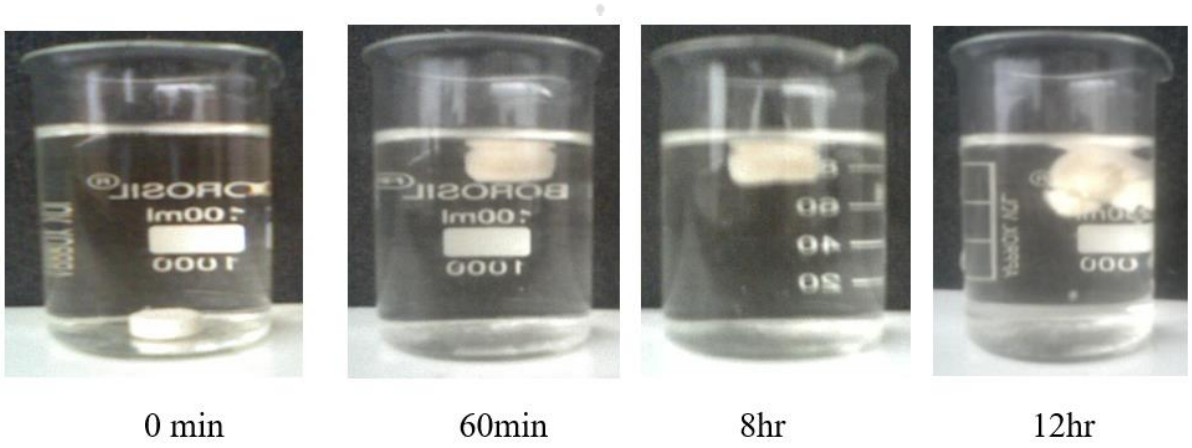

Figure No. 21. Floating behaviour of Bilayer tablet at various interval of time

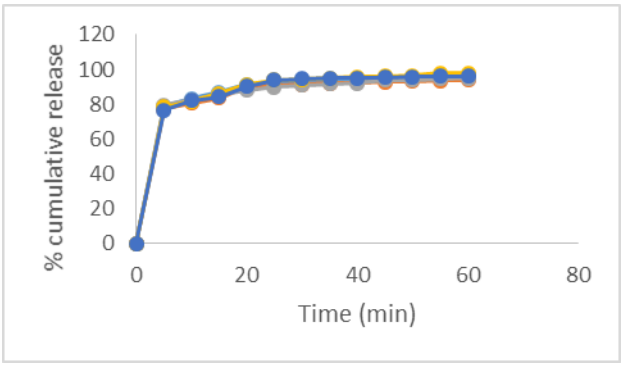

Figure No. 22. Bilayer floating bio adhesive tablets (Immediate release layer)

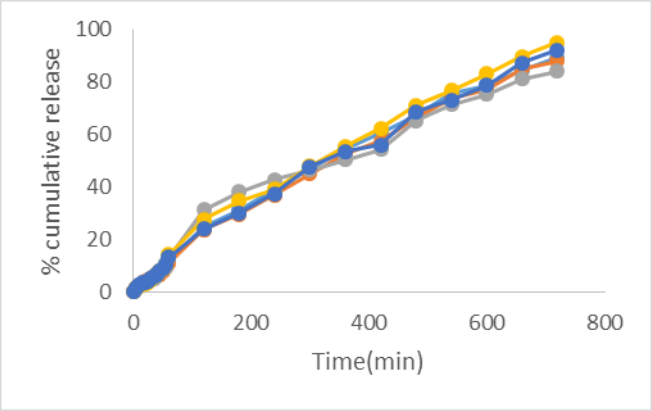

Figure No. 23. Bilayer floating bio adhesive tablets (sustained release layer)

3.7 Stability Study of Bilayer Floating Bio adhesive tablets

Table No. 13. Evaluation parameters for stability study

Parameters	**Before Storage**	**1month**	**2months**	**3months**
Hardness(kg/cm^2)	5.6± 1.6	6.2 ± 0.3	6.1 ± 0.7	6.5 ± 0.8
Friability (%)	1.4 ± 1.2	1.4 ± 0.7	1.6±0.8	1.7± 0.3
Weight variation (mg)	162 ± 1.4	158± 1.2	160 ± 1.5	158 ± 2.0
Disintegration time (sec)	38± 1.2	39± 2.5	38± 2.6	49± 2.9
Drug content for immediate release layer (%)	98.5±1.4	96.97 ± 1.9	96.45 ± 1.2	96.78 ± 1.6
Drug content for floating sustained release layer (%)	99.56±1.6	98.67±1.5	96.48±1.4	98.67±1.4
In-vitro drug release at the end of 60min.for immediate rerelease layer.	96.58±2.9	95.68±2.7	95.58± 1.2	96.75±1.7
In-vitro drug release at the end of 12 hrs for floating bioadhesive sustained release layer.	95.63±2.9	96.58± 1.8	92.58± 1.6	93.89± 1.8
FLT (sec)	142± 2.6	142± 2.9	145± 2.9	146± 2.6
TFT (hrs)	>15	>15	>15	>15

In stability study, for the determination of different parameters sample is withdrawn periodically and analysed. There were no major different were shown in formulation.

4. DISCUSSION AND CONCLUSION

The research study was used to develop the bilayer tablets of repaglindine and glipizide for the management of diabetes. The conventional dosage form in oral administration shows less bioavailability due to the shortage of gastric transition. The resident time may be increased by gastro retentive drug delivery system. It improves the bioavailability in gastric region. Literature survey was done for the depth of the topic and different types of polymers which may increase the release of repaglindine and glipizide. It produces the therapeutic effect. Polymers combination which are used in the study was extended and achieve the release of drugs in gastric retention. Gas generating technique is used for the preparation of tablets by using the polymers (HPMC, hydroxyl ethyl cellulose, polyethylene oxide). The combination of HPMC (hydrophilic) and glyceryl behenate (hydrophobic) is used for the formulation of repaglindine and glipizide.

Selection of drugs are the first steps in analytical development. UV-spectrophotometric is been used for the precise, accurate and development of bulk solution and product finished. Precision, accuracy, limit of detection and quantification and specificity were done by this method. The maximum absorbance shown by repaglindine and glipizide is 241nm and 276nm. Beer's law is used for the standard curve preparation with the coefficient correlation (r^2) = 0.999.

For the development of formulation, a selection and understanding of excipient is very much important. The compatibility study was done by the use of polymers and swelling polymers. There was no major endothermic peak during the DSC thermograms of pure and physical mixture. FTIR shows very weak interaction between the polymers and drugs. So, a strong excipient is used for the development of formulations.

The polymers which are used for the preparation of formulation such as polyethylene oxide, HPMC and hydroxyl ethyl cellulose. Direct compression technique is used for this preparation. The physiochemical property like flow properties, drug content, hardness, friability, thickness, in vitro release and buoyancy study. These tablets were sustained up to 23 hours. the percentage of PEO and HEC may decrease the % drug release. According to

ICH guidelines the stability study was carry out and found that the F7 batches were stable for 6 months.

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