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Preparation and Evaluation of Floating Tablets of Glipizide

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ABSTRACT

This work presents a methodical approach to the design and development of Glipizide cocrystal floating tablets, with the aim of improving the drug's bioavailability and therapeutic effectiveness. Glipizide cocrystal floating tablets are intended to extend the period of stomach residency following oral delivery. They have demonstrated regulated release, allowing for appropriate duration of action at a specific region. Using sodium bicarbonate as a gas-generating agent and Xanthan gum and HPMC K100M as a floating agent, many formulations were created by wet granulation. There was an evaluation of the formulations' physicochemical properties, total floating time, swelling index, buoyancy lag time, and in vitro drug release. It was discovered that the tablets' hardness had an impact on the dosage form's buoyancy feature. Each of the nine formulations had a cumulative floating time of eight to twelve hours and had good floating qualities.

INTRODUCTION

Floating Drug Delivery System may also result in fewer doses being required while enhancing patient compliance since it releases a medication in a regulated or sustained manner with a relatively short half-life. The creation and assessment of a floating medication delivery system for Diabetic medications. Drug absorption throughout the body can be greatly enhanced. This system is expected to float on the stomach fluid without affecting the normal pace of gastric emptying due to its low density. FDDS effectively treats diseases affecting the stomach and small intestine by delivering a longer and sustained medication release in these areas. It reduces variations in the concentration and site specificity of medications, hence reducing unfavorable effects or side effects. Swellable polymers (e.g., methyl cellulose, HPMC, gums) and effervescent chemicals (e.g., acids, tartaric acid) are combined to form gas generating matrix systems. As the system enters the stomach, CO2 is released and then retained by the larger hydrocolloids.

Experimental Work

Glipizide Drug Authentication:

Description

Color: This investigation can be conducted using an instrumental approach or based on visual perception.

Olfactory perception and palatability: The medications' color, smell, and overall look were all visually assessed.

Melting point determination: The Thiele tube is a capillary cylinder that holds a sample and is connected to a glass tube that is used to hold warming oil and a thermometer. At the point when oil is warmed, convection currents can happen in it thanks to the Thiele cylinder's design.

Solubility study: By introducing an excess of the drug to 10 milliliters of distilled water in glass tubes that were sealed with aluminum foil, the solubility of the drug was assessed. The resulting suspension was filtered after being agitated for 48 hours on a mechanical shaker. After diluting the resulting filtrate with distilled water, a UV spectrophotometer was used for spectrophotometric analysis.

Spectroscopic studies:

UV spectroscopy

Standard calibration curve for Glipizide

Preparation of dissolution medium (0.1NHydrochloricAcid):

0.1NHCl solution was prepared as per procedure reported in IP1996.

Dissolve 8.5ml of concentrated hydrochloric acid in 1000ml of distilled water to get 0.1 N hydrochloric acid.

Preparation of standard calibration curve for Glipizide:

The exact dosage of Glipizide (15 mg) is measured out using a precise measuring device. To make 50 millilitres, dissolve the tablet in a small quantity of distilled water and add 0.1N HCl. The 10 mL pipette contains this vital stock solution, while the 100 mL solution is prepared with 0.1N HCl. To get 2, 4, 6, 8, and 10 µg/ml, portions are taken from this secondary solution and mixed with 0.1 NHCl to a volume of 100 ml. After adding 0.1N HCl as a transparent solution, the absorbance of the final product is measured at 233 nm using a UV-Visible Spectrophotometer. Plotting the absorbance against the fixation on the X-axis yields the standard bend. During in vitro dissolving investigations, the alignment bend is utilised to evaluate the quantity of drug fixation released.

Fourier Transform Infrared Spectroscopy (FTIR): Using the KBr powder press method, the FT-IR spectra of glipizide was recorded to verify their purity on the FTIR spectrophotometer (FTIR 8400S, Shimadzu). Dried potassium bromide was used to do the baseline correction. Over the 4000-400 cm-1 range, the instrument was operated under dry air purge with a resolution of cm-1. The primary drug peaks in the scans were assessed for their existence. The principal peaks of the published infrared spectra were compared with the identified peaks.

Differential Scanning Colorimeter (DSC): To confirm the virtue of Glipizide, a DSC thermogram was performed. Differential Scanning Calorimetry (METTLER TOLEDO, Star SW 920) was used to record the DSC thermogram.

Design of Factorial batches

A 32-factorial design was implemented to enhance the formulation of Glipizide cocrystal gastroretentive drifting tablets. The model indicated that it contained two independent variables at three levels (+1, 0, and -1). The model indicates that nine formulations are feasible; Table illustrates the essence of each formulation. The two independent variables were the concentrations of HPMC K100M (X1) and Xanthan gum (X2). The dependent variables included in vitro drug release (Y3), swelling index (Y2), and drifting delayed time (Y1).

Table: Factorial design for the preparation of batches F1-F9.

Batches code	**Variable level in coded form**	
	X1(HPMCK100 M)	**X2**(Xanthan gum)
F1	-1	-1
F2	-1	0
F3	-1	+1
F4	0	-1
F5	0	0
F6	0	+1
F7	+1	-1
F8	+1	0
F9	+1	+1

Table Translation of coded value in actual unit.

Variable level	**Coded Level**		
	-1	**0**	**+1**
X1=Concentration of HPMC K100M (mg)	20	25	30
X2=Concentration of Xanthan gum (mg)	25	30	35

Table Composition of Factorial Batches.

Formulation code / Ingredients (mg)/tablet	F1	F2	F3	F4	F5	F6	F7	F8	F9
Glipizide cocrystal equivalent to	16	16	16	16	16	16	16	16	16
HPMCK100M	20	20	20	25	25	25	30	30	30
Xanthan gum	25	30	35	25	30	35	25	30	35
Sodium Bicarbonate	80	80	80	80	80	80	80	80	80
PVPK30	10	10	10	10	10	10	10	10	10
Mg. Stearate	10	10	10	10	10	10	10	10	10
Talc	7	7	7	7	7	7	7	7	7
MCC	32	27	22	27	22	17	22	17	12
Total weight(mg)	200	200	200	200	200	200	200	200	200

Preparation of factorial batches

Table describes the manufacturing technique used to create floating tablets containing glipizide cocrystal. It involves a wet granulation process with varied proportions of different grades of polymers. All components are precisely weighed prior to being filtered through a variety of mesh sieves. Powder and magnesium stearate are introduced as a post-grease after the drug and other components have been consolidated, and the mixture is stirred for an additional few minutes. Before compression, the powder mix's properties were assessed. 200 mg of the powder mix is gauged and compressed into punches with a 12 mm breadth using a revolving punch tablet compression machine. An experimental design known as a two-factor factorial

design gathers information for each possible mix of the two factors of interest's values. The design is a reasonable two-factor factorial design in the event that equivalent sample sizes are gotten for each feasible factor blend. A reasonable a × b factorial design has n separate replications at each of the a × b treatment combinations, a degree of factor A, and b levels of factor B. As N = abn, the design size is. The typical change in the response correlated with an adjustment of the factor's level is known as the impact of the factor. Usually, we allude to this as the chief impact. There is an interaction between the factors if the average change in response at all levels of one factor is different from all levels of the other component.

Method of Preparation of Floating Effervescent Tablet:

The following techniques are used to prepare the floating effervescent tablet:

Wet granulation:

This is the most widely used and comprehensive method for creating tablets. Granules containing the medication and effervescent ingredients form. When granulating with pure water or solvents that include water, the effervescent reaction will start. To keep proper control over the process, caution must be exercised. Because vacuum processing can regulate both the effervescent response and the drying process, it is frequently advantageous.

PRE-COMPRESSIONAL EVALUATION OF POWDER BLEND

It was performed for bulk density, tapped density, compressibility index, housner’s ratio and angle of repose.

POST COMPRESSIONAL EVALUATION OF GLIPIZIDE COCRYSTAL FLOATING TABLETS

It was performed for Tablet thickness, hardness, friability test, weight variation, drug content, In vitro buoyancy studies, swelling studies and drug release studies.

Result and Discussion

Drug Authentication

Sr.No	Test	Specification	Observation	Interference
1	State	Solid crystalline	Solid crystalline	Complies
2	Colour	White	White	Complies
3	Odour	Odour less	Odour less	complies

Melting Point:

The capillary technique was used to calculate the drug's melting point, which came out to be 202^0C.

Solubility Study:

It dissolves very little in ethanol and water and very marginally in acetone and dichloromethane.

EVALUATION OF FACTORIAL DESIGN FORMULATIONS

PRE-COMPRESSIONAL EVALUATION OF POWDER BLEND:

The particle mix of the numerous plans was evaluated for the pre-pressure boundaries, including the mass thickness, tapped thickness, compressibility file, Hausner's proportion, and point of rest.

Bulk Density:

Indicates that the powder mix were not massive. The results were shown in Table. By emptying the mix into a graduated cylinder, the clear mass density (ρb) was ascertained. The powder's mass volume (Vb) and weight (M) were determined.

Tapped density:

The powder mix's tapped thickness went from 0.923 to 0.930 grams per milliliter. The results were shown in Table. The estimating chamber containing the assigned mass of blend was tapped for a specific timeframe.

Compressibility index (CI):

The compressibility index ranged from 6.82% to 10.33%, suggesting that the powder mix has adequate flow characteristics for compression. The outcomes were displayed in Table. Since compressibility reveals how readily a material may be made to flow, it is the easiest way to measure the free flow of powder.

Hausner's ratio:

The powder mix's Hausner's ratio was determined to be between 1.07 and1.22, indicating that the blend has good flow qualities. The outcomes were displayed in Table.

Angle of repose:

The point of repose for the formulated powder mix was viewed as in the scope of 23º.19' to 24º.7', which indicates great stream properties of powder mix and thus direct compression technique was taken on. The results were shown in Table.

Table Pre-compressional examination of the powder blend's results

Batch	Bulk Density (gm/ml)	Tapped Density(gm/ml)	Angle of Repose (θ)	Hausner'sRatio	Carr's Index (%)
F1	0.566 ±0.166	0.627±0.17	24±0.534	1.13±0.026	11.8 ±0.20
F2	0.589±0.876	0.676±0.3	28 ±0.333	1.12±0.034	11.06 ±0.13
F3	0.612 ±0.242	0.685±0.11	23±0.768	1.10±0.089	11.75 ±0.27
F4	0.559 ±0.495	0.695±0.7	24±0.373	1.09±0.096	8.69 ±0.56
F5	0.591±0.293	0.689±0.9	25±0.635	1.10±0.034	11.47±0.47
F6	0.627±0.174	0.695±0.11	25±0.635	1.10±0.089	9.64 ±0.18
F7	0.614±0.151	0.694±0.5	24±0.534	1.10±0.034	11.56 ±0.32
F8	0.549 ±0.583	0.662±0.3	24 ±0.847	1.09±0.089	9.86 ±0.34
F9	0.561 ±0.912	0.669±0.6	25 ±0.635	1.08±0.096	8.87 ±0.16

*All values represent mean±SD(n=3).

POST-COMPRESSIONAL EVALUATION OF GLIPIZIDE FLOATING TABLETS :

Assessment tests were conducted on tablets with varying formulations, including thickness, width, hardness, friability, weight variety, drug content, in-vitro buoyancy studies, swelling index, and in-vitro drug release**.**

Tablet thickness:

The thickness of the tablet was determined using a vernier calliper, and the results are presented in Table.

Table: Thickness of F1-F9 formulation

Evaluation Parameter	Thickness(mm)*
F1	3.34±0.09
F2	3.35±0.08
F3	3.5±0.07
F4	3.44±0.08
F5	3.51±0.06
F6	3.29±0.03
F7	3.34±0.05
F8	3.46±0.09
F9	3.33±0.06

*All values was represented as mean ±SD (n=3)

Hardness

The tablets' hardness was measured and it was found to be between 5.1 and 5.9 kg/cm2. This suggests that the tablets have strong mechanical strength and can tolerate handling-related physical and chemical stress. Table displayed the findings.

Table: Hardness of F1-F9 formulation

Evaluation Parameter	Hardness(kg/cm²)*
F1	8.17±0.48
F2	8.16±0.43
F3	8.28±0.53
F4	9.23±0.3
F5	8.86±0.42
F6	9.92±0.41
F7	9.76±0.57
F8	9.42±0.37
F9	9.35±0.55

*All values was represented as mean ±SD (n=3).

Friability Test:

All of the formulations had a percentage friability ranging from 0.45% to 0.30%. In every formulation, the percentage friability was less than 1%, indicating that the tablet has strong mechanical resistance.

Table: Friability of F1-F9 formulation

Evaluation Parameter	Friability (%)*
F1	0.40±0.04
F2	0.55±0.5
F3	0.49±0.5
F4	0.46±0.3
F5	0.52±0.4
F6	0.47±0.2
F7	0.49±0.7
F8	0.42±0.1
F9	0.45±0.3

*All values was represented as mean±SD (n=20).

Weight variation Test:

Table : Weight variation of F1-F9 formulations

Evaluation Parameter	Weight variation(mg)*
F1	200.2±1.2
F2	199.3±2.3
F3	201.4±1.1
F4	199.3±2.1
F5	200.1±0.4
F6	199.5±1.7
F7	201.8±1.5
F8	200.4±0.8
F9	199.9±2.4

All values was represented as mean±SD (n=20)

Estimation of drug content for tablets:

The drug was evenly distributed throughout all of the formulations, as evidenced by the rate at which the drug content of the relative variety of formulations fell between 99.16% and 99.89%. Limits: not less than 90% and not more than 110%, according to U.S.P.

The results were shown in Table

Table: Drug content of F1-F9 formulations

Evaluation Parameter	Drug Content(%)
F1	98.06±0.23
F2	97.03±1.13
F3	99.27±0.31
F4	99.36±0.71
F5	99.72±0.34
F6	99.51±1.07
F7	98.13±0.75
F8	98.37±0.83
F9	99.16±0.14

*All values was represented as mean ±SD(n=3)

In vitro buoyancy studies:

Total Floating Time (TFT), also known as Floating Lag Time (FLT) or Lightness Lag Time (BLT), is the amount of time that a dosage form stays light once it emerges on the medium.

Table: Data of In-vitro buoyancy study of F1-F9 formulation

Formulation Code	Floating Lag Time (min)	Total Floating Time(hrs)
F1	2 min	>7
F2	3 min	>8
F3	3 min	>8
F4	3min35sec	>8
F5	3min50sec	>7
F6	2min35sec	>8
F7	1min50sec	>8
F8	2min15sec	>8
F9	4min10sec	>9

Swelling studies:

For eight hours, a swelling research was conducted on all of the batches (F1 through F9). Table presented the swelling index data

Table: Swelling index of F1-F9 formulations

Time (hr.)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	38.89	44.71	43.08	42.08	55.80	52.08	46.94	61.40	56.84
2	47.72	52.81	55.47	56.75	66.93	68.45	56.02	77.84	88.54
3	51.17	57.18	60.71	60.86	75.67	90.37	75.25	86.24	101.28
4	54.19	63.37	70.75	75.78	95.54	115.20	90.10	94.49	118.02
5	67.48	75.86	86.24	91.08	110.72	121.59	95.75	101.84	131.08
6	78.45	98.45	99.75	98.65	124.32	136.21	103.42	119.54	146.66
7	102.58	114.58	123.14	109.56	135.41	143.87	110.48	122.42	159.24
8	90.12	122.37	132.25	114.78	141.58	154.87	119.26	125.65	167.54

In vitro drug release studies:

HPMC K100M and Xanthan gum were used to make the formulations in order to boost the drug's release retardation. When the high viscosity grade polymer comes into contact with the aqueous medium, it causes a highly viscous gel layer to develop, slowing down the pace at which the medium diffuses into the tablet. This might delay or lessen the release of the medicine. Drug release was shown to decrease when Xanthan gum content increased when combined with HPMC K100M. The findings are displayed in Table and Figure.

Table: Drug release (%)of formulationF1-F9

Ti (hrs.)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	8.50	8.21	5.21	7.98	7.22	6.55	8.64	8.93	3.69
2	12.97	11.34	13.39	12.74	12.34	13.62	17.97	14.87	8.50
3	24.74	19.37	18.93	20.70	25.77	20.62	31.77	27.65	12.97
4	39.04	37.71	27.26	36.70	45.76	36.86	48.00	42.67	24.73
5	46.81	45.27	41.26	55.47	57.54	42.89	57.08	50.32	39.04
6	63.49	58.29	67.48	61.75	82.50	56.79	76.00	58.08	46.81
7	74.55	80.68	76.55	75.77	89.79	67.26	86.13	67.46	55.08
8	84.26	89.68	91.19	90.67	95.72	74.83	98.13	76.46	63.99

The best formulation, F7 (HPMC K100M 60% and Xanthan gum 40%), was chosen out of the nine formulations because it had the highest retardant impact (98.13% in 8 hours).

Research has indicated that some polymers, including xanthan gum and hydroxypropyl methylcellulose, are classified as floating polymers that exhibit more floating qualities than other polymers. These polymers have tracked down application in the assembling of floating tablets. These polymers' qualities are improved since they are very much hydrated and can drift, especially when used in blend (Ahuja, et al.1997). To improve the drug absorption process in a site-specific way, floating systems are used to confine a conveyance gadget inside the body's lumen and cavity (Chickering and Mathiowitz 1999). The technique makes use of polymers that might drift to the gastrointestinal plot's. Studies on drug release were conducted to ascertain if the medication was released at a sufficiently slow pace, or, alternatively, what proportion of polymer was required to maintain the drug's release for a minimum of eight hours. The proportion of medication released at comparable periods rose dramatically when the HPMC content of the tablets was increased. This resulted from HPMC rapidly eroding and expanding when it came into touch with stomach contents. Comparing tablets with identical formulations but varying effervescent base concentrations reveals that the drugs release more

quickly from tablets containing 10% gas-generating agent than from those containing 5%. This was caused by the medication diffusing more quickly, the polymer matrix expanding more, and the liquid medium penetrating the tablet better.

Conclusion

The F7 formulation yields the best results out of the relative multitude of formulations in terms of floating time (1 moment and 50 seconds) and drug release profile (97.94% in 8 hours).

According to the study, Xanthan gum and HPMC K100M may be promising polymers for gastroretentive drug conveyance systems.

The formulation batch F7, which was made using the wet granulation process and contained 30 mg of HPMC K100M and 25 mg of Xanthan gum, showed the least amount of floating time and the highest rate of drug release, according to the data. Thus, it was thought that this formulation was optimal. Therefore, glipizide floating tablets provide a better option than traditional dose forms for increasing patient compliance.

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