Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2013, 5(2):82-96

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Formulation and *invitro* evaluation of gastroretentive floating tablets of glipizide

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ABSTRACT

Glipizide an oral anti-diabetic agent a second generation sulfonylurea is poorly soluble in water and majorly absorbed from upper GI tract. It has an elimination half-life of about 2–4 h. It is a rapidly absorbed drug having faster elimination rate. In the present study an attempt was made to prepare the Floating matrix tablets of Glipizide were prepared by Effervescent floating technique. The formulations were prepared by polymers HPMC 5cps and carbopol 940 used for matrix system, and incorporating $NaHCO_3$ into tablets resulting in floating of tablet in simulated gastric fluid. Physical mixtures were evaluated for bulk density, tapped density, Carr's index and Hausner ratio. Characterization of drug and polymer mixture were done by performing FTIR and it was concluded that there was no interaction between the drug and polymer as the principle peaks of the drug were found unaltered in the IR spectra of drug polymer physical mixture. Tablets were formulated with different ratios of HPMC 5cps and carbopol 940 individually and combination of polymers. The formulations were evaluated for physical tests, buoyancy lag time and dissolution.

Key words: Carbapol 940, HPMC,Gastro retentive floating tablet,

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INTRODUCTION

In an attempt to retain the dosage form for a prolonged period, gastroretentive system has been developed for the last two decades and is a topic of interest in terms of their potential for the controlled drug delivery at the target site. Davis firstly described the concept of floating drug delivery system (FDDS). Gastric emptying of dosage forms is an extremely variable process and placement of drug delivery system in a specific region of the GI tract offers numerous advantages, especially the drugs having narrow absorption window in GI tract, primary absorption in the stomach, stability problem in the intestine, poor solubility at alkaline pH, local activity in stomach, and property to degrade in the colon. It has been suggested that compounding the drugs with narrow absorption window in a unique pharmaceutical dosage form which prolongs the gastric residence time would enable and extended absorption phase of these drugs[1].

EXPERIMENTAL SECTION

Various chemicals used are Glipizide- Franco India, Chennai , HPMC 5cps- CDH, New Delhi ,Carbopol 940- Ranikem Ltd, Mumbai, Sodium bicarbonate- Loba chemie, Mumbai , Citric acid- Loba chemie, Mumbai, Micro crystalline cellulose, Poly vinyl pyrollidine K 30, Talc, Magnesium stearate, - CDH, New Delhi, N N Dimethyl Formamide- Merck India Ltd, Hydrochloric acid- S.D Fine chemicals Ltd, Ethanol- SISCO Research Lab Pvt Ltd, Demineralised Water- Ind.Scientific enterprises.All are of analytical grade.

Equipments used are- FTIR- ABB BOMEM 104 series, UV Spectrophotometer- Shimadzu, UV-1601 Japan, Dissolution apparatus- Electro Lab TDT-08L, Mumbai, Rotary punching machine- Rimek mini press-I, Bulk density

apparatus- Pharmatools Mumbai, Hardness tester- Pfizer, Friabilator- Electro Lab, India, Electronic balance- Metter, Japan.

PREFORMULATION [3]

Preformulation testing is the first step in the rational development of dosage forms of a drug substance. It can be defined as –"an investigation of physical and chemical properties of a drug substance alone and when combined with excipients". The overall objective of preformulation testing is to generate information useful to the formulation in developing stable and bioavailable dosage forms that can be mass produced. The formation preformulation should start at the point after biological screening, when a decision is made for further development of compound in clinical trials.the preformulation scientist should consider the following before going through the formal program which includess:

Available physico chemical data (including chemical structure and different salts available),Anticipated dose,Supply situation and development schedule,Availability of stability,assay,Nature of information the formulator should have or would like to have. The overall objective of preformulation studies is to generate information useful to the formulator in developing stable and bioavailable dosage forms.

Organoleptic properties The Organoleptic character of the drug like color, odour, taste and appearance play an important role in the identification of the sample and hence they should be recorded in an descriptive terminology.

Bulk density Bulk density of a compound varies substantially with the method of crystallization, milling or formulation. Bulk density is determined by pouring pre sieved blend into a graduated cylinder via a large funnel and measure the volume and weight is given by.

Bulk density = weight of the blend /bulk volume of the blend

Tapped density Tapped density is determined by placing a graduated cylinder containing known mass of blends on a 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 drug in the cylinder and this minimum volume, the tapped density may be computed.

Tapped density =weight of blends/ tapped volume of blends

Hausners ratio

Hausener ratio was determined as the ratio between the tapped density to that of the bulk density.

H.R = Tapped Density / Bulk Density

Carr's index Carr's index is measured using the values of the 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

Table No.1

Compressibility Index (%)	Flow character	Hausners Ratio
≤10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very poor	1.46-1.59
>38	Very very poor	>1.60

Angle of repose The manner in which stresses are transmitted through a bed and the beds response to applied stress are reflected in the various angles of friction and repose. The most commonly used of these is angle of repose, which may be determined experimentally by a number of methods. The method used to find the angle of repose is to pour the powder in a conical heap on a level, flat surface and measure the inclined angle with the horizontal pile

$\tan\theta = h/r$

$\theta = \tan\text{-}1\ h/r$

Where, h- Height of the heap, r- Radius of the heap

Table No.2 Relationship belongings angle of repose & powder flow

S.No.	Angle of repose (a) degrees	Flow
1	< 25	Excellent
2	25-30	Good
3	30-40	Passable
4	40 & above	Very poor

Solubility Studies

It is important to know about solubility characteristics of a drug in aqueous systems, since they must possess some limited aqueous solubility to elicit a therapeutic response. Quantitative determination of solubility was made by preparing saturated solution of drug in a constant volume of pH 1.2, buffers and resulting solutions were kept at room temperature for 24 hours with intermediate shaking.

The resulting solutions were filtered and analyzed for dissolve drug by U.V spectrophotometry at λmax of 275 nm.

By I.R Spectroscopy

Glipizide discs were prepared by pressing the Glipizide with potassium bromide and the spectra between 4000^{-1}cm -500^{-1}cm was obtained under the operational conditions. The absorption maxima in spectrum obtained with the substance being examined correspond in position and relative intensity to those in the reference spectrum represented in Table 6 & Fig2.1 respectively

STANDARD CURVE OF GLIPIZIDE

Preparation of 0.1N HCL

8.5 ml of concentrated HCL is dissolved in water and the final volume was made upto1000ml with distilled water.

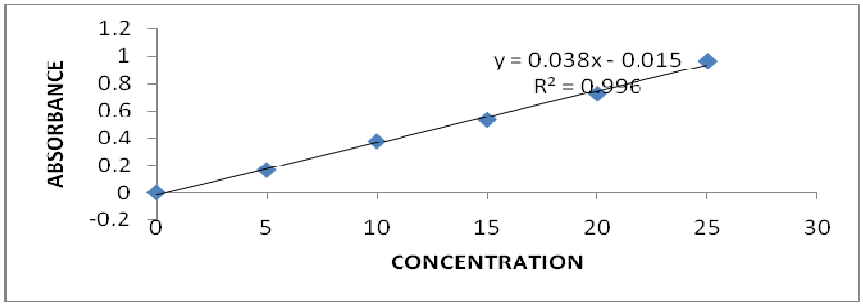
PREPARATION OF STOCK SOLUTION IN 0.1N HCL:

100 mg of Glipizide was dissolved in 0.1N HCl in a 100ml standard flask and the volume was made upto 100ml, Serial dilutions were made in 0.1N HCl in order to obtain 5 µg/ml, 10 µg/ml, 15µg/ml, 20 µg/ml, 25 µg/ml,. Absorbances of these solutions were measured at 275nm using UV-Visible Spectrophotometer [Schimadzu 159] and standard graph was plotted[7].

Table No.3 Standard Curve of Glipizide in 0.1N HCl

S.NO	CONCENTRATION (mcg/ml)	ABSORBANCE
1	5	0.165
2	10	0.375
3	15	0.534
4	20	0.725
5	25	0.965

Figure No.1 STANDARD CURVE OF GLIPIZIDE



PROCEDURE:
5.3 PREPARATION OF GLIPIZIDE FLOATING TABLETS

- Nine formulations (GFT1, GFT2, GFT3, GFT4, GFT5, GFT6, GFT7, GFT8, and GFT9) of varying constituents were prepared.
- Nine floating matrix formulations of Glipizide based on gas forming agent were prepared. HPMC 5cps and Carbopol 940P were used in formulating the matrix system. Incorporation of sodium bicarbonate into matrix resulted in the tablet floating over simulated gastric fluid for sustained release.

DIRECT COMPRESSION:
Manufacturing process:
Step I: Sifting of Raw Materials
Sift Glipizide, HPMC5cps, sodiumbicarbonate , citric acid, microcrystalline cellulose, magnesium stearate, magnesium stearate,and talc through #40 mesh seperately, collect in poly bags.

Step II: Pre blending
Sift Glipizide, HPMC 5cps, sodium bicarbonate, citric acid, microcrystalline cellulose, magnesium stearate, magnesium stearate blender and mix for 10 minutes

Step III: Compression
Fix the tablet machine and compress the powder blend using 10x10mm round punches as per the SOP.

Table No.4 FORMULATIONS

Name of the ingredient	GFT1	GFT2	GFT3	GFT4	GFT5	GFT6	GFT7	GFT8	GFT9
Glipizide	15	15	15	15	15	15	15	15	15
HPMC 5cps	30	45	60	-	-	-	60	60	60
Carbopol 940	-	-	-	30	45	60	15	30	45
Sodium bicarbonate	20	20	20	20	20	20	20	20	20
Citric acid	5	5	5	5	5	5	5	5	5
Poly vinyl pyrrolidine K -30	5	5	5	5	5	5	5	5	5
Micro crystalline cellulose	120	105	90	120	105	90	75	60	45
Magnesium stearate	5	5	5	5	5	5	5	5	5

CHARACTERIZATION OF GLIPIZIDE FLOATING TABLETS (GFT1-GFT9)

Tablet Size
Thickness of the tablet was measured by using Vernier caliper in mm. Thickness of fabricated tablets (GFT1-GFT9) is presented in Table no.10.

Hardness test
Hardness test was carried out by using Pfizer hardness tester. Hardness of fabricated tablets (GFT1-GFT9) is presented in Table 10.

Friability test
Friability of the tablets was tested using Roche friabilator. Loss of less than 1% in weight is considered to be acceptable. The weight of 10 tablets was noted initially (W1) and placed in the friabilator for 5 min / 100 rpm. The tablets were reweighed and noted as (W2). The difference in the weight is noted and expressed as percentage. Friability[12] of fabricated tablets (GFT1-GFT9) is shown in Table 10.

Percentage Friability = (*W1 – W2)/W1 * 100*
Official Limit not more than 1%

Weight variation test
Twenty tablets were selected at random and the average weight was determined. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in table no.15 and none deviates by more than twice the percentage.

Official limit[6] of Glipizide Floating formulations (GFT1-GFT9) percentage deviation is ±7.5%.

S.NO	Average weight of tablet	Percentage
1	80 gm or less	±10 %
2	More than 80 mg and less than 250 gm	±7.5 %
3	250 mg or more	± 5 %

The average weight and percentage deviation of (GFT1-GFT9) are presented in Table 5.

Buoyancy determination:
In practice floating time and buoyancy lag time was determined by using beaker[2] containing 100 ml of 0.1N HCl, which was maintained at 37ºC. The time required for the tablet to rise to the surface of the medium was determined as Buoyancy Lag time and the duration of which the tablet floats on the surface of the medium was noted as the Buoyancy floating time. Results (GFT1-GFT9) are presented graphically in Table 11.

Drug content
Drug content of the tablets were determined by using UV visible spectrophotometer.10 tablets were taken and powdered. The tablet powder equivalent 100 mg of Glipizide was accurately weighted and transferred to 100 ml volumetric flask and the volume was made up to 100 ml with 0.1N HCL of pH1.2, 1ml of the aliquot was further diluted to 100 ml with 0.1N HCl. The absorbance was measured at 276 nm. Results were presented in table 10.

***In vitro* Dissolution of Fabricated Tablets** (GFT1-GFT9)
Tablet's dissolution was assessed using standard USP Dissolution apparatus (paddle) equipment in 900 ml of 0.1N HCl. The stirring speed of 100 rpm for the basket was used. The Glipizide tablets were subjected to dissolution testing in 900 ml dissolution medium. Three tablets were taken in each batch and a temperature of 37 ºC was maintained throughout the experiment. Dissolution studies were carried out for 24 h. 5ml of the Aliquot was taken at intervals of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12 and 24 h. After collecting the sample, the dissolution medium was replenished with the same volume of fresh medium, and the sample was filtered 1ml of the filtrate was diluted to 10ml with the phosphate buffer and analyzed spectrometrically at 275 nm. The results were shown in table 12.1-12.4 and in Fig.5.1-5.4 respectively.

RELEASE KINETIC STUDY[7, 8] The rate and mechanism of release of Glipizide through the prepared Floating matrix tablets were analyzed by fitting the drug release data into

Zero order equation:

$Q = Q0 - K0\ t$

In this equation Q is the amount of drug remaining undissolved at time t, Q0 is the amount of drug undissolved at t = 0 and K0 is the corresponding release rate constant .

First order release equation:

$\ln Q = \ln Q0 – K1t$

Where M is the amount of drug undissolved at time t, M0 is the amount of drug undissolved at t = 0 and K1 is the corresponding release rate constant.

Higuchi Square Root Law equation:

$Q = K2t0.5$

Where Q (Q = 100 - M) is the amount of drug dissolved at time t and K2 is the diffusion

The diffusion data was further analyzed to define the mechanism of release by applying the diffusion data into

The Korsmeyer - peppas equation:

$Mt / M_{\infty} = K\ tn$

Where Mt / M_{∞} is the fraction of drug released at time t, K is the Korsmeyer release rate constant and n characterizes the mechanism of drug release from formulations during diffusion process. If n = 0.45 it is case I or Fickian

diffusion, 0.45, n, 0.89 is for anomalous diffusion or non- Fickian transport, n = 0.89 for case II transport, n .0.89 for super case II transport.

RESULTS AND DISCUSSION

Description
Observation: The sample of Glipizide is a white or almost white, odourless or almost odourless crystalline powder.

Solubility:
Observation: solubility of Glipizide in 0.1 N HCl was found to be 0.72 mg/ml at 37°C.

Infrared absorption spectrum:
Observation: The spectrum shows all prominent peaks of Glipizide

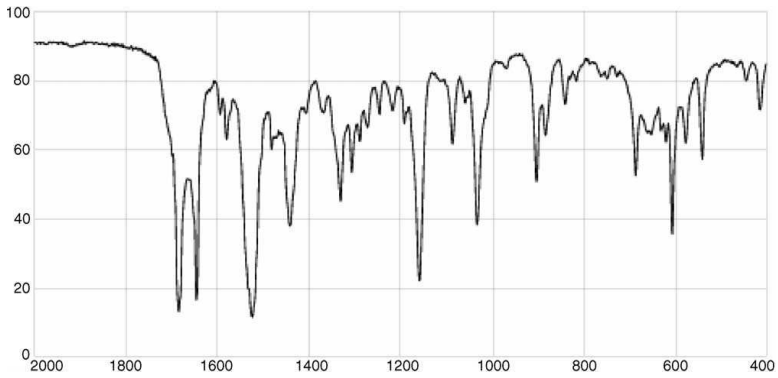


Figure No.2 IR spectroscopy of Glipizide

IR Interpretation:
IR spectrum indicated characteristics peaks belonging to measure functional groups such as principal peaks at wave numbers 1640, 1370, 1142, 1651 cm^{-1}

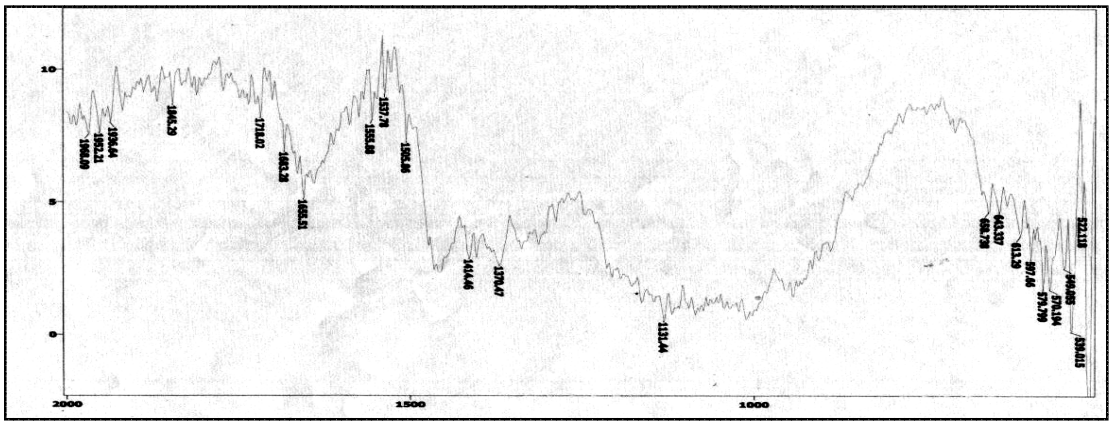


Figure No.2.1 HPMC

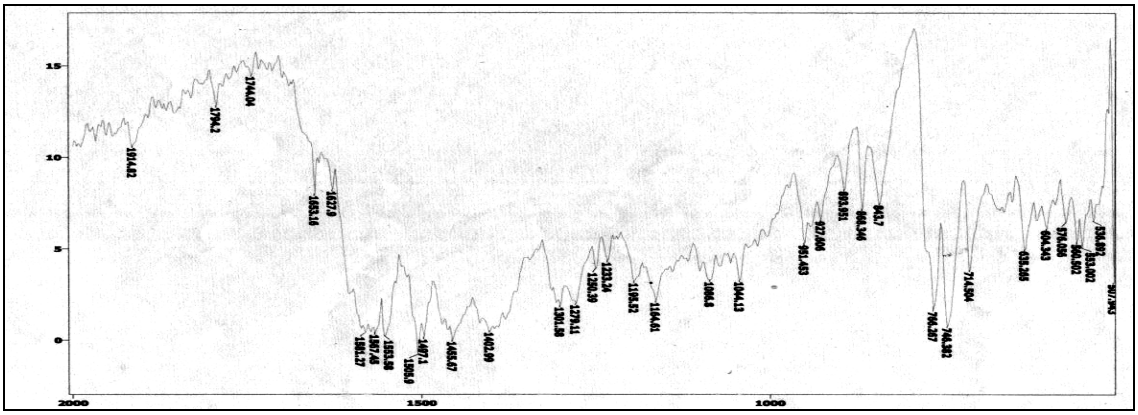


Figure No.2.2 GLIPZIDE+HPMC

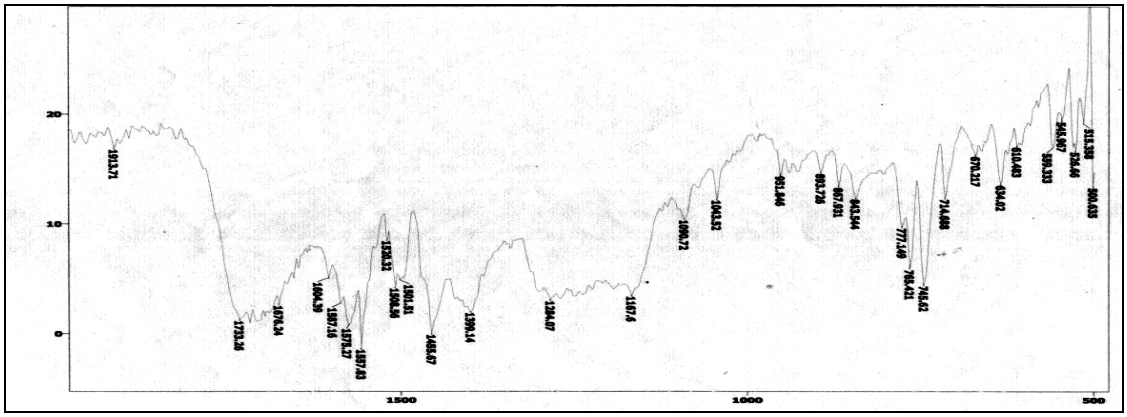


Figure No.2.3 GLIPIZIDE + CARBOPOL 940

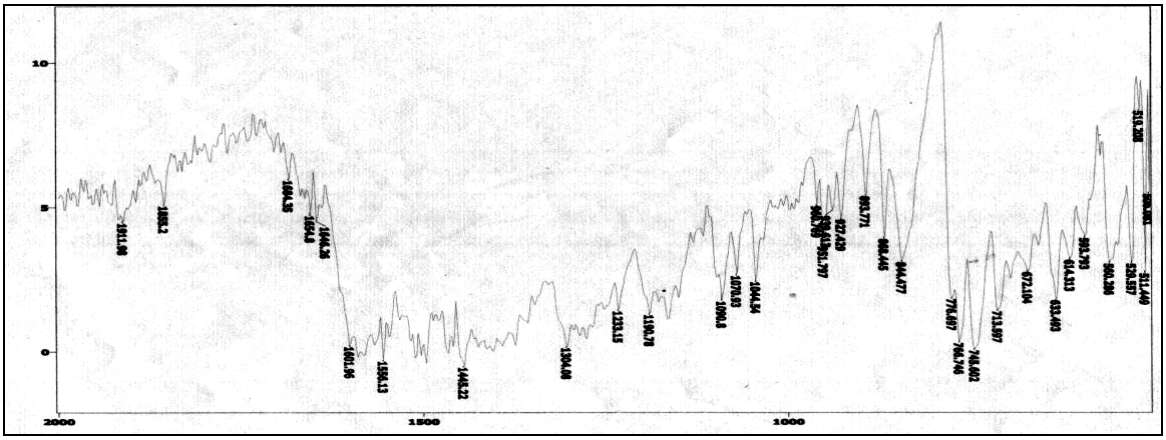


Figure No.2.4 Glipizide+$NaHCO_3$

Table No.6 IR INTERPRETATION OF GLIPIZIDE

S.No	Peaks (cm^{-1})	Groups
1	1640	CONH Stretching
2	1370	SO_2NH Stretching
3	1142	Cyclo hexyl stretching
4	1651	-C=O, Urea

The major IR peaks observed in GLIPIZIDE were 1640 (CONH stretching), 1370 (SO_2NH Stretching), 1142 (cyclo hexyl stretching), 1651 (C=O, Urea). In FTIR study of drug and polymers they show all prominent peaks.

Physical Properties of drug and polymer[3, 5]

Observation: The physical properties of drug and excipients are as follows.

Carr evaluated interparticulate cohesive properties with angle of repose measurements and found that density of a powder depends on particle packing and that density changes as the powder consolidates. The degree of consolidation is unique to the powder and ratio of these densities is related to interparticulate friction. This ratio, percent compressibility, was used as an index of flow. Adhesive/cohesive forces of particles as they relate to flow behavior by examining normal and shear stresses on powder beds. Values of Carr's index below 15 % usually show good flow characteristics, but readings above 25 % indicate poor flow ability. The range obtained is in between 21.2 to 27.97. Here all polymers (HPMC 5cps, Carbapol 940) and microcrystalline cellulose showed the Carr's index above 25% wish mean that the particle size distribution of this polymer is towards narrower distribution and these are very fine in nature.

Table No.7 Physical characteristics of Drug (Glipizide)

S.No	Parameter	Specifications
1	Loss on Drying (%)	0.80
2	Bulk density (g/cc)	0.423
3	Tapped Density (g/cc)	0.537
4	Hausners ratio	1.269
4	Compressibility index (%)	21.2
5	Angle of repose (° ')	39°71'

Table No.8 Physical Characteristics of Polymer and Excipient

Parameters	HPMC 5cps	Carbopol 940p	MCC
Bulk density (g/cc)	0.502	0.432	0.557
Tapped density (g/cc)	0.697	0.623	0.718
Compressibility Index (%)	27.97	27.73	22.46
Angle of repose (º')	37º48'	41 º56'	30º27'
Hausners ratio	1.388	0.695	1.289

CHARACTERIZATION OF GLIPIZIDE POWDER BLEND

The physical characteristics of the granules (GFT1 to GFT9) such as bulk density, tapped density, angle of repose, and compressibility index were determined. The results are given in the table. The bulk density and tapped density ranged from 0.483-0.535 and 0.549-0.627 respectively. The compressibility Index was in the range of 17.3-27.1. The angle of repose was below 30 indicating good flow properties.

Table 9 Physical characteristics of powder blend (FI – FIX)

Batch No	Bulk Density (g/cc)	Tapped Density (g/cc)	Angle of repose Tan θ=h/r	Compressibility index (%)
FI	0.486±0.12	0.605±0.35	24º66'±0.83	24.4±0.33
FII	0.483±0.36	0.614±0.49	27°27'±0.24	27.1±0.17
FIII	0.488±0.19	0.627±0.32	29°16±'0.36	28.48±0.12
FIV	0.519±0.37	0.579±0.18	26°41'±0.18	19.56±0.24
FV	0.535±0.43	0.590±0.24	27°89'±0.21	18.2±0.35
FVI	0.507±0.71	0.529±0.66	28°96'±0.39	17.9±0.46
FVII	0.502±0.64	0.589±0.54	25º31°'±0.47	17.3±0.68
FXIII	0.509±0.09	0.573±0.25	27°30'±0.58	19.96±0.53
FIX	0.503±0.16	0.549±0.37	29°48'±0.27	20.34±0.16

Evaluation of floating tablets

The physical properties of the tablets (GFT1 to GFT9) obtained by compressing the blend using Cadmach eight punches tablet machine .The physical properties such as tablet size, hardness, friability and weight variation were determined and results of the formulations (GFT1 to GFT9) found to be within the limits specified in Pharmacopoeia.

1. Tablet Thickness and Hardness

Observation: All the formulations were evaluated for various parameters. The thickness, diameter and Hardness of all tablets from batch GFT1 to GFT9are shown in table 15, as there was no much variation in thickness of tablets in each formulation, it shows that powder blends were consistent in particle size and uniform behavior during compression process.

The hardness of tablet was measured on Pfizer hardness tester. The hardness was in range of 5.2-5.8 Kg/cm^2. Tablets hardness was found to be a determining factor with regard to the buoyancy of the tablets. Tablet hardness

reflects differences in tablet density and porosity, which are supposed to result in different release patterns of the drug by affecting the rate of penetration of the dissolution fluid at the surface of the tablet[4].

2. Friability
Observation: The values of friability are given in below table no.10, and are within the limit. The present study of tablets is in within the limit and the slight variation in friability because of the variation in compression force applied and its total weight. Friability of tablets found in the range of (0.46%-0.83%)[4].

3. Uniformity of Weight
Observation: The values of average weight are given in below table 8 and are in within limit[60].

4. Drug content
Observation: The values of drug content are given in table 8.

The drug content was found spectrophotometrically for all formulations (GFT1 to GFT9). The values are shown in the Table.15.The drug content was found to be within a narrow range as specified in the Pharmacopoeia (90- 110%) in all formulations.

Table 10 Physical Characteristics of Glipizide Floating Tablets (GFT1-GFT9)

Batch No	Thickness (mm)	Friability (%)	Hardness (kg/cm^2)	Weight Variation (mg±SD)	Assay
GFT1	3.4±0.12	0.47	5.5±0.34	202±2.99	98.76±0.19
GFT 2	3.2±0.21	0.68	5.2±0.73	205±1.98	97.16±0.27
GFT3	3.4±0.53	0.47	5.4±1.92	202. 5±3.7	98.87±0.41
GFT4	3.2±0.16	0.46	5.3±0.34	198±6.5	97.26±0.33
GFT5	3.3±0.42	0.72	5.6±0.28	204±1.3	97.48±0.26
GF T6	3.1±0.53	0.74	5.5±0.37	199±6.59	98.67±0.17
GFT7	3.3±0.24	0.63	5.4±0.89	204±1.6	98.83±0.32
GFT8	3.2±0.16	0.45	5.3±0.42	194±3.06	97.92±0.21
GFT9	3.4±0.29	0.83	5.8±0.56	207±3.9	99.27±0.16

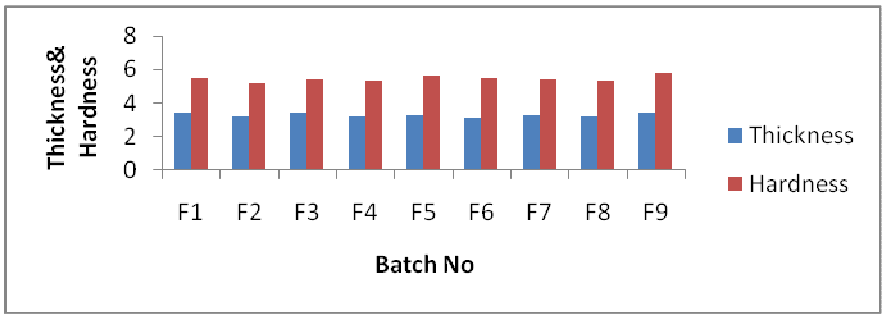


Figure No.3.1 Thickness and Hardness of Glipizide Floating tablets

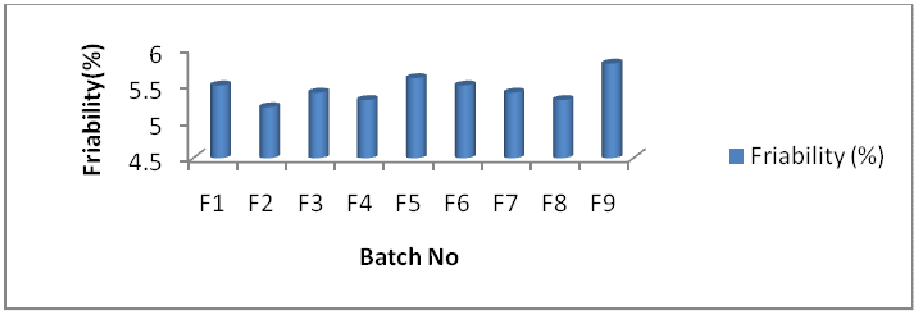


Figure No.3.2 Friability of Glipizide Floating tablets

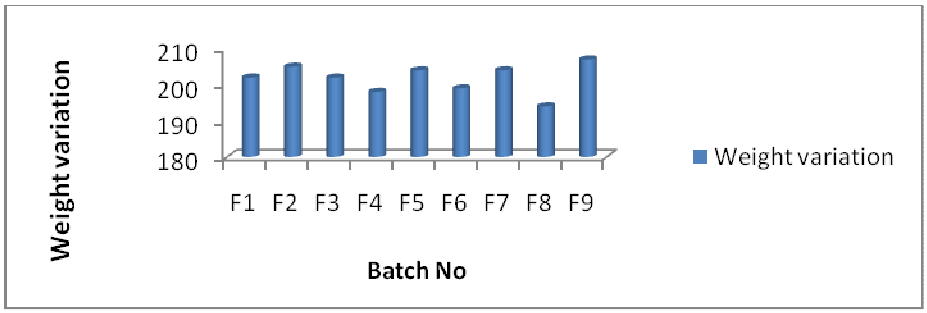


Figure No.3.3 Weight variation of Glipizide Floating tablets

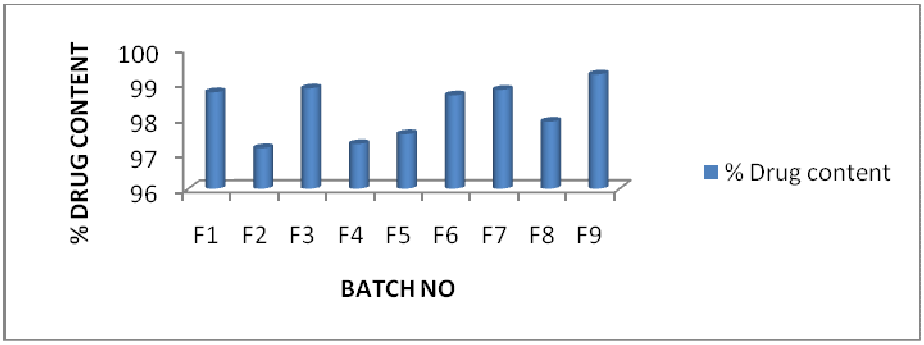


Figure No.3.4 % Drug Content of Glipizide Floating tablets

5. Buoyancy and floating time of Glipizide Floating Tablets (GFT1-GFT9)

Buoyancy lag time and duration of floating were determined using USP dissolution test apparatus in 0.1N HCl Maintained at 37ºC. Buoyancy lag time of GFT1-GFT F9 was in the range of 45-90secs.The Floating time was found to be 24 hours for GFT F9. The reports are presented in the Table 9 respectively. Based upon the floatation time, the formulation GFT9 was selected as the best formulation.

Table No.11 Buoyancy and floating time of Glipizide Floating Tablets (GFT1-GFT9)

S.No	Batch No	Buoyancy lag time (sec)	Floating duration (hrs)
1	GFT1	60	10
2	GFT2	55	12
3	GFT3	50	16
4	GFT4	65	11
5	GFT5	55	12
6	GFT6	60	16
7	GFT7	60	18
8	GFT8	55	20
9	GFT9	45	23

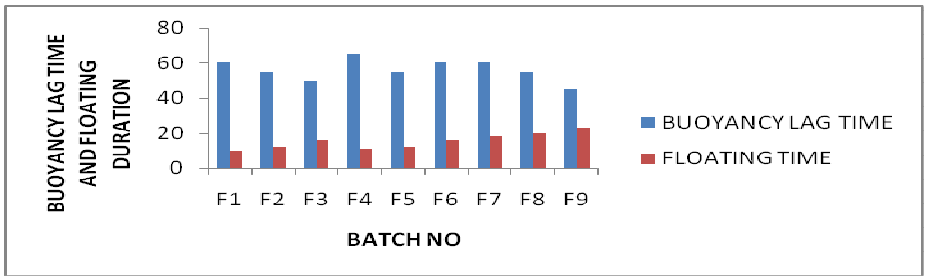


Figure No. 4 Buoyancy lag time and Floating time of Floating tablets

Dissolution Studies:

Observation: Dissolution data of batch GFT1-GFT9 are shown in Table 15.1-15.3

From the dissolution study it was concluded that release from the matrix is largely dependent on the polymer swelling, drug diffusion and matrix erosion. It was observed that all the tablets ascended to the upper one third of the

dissolution vessels within a short time, and remained floated until the completion of release studies. The drug release study is carried out up to 24hrs.

The percentage drug release of batch GFT9 shows 98.68% drug release at the end of 24 hours, where as other batches showing drug release before 24 hours. Large concentration of polymer induces the formation of strong matrix that slowed down the rate of water diffusion into the tablet matrix, which may result in the retardation of drug release. Being water-soluble polymers, they dissolve and form pores filled liquid in which drug can thereafter diffuse in dissolution medium. All the formulations were designed as dosage form for 24 hrs. In order to check the 100 % dissolution release profile, optimized formulations were subjected to dissolution studies for 24 hrs.

The dissolution studies of the formulation (GFT1-GFT9) were carried out in USP dissolution apparatus (paddle) in 900 ml of 0.1N HCl as dissolution medium. The reports are represented in the tables 17.1-17.3 and Fig10.1-10.3 respectively. The formulation GFT9 showed a constant release in a sustained manner with 98.68% at the end of 24th hour and hence ***GFT9*** was ***chosen as the best formulation.***

Table No.12.1 *In Vitro* release profile of Glipizide floating Tablets (GFT1-GFT3) in 0.1N HCl

S.No	Time(hrs)	Cumulative % Drug release		
		GFT1	GFT2	GFT3
1	1	5.41±0.46	4.89 ± 0..35	3.89±0.57
2	2	9.82 ± 0.21	8.24 ± 0.38	9.16 ± 0.29
3	3	13.57 ± 0.39	12.69 ± 0.41	11.47 ± 0.69
4	4	16.39 ± 0.48	15.97 ± 0.19	14.70 ± 0.49
5	5	19.92 ± 0.11	22.28 ± 0.34	20.66 ± 0.55
6	6	25.76 ± 0.42	33.6 ± 0.56	28.70 ± 0.81
7	7	32.51 ± 0.44	41.25±0.47	37.68 ±0.65
8	8	39.34 ± 0.40	52.39±0.32	45.99 ± 0.52
9	9	68.15 ± 0.21	64.28±0.56	56.51 ± 0.54
10	10	82.37 ± 0.40	73.54 ± 0.42	65.27 ± 0.25
11	12	95.87 ± 0.19	89.36±0.28	76.56±0.33
12	14		96.42±0.59	81.24 ± 0.38
13	18			97.14±0.61

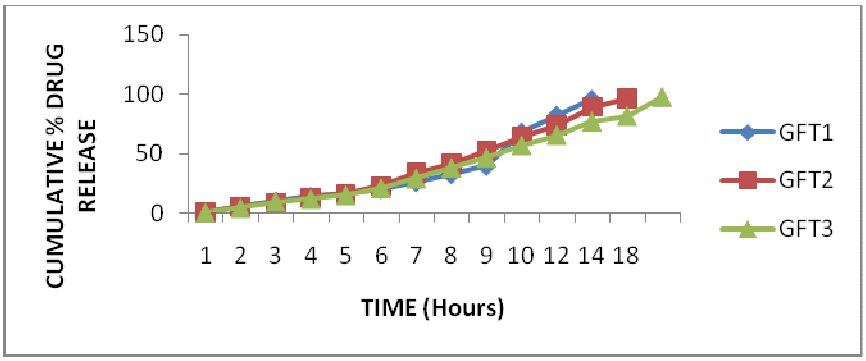


Figure No.5.1 In vitro release profile of Glipizide Floating Tablets (GFT1-GFT3) in 0.1N Hcl

Table 12.2 *In Vitro* release profile of Glipizide floating Tablets (GFT4-GFT6) in 0.1N HCl

S.no	Time(hrs)	Cumulative % Drug release		
		GFT4	GFT5	GFT6
1	1	8.56 ± 0.51	6.18 ± 0.19	3.68 ± 0.31
2	2	12.11±0.29	9.24 ± 0.31	6.45 ± 0.31
3	3	16.19 ± 0.31	11.01 ± 0.32	9.90 ± 0.12
4	4	21.80 ± 0.45	17.48 ± 0.32	14.39 ± 0.49
5	5	29.23 ± 0.53	23.84 ± 0.55	19.46 ± 0.20
6	6	34.41 ± 0.19	27.26 ± 0.32	23.58±0.39
7	7	48.25 ± 0.50	33.48 ± 0.24	28.51 ± 0.52
8	8	61.58 ±0.41	49.52 ± 0.46	41.21 ± 0.47
9	9	76.63 ± 0.55	61.35 ± 0.50	58.58 ± 0.32
10	10	88.45 ± 0.41	79.81 ± 0.45	69.65 ± 0.43
11	12	96.27±0.25	84.85 ± 0.29	76.57 ± 0.43
12	14		95.03±0.83	87.56 ±0.29
13	18			96.08± 0.30

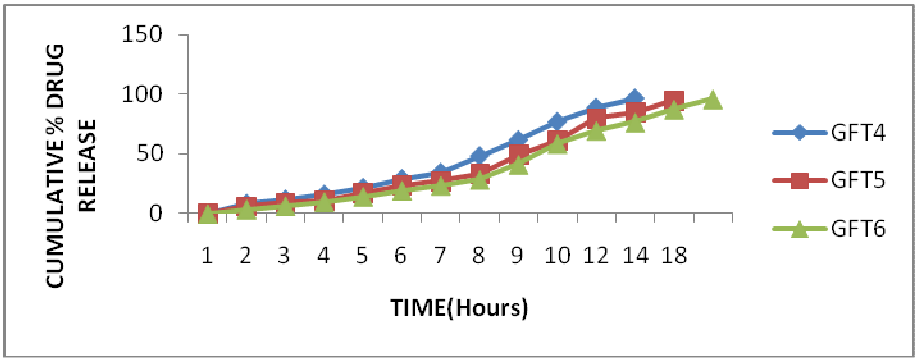


Figure No.5.2 *In Vitro* release profile of Glipizide floating Tablets (GFT4-GFT6) in 0.1N HCl

Table 12.3 *In Vitro* release profile of Glipizide floating Tablets (GFT7-GFT9) in 0.1N HCl

S.No	Time (hrs)	Cumulative % Drug release		
		GFT7	GFT8	GFT9
1	**1**	5.81 ± 1.26	4.14 ± 0.25	3.92 ± 0.42
2	**2**	11.46 ± 1.35	8.52 ± 0.51	7.21 ± 0.31
3	**3**	16.89 ± 2.51	15.36±0.24	13.85±0.67
4	**4**	21.52 ± 1.04	20.21± 0.62	17.46±0.34
5	**5**	26.5±12.36	24.36± 0.59	19.85±0.69
6	**6**	32.78 ± 2.11	29.33±0.24	25.21 ± 0.59
7	**7**	38.21 ± 2.31	33.12 ± 0.47	30.27 ± 0.56
8	**8**	45.43 ± 2.83	39.57±1.29	35.25 ± 0.69
9	**9**	56.46 ± 1.85	45.68±0.28	42.58 ± 0.42
10	**10**	65.34 ± 2.28	51.36±0.25	49.63 ± 0.42
11	**12**	74.22 ± 1.47	65.12±1.34	55.72 ± 0.52
12	**14**	87.65 ± 0.25	78.36±0.16	61.50 ± 0.49
13	**18**	96.68±0.39	85.21±0.73	76.41±0.26
14	**22**		97.17±0.24	89.53±0.64
15	**24**			98.68±0.73

Table No.12.4 COMPARISON OF SELECTED FORMULATION GFT9 WITH MARKETED FORMULATION

S.NO	TIME	Cumulative % Drug release	
		GFT9	MARKETED
1	1	3.92 ± 0.42	3.23±1.06
2	2	7.21 ± 0.31	8.31±0.24
3	3	13.85±0.67	12.54±3.29
4	4	17.46±0.34	15.21±1.46
5	5	19.85±0.69	19.34±0.67
6	6	25.21 ± 0.59	24.41±1.71
7	7	30.27 ± 0.56	29.51±2.62
8	8	35.25 ± 0.69	34.36±5.78
9	9	42.58 ± 0.42	40.24±2.92
10	10	49.63 ± 0.42	46.25±0.16
11	12	55.72 ± 0.52	51.26±0.78
12	14	61.52 ± 0.49	60.53±0.96
13	18	76.52±0.26	74.51±0.42
14	22	89.53±0.64	88.57±0.77
15	24	98.68±0.73	99.21±0.23

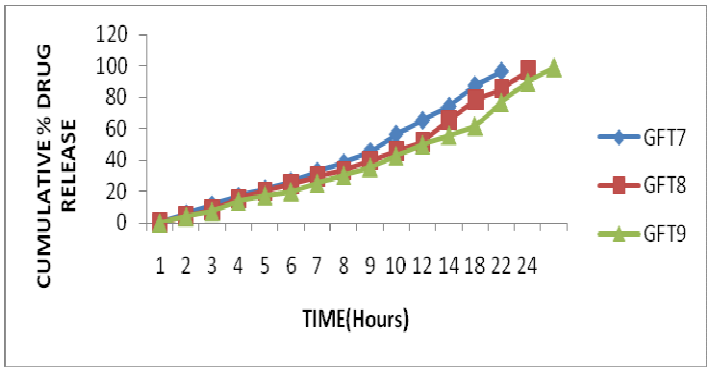


Figure No.5.3 *In Vitro* release profile of Glipizide floating Tablets (GFT7-GFT9) in 0.1N HCl

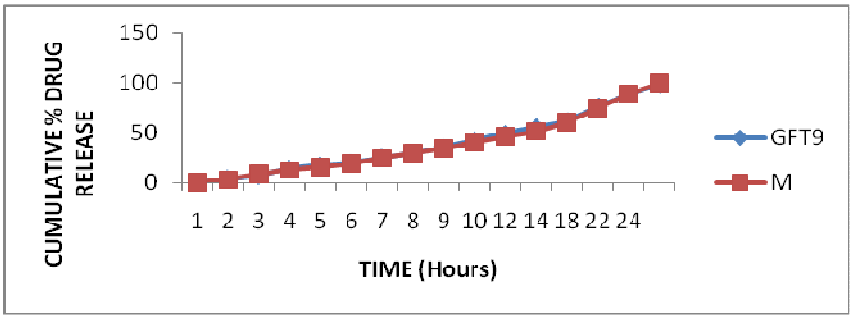


Figure No.5.4 comparison of selected GFT9 with Marketed Formulation

COMPARISON

It had been shown that when compared the selected formulation GFT9 with marketed formulation, Marketed product of Glipizide released 99.21%, at the end of the 24thhour of dissolution study. Selected formulation GFT9 had released the 98.68% of drug, which is almost similar to that of marketed product.

RELEASE KINETICS OF OPTIMIZED FORMULATION

ZERO ORDER KINETICS

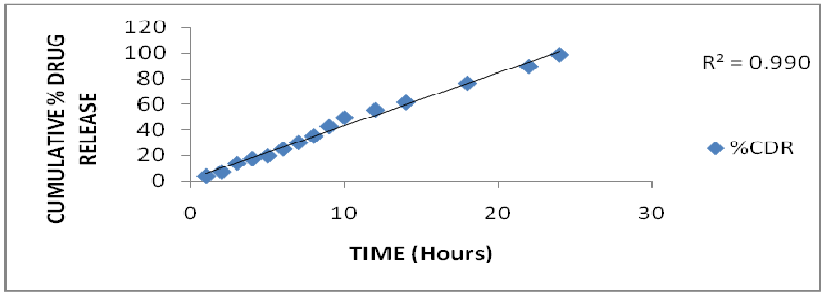


FIGURE No.6.1: Zero order plots for optimized Formulation

FIRST ORDER KINETICS

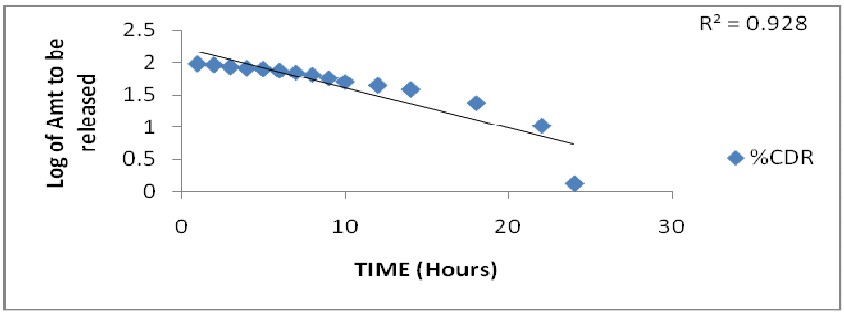


Figure No 6.2 First order plots for optimized Formulation

HIGUCHI MODEL

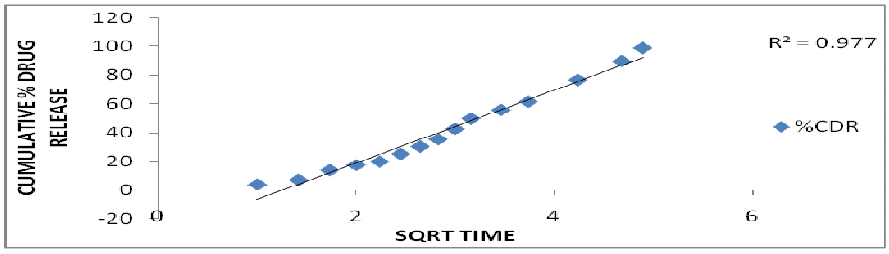


Figure No 6.3 Higuchi Plot for optimized formulation

KORSEMEYER PEPPAS MODEL

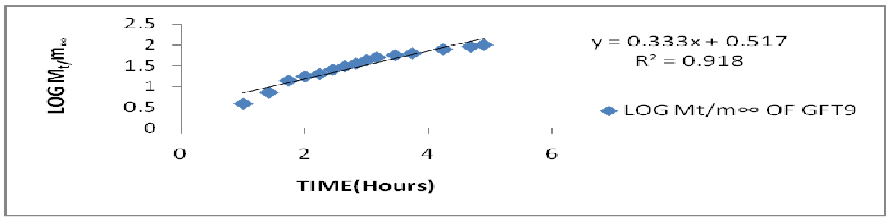


Figure No 6.4 Korsemeyer Peppas Model for optimized formulation

Table No.13 Release Kinetics of Optimized formulation

Formulation	Zero Order	First order	Higuchi	Korsemeyer peppas	
				R^2	n
GFT9	0.990	0.928	0.977	0.918	0.333

To know the mechanism of drug release from these formulations, the data were treated according to zero order (cumulative amount of drug released vs time), first-order (log cumulative percentage of drug remaining vs time), Higuchi's (cumulative percentage of drug released vs square root of time), and Korsmeyer (log cumulative percentage of drug released vs log time) equations.
From Korsemeyers peppas model,

- The value of n falls between 0.5 to 1 (0.5 < n <1) indicating non-fickian release.
- The value of n < 0.5 indicating Fickian diffusion i.e. first order release
- The value of n = 1, indicating the Zero order release or case 2 transport
- The value of n >1, indicating the Super case 2 transport.

Different kinetic models were applied for best formulation and n value obtained is 0.333 and r^2 is 0.918 indicating Fickian Diffusion and first order release.

CONCLUSION

On the performance with respect to buoyancy lag time, floating time and the release characteristics, the formula (GFT9) was selected as the best formula as it showed a buoyancy time 45 seconds, floatation time of 23 hours, and Cumulative % drug release of 98.68%. This Formulation (GFT9) showed a sustained release rate throughout its release period. And the selected formulation (GFT9) was compared with the marketed formulation. Selected formulation GFT9 had released the 98.68% of drug, which is almost similar to that of marketed product (99.21%). Different kinetic models were applied to optimized formulation (GFT9) the 'n' value is 0.333, r^2 value is 0.918 indicating Fickian Diffusion and first order release. Hence this formulation can be considerd for further studies to locate dosage form with in desired region of gastrio intestinal region from where the drug has maximum absorption.

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