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Research Article

FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLET OF GLIPIZIDE BY USING COMBINATION OF NATURAL AND SYNTHETIC POLYMER

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ABSTRACT

Controlled release delivery system provides a uniform concentration or amount of the drug at the absorption site and thus, after absorption allow maintenance of plasma concentrations within a therapeutic range, which minimizes side effects and also reduces the frequency of administration. The overall objective of this work was to develop a tablet glipizide oral sustained release prepared by the method of direct compression, using hydroxy propyl methyl cellulose (HPMC K-100M) and xanthan gum polymer alone and in combination at various concentrations. Glipizide has a relatively short plasma half-life and low absolute bioavailability. All batches were evaluated for the precompression and post compresson. The hydrophilic matrix of HPMC alone cannot control the release glipizide effective for 12 h while when combined with xanthan gum, may slow down the release of the drug and, therefore, can be successfully employed for the formulation of matrix tablets SR.

KEYWORDS: *Glipizide, Matrix, Polymers, Retardant.*

INTRODUCTION [1]

Oral ingestion is traditionally preferred route of drug administration, providing a convenient method of effectively achieving both local and systemic effects. In conventional oral drug delivery systems, there is very little control over release of drug. The effective concentration at the target site can be achieved by intermittent administration of grossly excessive doses, which in most situations, often results in constantly changing, unpredictable and often sub or supra therapeutic plasma concentrations leaving the marked side effects. An ideal oral drug delivery system should steadily deliver a measurable and reproducible amount of drug to the target site over a prolonged period.

MATERIALS AND METHODOLOGY

Preparation of Standard Curve: [2]

Preparation of Phosphate Buffer pH 6.8:

Placed 11.45 gm of potassium dihydrogen phosphate and 28.80 gm of disodium hydrogen phosphate and made up to 1000 ml with distilled water.

Preparation of Standard Curve of glipizide with Phosphate Buffer pH 6.8:

A standard graph of pure drug in suitable medium was prepared by plotting the concentration on X-axis and absorbance on Y-axis. An accurately weighed 100 mg of Glipizide was dissolved in methanolic phosphate buffer of pH 6.8 as per I.P and make up the volume up to 100 ml in a volumetric flask, (Stock Solution: I, This stock solution concentration is 1mg/ml or 1000 µg/ml). From this stock solution 10 ml of solution were pipette out and make up the volume up to 100 ml (Stock Solution: II, 100µg/ml). Then the aliquots were prepared, whose concentration ranging from 5 to 25µg/ml and the absorbance were measured at 226 nm by using UV Spectrophotometer against the reagent blank. The coefficient of variation and correlation coefficient were determined.

Preparation of 0.1 N Hydrochloric Acid:

8.5 ml of concentrate hydrochloric acid was taken and diluted with distilled water up to 1000 ml.

Preparation of Standard Curve of glipizide with 0.1 N HCI:

A standard graph of pure drug in suitable medium was prepared by plotting the concentration on X-axis and absorbance on Y-axis. An accurately weighed 100 mg of Glipizide was dissolved in methanolic 0.1 N HCI as per I.P and make up the volume up to 100 ml in a volumetric flask, (Stock Solution: I, This stock solution concentration is 1mg/ml or 1000 µg/ml). From this stock solution 10 ml of solution were pipette out and make up the volume up to 100 ml (Stock Solution: II, 100µg/ml). Then the aliquots were prepared, whose concentration ranging from 5 to 25 µg/ml and the absorbance were measured at 226 nm by using UV Spectrophotometer against the reagent blank. The coefficient of variation and correlation coefficient were determined.

Drug Excipient Compatibility Studies:

The interaction between the drug and excipients are determined after a specific time period by using suitable analytical techniques like FTIR.

Preformulation Studies: [3-7]

Angle of Repose:

The angle of repose is the maximum angle that the plane of powder makes with the horizontal surface on rotation.

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

Where, h = height of the powder heap

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r = radius of the powder heap
θ = is the angle of repose.

Determination of Bulk Density and Tapped Density:

The bulk density and the tapped density were calculated using the following formulae.

Bulk density = Weight of the powder / Initial volume
Tapped density = Weight of the powder / final volume

Carr's Compressibility Index:

Carr's index of each formulation was calculated according to equation given below:

Carr's index = [Tapped density − Bulk density/Tapped density] X 100

Hausner's Ratio:

Hausner's Ratio indicates the flow properties of the powder and is measured by the ratio of tapped density to bulk density.

Hausners Ratio = Tapped density/Tapped density

Formulation Table: The formulation blend was mixed thoroughly by using mortar and pestle and the tablets of glipizide were punched by using Cemach tablet punching machine using 8 mm punch.

Table No. 1: Actual values of Ingredients taken for Matrix Tablet

Sr. No.	Ingredients	Formulation Codes								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Glipizide	10	10	10	10	10	10	10	10	10
2	HPMC K100-M				15	20	25	15	20	20
3	Xanthan Gum	5	10	15				5	10	12.5
4	Microcrystalline Cellulose	177	172	167	167	162	157	162	152	149.5
5	Magnesium Stearate	4	4	4	4	4	4	4	4	4
6	Talc	4	4	4	4	4	4	4	4	4
	Total weight (mg)	200	200	200	200	200	200	200	200	200

In vitro dissolution studies: [8-9]

The release rate of glipizide from sustain tablets was determined. The dissolution test was performed using United States Pharmacopoeia (USP) type II (paddle) apparatus, 900 ml of phosphate buffer of PH 6.8 at 37 ± 0.5°C and 50 rpm. A sample (10) of the solution was withdrawn from the dissolution apparatus at the appropriate time for 12 hours, and the samples were replaced with fresh dissolution medium. The samples were diluted into a suitable concentration with phosphate buffer. Absorbance of these solutions was measured at 226 nm using a UV/Visible double-beam spectrophotometer.

Data analysis: [10-16]

To analyze the mechanism of release and release rate kinetics of the dosage form, the data obtained were fitted into Zero order, First order, Higuchi matrix, Korsmeyar-Peppas and Hixson Crowell model of optimized formulation.

Accelerated stability study: [17]

In order to determine the change in vitro release profile on Storage, stability study of batch F9 was carried out at 40 °C in a Humidity chamber having 75% RH. Sample was withdrawn at various time intervals and the study was conducted for 90 days. The sample was evaluated for change in vitro drug release pattern, hardness, Wetting time, percent drug content and disintegration time.

RESULT AND DISCUSSION

Identification Tests:

Preparation of Standard Curve of glipizide in Phosphate Buffer pH 6.8:

Table No. 2: Calibration Curve of Glipizide

Sr. No.	Concentration (ug/ml)	Absorbance
1	0	0
2	5	0.181
3	10	0.363
4	15	0.544
5	20	0.713
6	25	0.869

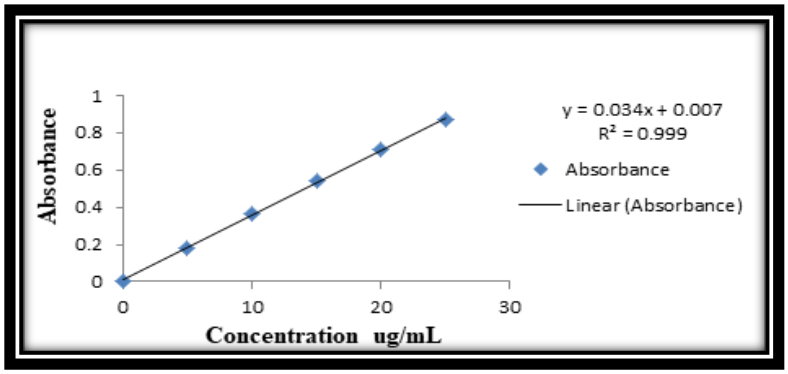

Fig. 1: Calibration curve of glipizide pH 6.8 phosphate buffer at 226 nm

Preparation of Standard Curve of glipizide with 0.1 N HCI:

Table No. 3: Calibration curve of glipizide

Sr. No.	Concentration (ug/ml)	Absorbance
1	0	0
2	5	0.12
3	10	0.258
4	15	0.371
5	20	0.523
6	25	0.624

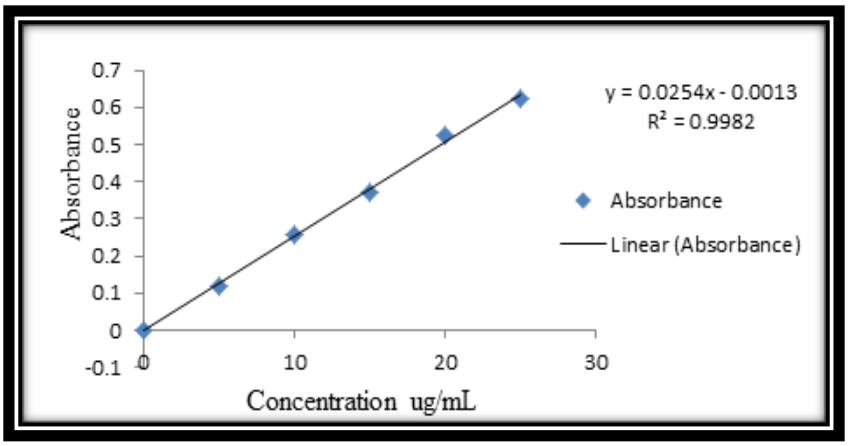

Fig. 2: Calibration curve of glipizide in 0.1 N HCL at 226 nm

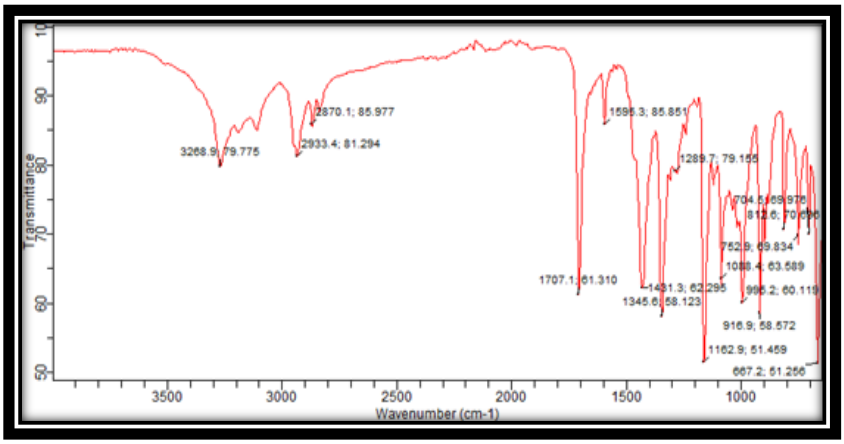

Fig. 3: FTIR Spectrum of glipizide

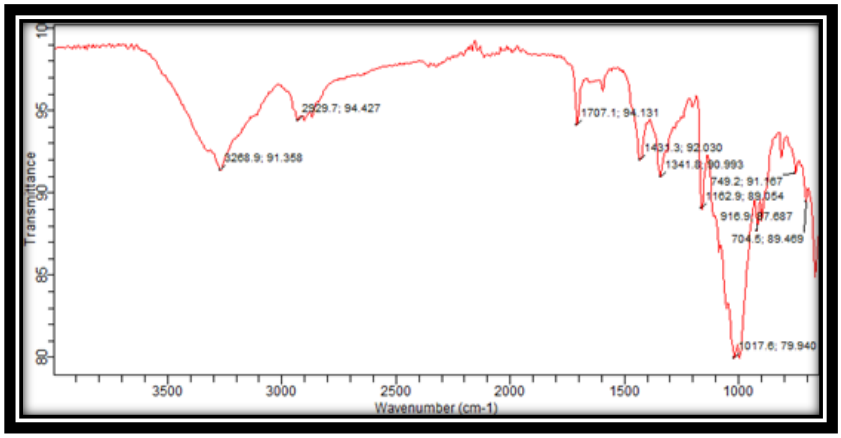

Fig. 4: FTIR spectrum of glipizide with xanthan gum

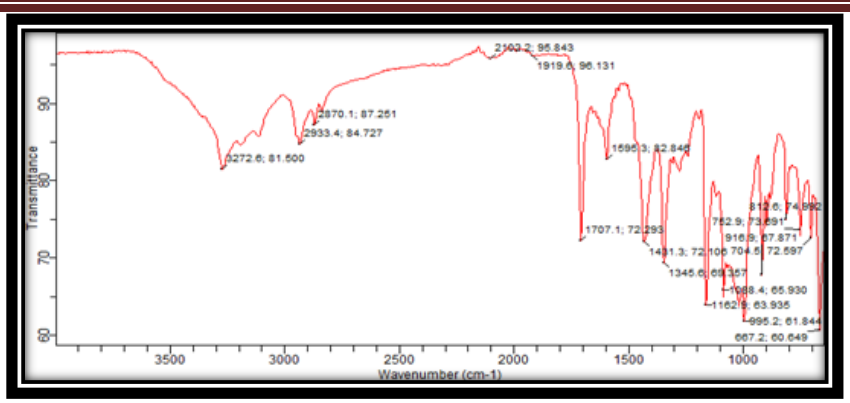

Fig. 5: FTIR spectrum of formulation blend

Preformulation Studies:

Preformulation testing was done for each batch and the result were tabulated in the above table which concluded that all batches are passes with good flow ability and were further proceed for compression of tablets (Table 4).

Evaluation of matrix tablets:

All the prepared matrix tablets were evaluated for following official parameters (Table 5).

After the compression of tablet post compression parameter are evaluated such as hardness, thickness, friability, weight variation and drug content. All parameter possess the standards of Indian pharmacopoeia and found to be within limit. The percent drug content is calculated by performing an assay of glipizide tablet using UV spectrophotometer.

In vitro dissolution studies:

In the dissolution study of various batches formulation the following calculation are done and from that data a graph of various formulation were drawn and compared with marketed formulation (Table 6).

Accelerated Stability Studies:

The optimized batch of F9 glipizide matrix tablet were evaluated for accelerated stability studies at 40^{0}C / 75 % RH condition. The stability details of results are presented as below (Table 7).

Table No. 4: Precompression parameters of glipizide formulation

Formulation code	Bulk density (gm/ ml)	Tapped density (gm/ ml)	Compressibility Index %	Carr's Index (%)	Hausner's Ratio	Angle of repose
F1	0.50	0.617	18.96	18.96	1.23	26.30
F2	0.515	0.580	11.20	11.20	1.14	26.87
F3	0.512	0.595	13.94	13.94	1.16	27.16
F4	0.520	0.591	12.01	12.01	1.13	27.77
F5	0.526	0.606	13.20	13.20	1.15	28.09
F6	0.549	0.617	11.02	11.02	1.12	28.09
F7	0.529	0.602	12.12	12.12	1.13	29.42
F8	0.526	0.609	13.62	13.62	1.15	29.76
F9	0.543	0.632	14.08	14.08	1.16	27.04

Table No. 5: Post Compression parameters of glipizide formulation

Sr. No.	Formulation	Hardness (Kg/cm^2)	Friability (%)	Thickness	Weight variation	% Drug content (mg)
1.	F1	5.3	0.13	3.28	199	102.00
2.	F2	5.1	0.09	5.53	200	98.10
3.	F3	5.5	0.14	3.30	199	98.48
4.	F4	5.2	0.10	3.45	201	97.00
5.	F5	5.0	0.18	3.40	200	98.00
6.	F6	5.5	0.16	3.48	202	101.00
7.	F7	5.4	0.19	3.12	201	96.14
8.	F8	5.6	0.22	3.16	199	95.60
9.	F9	5.4	0.11	3.13	200	99.17

Table No. 6: In-vitro % drug release of formulation F1 to F9

Time	Innovator (Glynase)	% Drug release								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0	0
0.5	19.05	29.91	21.17	11.91	29.91	31.50	27.79	29.91	27.79	21.10
1	26.47	42.00	23.02	13.50	36.79	42.00	29.38	31.50	37.26	26.47
2	36.79	54.00	26.47	19.05	42.00	48.17	37.26	36.79	46.58	29.30
3	46.58	58.00	29.38	21.17	46.58	54.00	51.35	42.00	51.35	37.26
4	51.35	70.41	36.79	26.47	58.00	70.41	58.50	51.35	65.38	46.58
5	60.00	79.41	46.58	27.79	79.41	83.91	87.08	65.38	79.41	54.00

6	68.82	83.91	53.47	29.38	83.91	90.52	87.08	73.58	83.91	65.38
7	75.17	88.14	60.00	31.76	92.91	97.41	87.08	87.08	90.52	73.58
8	83.91	92.91	68.82	36.79	96.88	98.47	90.52	92.91	96.61	81.79
9	90.52	96.35	73.58	40.23	97.67	98.47	97.41	98.20	96.88	88.41
10	94.23	96.88	81.79	46.58	97.67	98.73	97.41	98.73	97.67	92.91
11	97.67	97.67	82.00	48.44	98.47	98.73	101.64	98.73	97.67	96.88
12	100.05	97.67	82.00	51.35	98.47	98.73	101.64	98.73	98.92	99.79

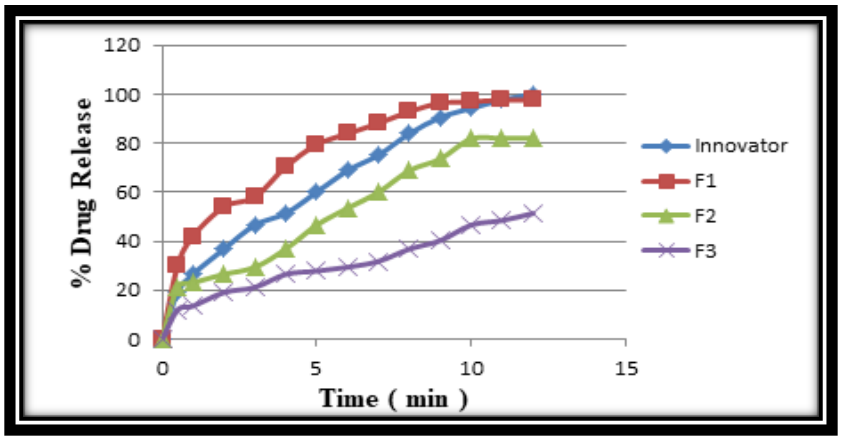

Fig. 6: In-vitro release profile of formulation F1, F2 & F3

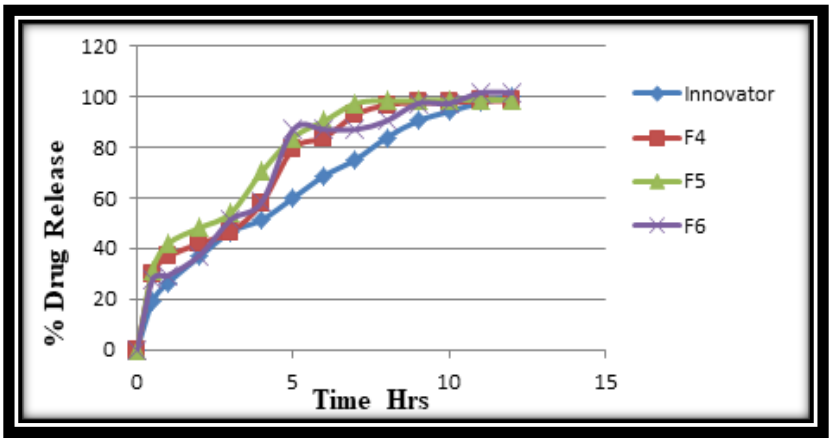

Fig. 7: In-vitro release profile of formulation F4, F5 & F6

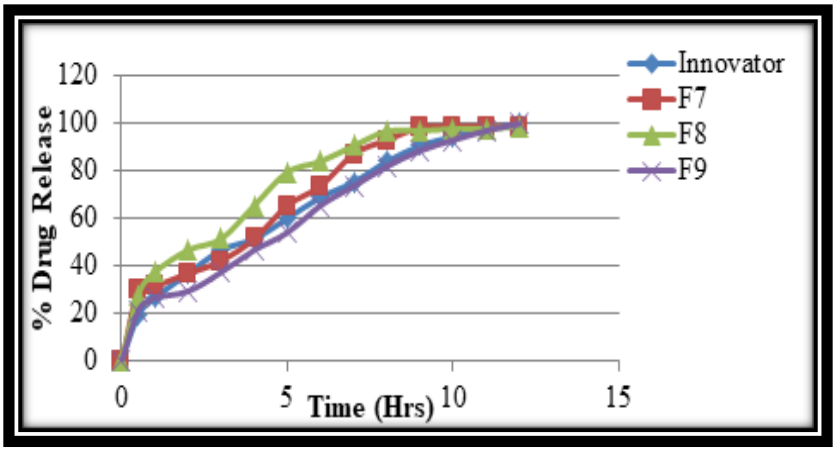

Fig. 8: In-vitro release profile of formulation F7, F8 & F9

Data analysis by various kinetic models:

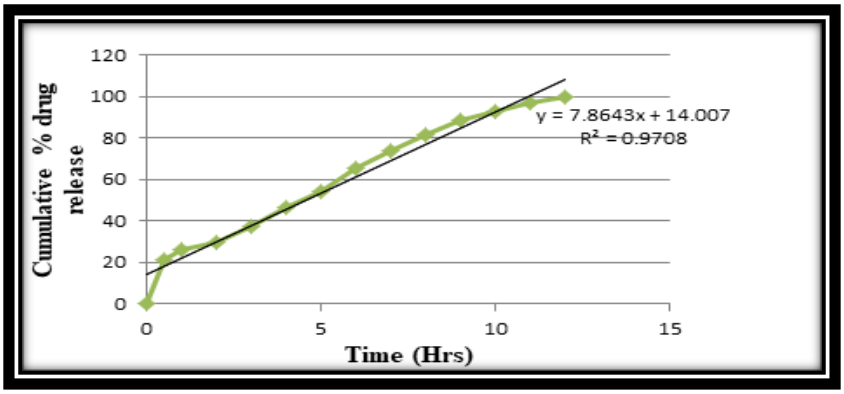

Fig. 9: Zero order kinetic model of optimized formulation

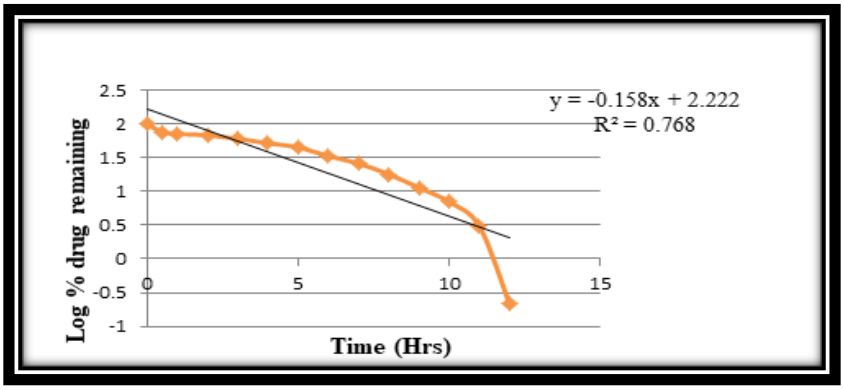

Fig. 10: First order kinetic model of optimized formulation

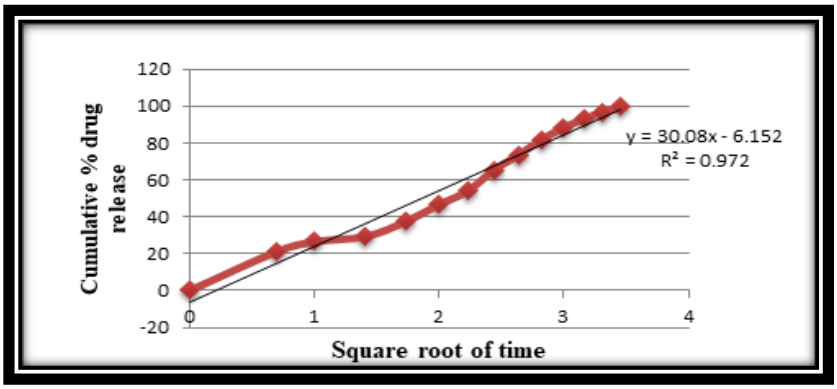

Fig. 11: Higuchi model kinetic release of optimized formulation

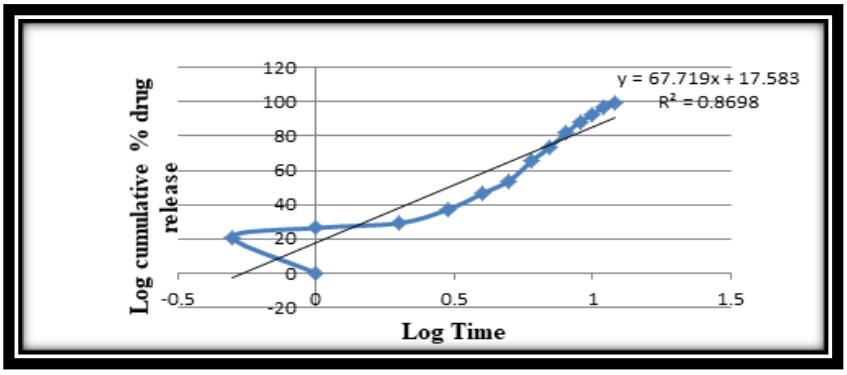

Fig. 12: Korsmeyer-Peppas model for drug release of optimized formulation

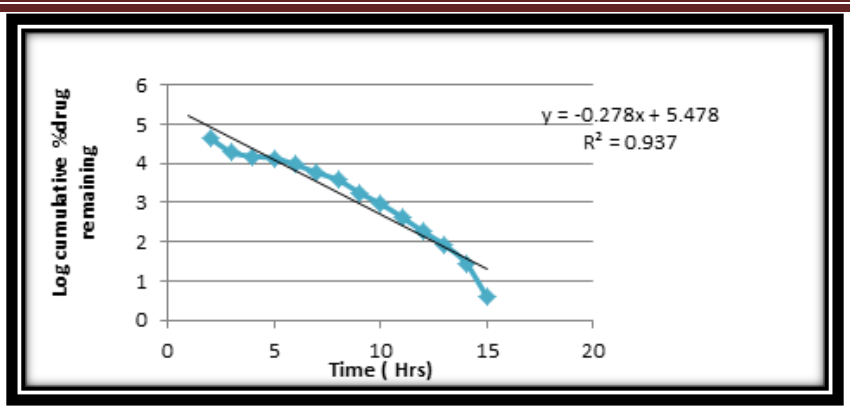

Fig. 13: Hixson-Crowell model kinetic release of optimized formulation

Table No. 7: Results of accelerated stability Study of optimized formulation

Sr. No.	Test	Specifications	Initial	After 1 month	After 2 months	After 3 months
1	**Description**	White/Off-white colored tablets	Complies	Complies	Complies	Complies
2.	**Assay by UV**	NLT 90.0 %and NMT 110.00 %	99.12 %	98.07 %	97.69 %	97.14 %
3	**Dissolution**	NLT 80% release after 12 hours	99.18 %	97.8 %	97.5 %	97.24%

CONCLUSION

The present work was to formulate and evaluate sustain release matrix tablets of glipizide by using natural and synthetic polymer to sustain the drug release from matrix tablet. The sustained release drug delivery was a promising approach to achieve a prolonged therapeutic action of drug. The matrix forming polymers, HPMC K-100M, Xanthan gum alone & in combination were studied.

The amount of drug release for optimized formulation F9 was found to be 99.79%. The cumulative percentage drug was decreased by increase in polymer concentration. The drug release of optimized formulation F9 correspond to Higuchi model and nearly comparative to zero order as result obtained from r^2 value. It is found be 0.979 for marketed formulation and 0.972 for the optimized formulation. Formulation F9 containing HPMC K-100M. (10%) & Xanthan gum (6.25%) in combination successfully release drug for more than 8 hrs, emerging as best formulation.

The total % drug release from batch F8 and F9 was found to be 98.92 and 99.79 respectively. It shows non-fickian diffusion as per the n value obtained in the Korsmeyer-Peppas release kinetic model was found to be 0.537. FTIR studies proved that there was no chemical interaction in drug and polymer of the developed matrix tablets.

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