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FORMULATION AND *INVITRO* EVALUATION OF GLIBENCLAMIDE SUSTAINED RELEASE TABLETS

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ABSTRACT

This research endeavor aims to design and develop a robust and efficacious formulation of an oral antihyperglycemic drug, encapsulated in a sustained-release matrix tablet. The oral route of administration is widely regarded as the most natural, convenient, and safe, owing to its ease of administration, enhanced patient compliance, and cost-effective manufacturing process. Sustained-release dosage forms are meticulously designed to release the medication at a predetermined rate, thereby achieving and maintaining optimal therapeutic blood levels. The incorporation of sustained-release technology offers a multitude of benefits, including sustained blood levels, attenuation of adverse effects, and improved patient compliance. This study will undertake a comprehensive investigation of the effects of various formulation variables, such as polymer type and concentration, filler type, and tablet compression force, on the release characteristics of the drug. The optimized formulation will subsequently be evaluated for its stability, scalability, and in vitro release properties.

KEYWORDS: Sustained, Antihyperglycemic, Matrix, Tablets.

INTRODUCTION

All the pharmaceutical products formulated for systemic delivery via the oral route of administration irrespective of the mode of delivery (immediate, sustained or controlled release) and the design of dosage forms (either solid dispersion or liquid), must be developed within the intrinsic characteristics of GI physiology, pharmacokinetics, pharmacodynamics and formulation design is necessary to achieve a systemic approach to the successful development of an oral pharmaceutical dosage form.[1-5]

The novel system of drug delivery offers a means of improving the therapeutic effectiveness of included drugs by providing sustained, controlled delivery and / or targeting the drug to desired site.[6]

Sustained release systems include any drug delivery system that achieves slow. Release of drug over a comprehensive period of time.[7] As sustained release (SR) has given a new. Breakthrough for novel drug delivery system (NDDS) in the field of pharmaceutical technology. It excludes multifaceted production procedures such as coating and pelletization during manufacturing and drug release rate from the dosage form is controlled mainly by the type and proportion of polymer used in the preparations. Hydrophilic polymer matrix is extensively used for formulating an SR dosage form.[8]

MATERIALS AND METHODS

Materials Used in Design of Formulation: Glibenclamide, MCC, Sodium alginate, Metolose, HPMC K4M, Carbopol 934P, Aerosil, Magnesium stearate.

Solubility studies: Solubility of Glibenclamide was determined in pH 1.2, pH 6.8 and pH 7.4 phosphate buffers. Solubility studies were performed by taking excess amount of Glibenclamide in different beakers containing the solvents. The mixtures were shaken for 24hrs at regular intervals. The solutions were filtered by using whattmann's filter paper grade no. 41. The filtered solutions were analyzed spectrophotometrically at 240 nm.

Determination of Melting Point: Melting point of Glibenclamide was determined by capillary method. Fine powder of Glibenclamide was filled in glass capillary tube (previously sealed at one end). The capillary tube was tied to thermometer and the thermometer was placed in the Thais tube and this tube was placed on fire. The powder at what temperature it melted was noticed.

Spectroscopic study

Determination of absorption maximum (λmax): The wavelength at which maximum absorption of radiation takes place is called as λmax. This λmax is characteristic or unique for every substance and useful in identifying the substance. For accurate analytical work, it is important to determine the absorption maxima of the substance under study. Most drugs absorb radiation in ultraviolet region (190-390nm), as they are aromatic or contain double bonds.

Accurately weighed 10mg of Glibenclamide was dissolved in 0.1N HCL (pH 1.2) taken in a clean 10 ml volumetric flask. The volume was made up to 10 ml with 0.1N HCL which will give stock solution-I with concentration 1000µg/ml.

From the stock solution-I, 1ml was pipette out in 10ml volumetric flask. The volume was made up to 10 ml using 0.1N HCL to obtain stock solution-II with a concentration 100µg/ml. From stock solution-II, 1ml was pipette out in 10 ml volumetric flask. The volume was made up to 10ml using 0.1N HCL to get a concentration of 10µg/ml. This solution was then scanned at 200- 400 nm in UV-Visible double beam spectrophotometer to attain the absorption maximum (λmax).

Construction of calibration curve using 0.1 N HCL

Standard calibration curve of Glibenclamide in 0.1N HCL

- Standard solution: Accurately weighed 10mg of Glibenclamide was dissolved in 0.1N HCL taken in a clean 10ml volumetric flask. The volume was made up to 10ml with 0.1NHCL which gives a concentration of 1000µg/ml.
- Stock solution: From this standard solution, 1ml was pipette out in 10ml volumetric flask and volume was made up to 10ml using 0.1N HCL to obtain a concentration of 100µg/ml. From the above stock solution, aliquots of 0.5, 1, 1.5, 2, 2.5, 3 ml each was transferred to a separate 10ml volumetric flask and solution was made up to 10ml using

0.1N HCL to obtain a concentration of 5, 10, 15, 20, 25 and 30µg/ml respectively. The absorbance of each solution was measured at 210 nm.

FORMULATION DEVELOPMENT

Development Strategy

The following ingredients were selected for formulation development of model drug based on the literature search and Preformulation studies.

Selection of formulation method

Sustained release tablets of model drug were formulated using following methods they are:

1. Direct compression
2. Wet granulation

1. DIRECT COMPRESSION

In this process the tablets are compressed directly from powder blends of active ingredient and suitable excipients, which will flow uniformly in to the die cavity and form a firm compact.

Brief manufacturing procedure for the preparation of tablets

Step 1- Weighed all the ingredients separately.

Step 2- The model drug and the other excipients were passed through 40# sieve together andblended for 10 minutes.

Step 3- The magnesium stearate was passed through 60# sieve and added to the blend of step2 and blended for 5 minutes.

Step 4- Compressed the blend of step 3 in to tablets by using 8.5mm, round punches.

Composition of model drug formulations for direct compression

Table 1: Composition of model drug formulations for direct compression.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Drug	20	20	20	20	20	**20**	20	20
MCC	72	67	72	67	72	**67**	72	67
HPMC-K4M	05	10	_	_	_	**_**	_	_
Metolose 60 SH50	_	_	05	10	_	**_**	_	_
Carbopol 971p	_	_	_	_	05	**10**	_	_
Sodium alginate	_	_	_	_	_	**_**	05	10
Aerosil	1	1	1	1	1	**1**	1	1
Mag.stearate	2	2	2	2	2	**2**	2	2
Total(mg)	100	100	100	100	100	**100**	100	100

RESULTS AND DISCUSSION

PREFORMULATION STUDIES

Solubility study

Table 2: The solubility of Glibenclamide was carried out at 25^0C using 0.1 N HCL, 6.8 phosphate buffer, and purified water.

S. No	Medium	Solubility (mg/ml)
01	Water	0.047
02	0.1 N HCL	0.451
03	6.8 pH phosphatebuffer	0.256

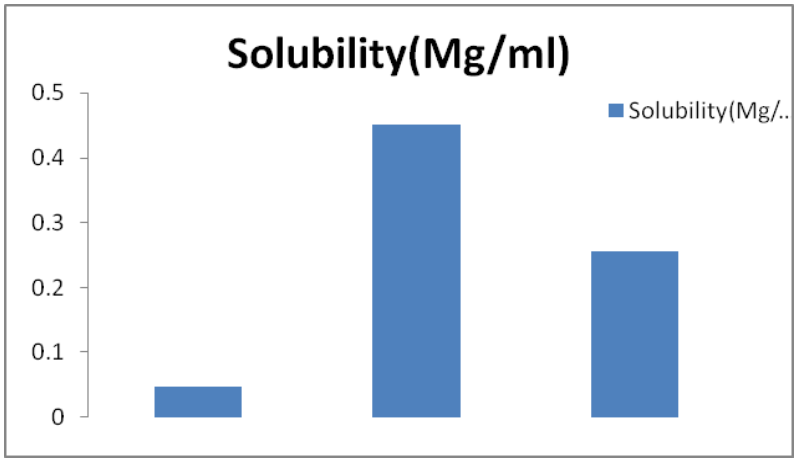

Fig. 1: Solubility of Glibenclamide.

Spectroscopic studies

Determination of λ_{max}

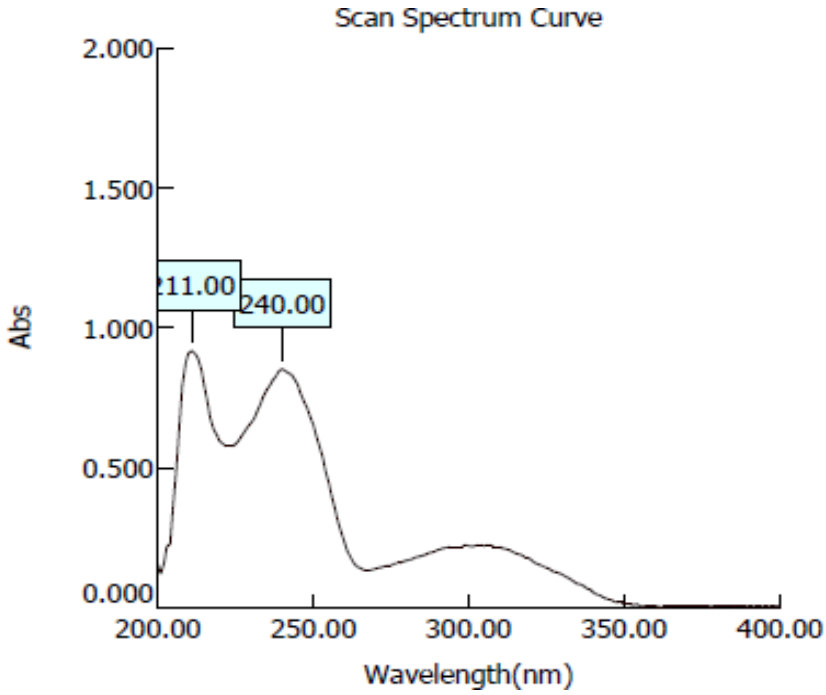

Fig 2: λmax of Glibenclamide in methanol (25µg/ml).

Calibration curve

Calibration curve of Glibenclamide at 0.1N HCl

Table 3: Standard calibration data of Glibenclamide in 0.1N HCL.

Concentration (µg/ml)	Absorbance
0	0
5	0.121
10	0.246
15	0.367
20	0.495
25	0.615
30	0.724

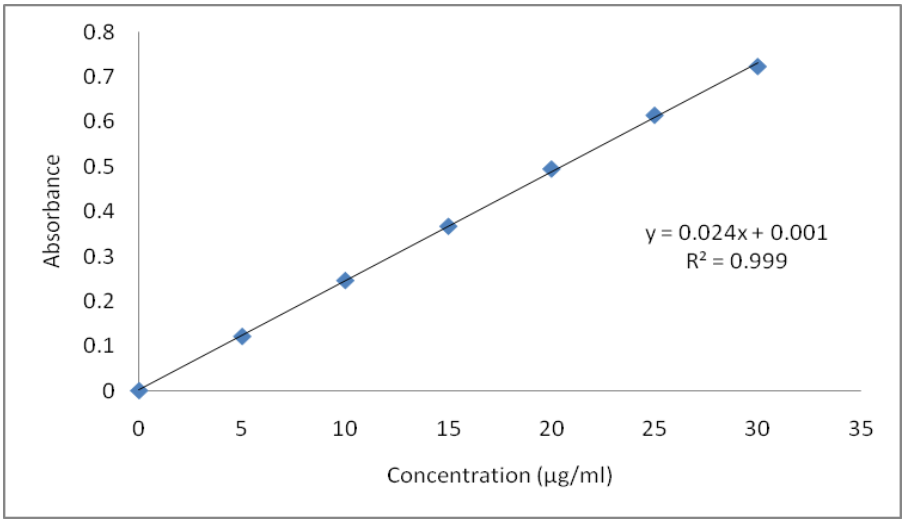

Fig 3: Standard calibration curve of Glibenclamide in 0.1N HCL.

For the developed UV method for estimation of Glibenclamide, the calibration curve data is presented in Table 3. The linearity range was found to be 5-30µg/ml. Goodness of fit of regression equation was supported by highly significant value of 'r' (0.999).

Drug polymer interaction (FTIR) study

From the spectra of Glibenclamide, and optimized formulation, it was observed that all characteristic peaks of Glibenclamide were present in the combination spectrum, thus indicating compatibility of the Drug and polymer.

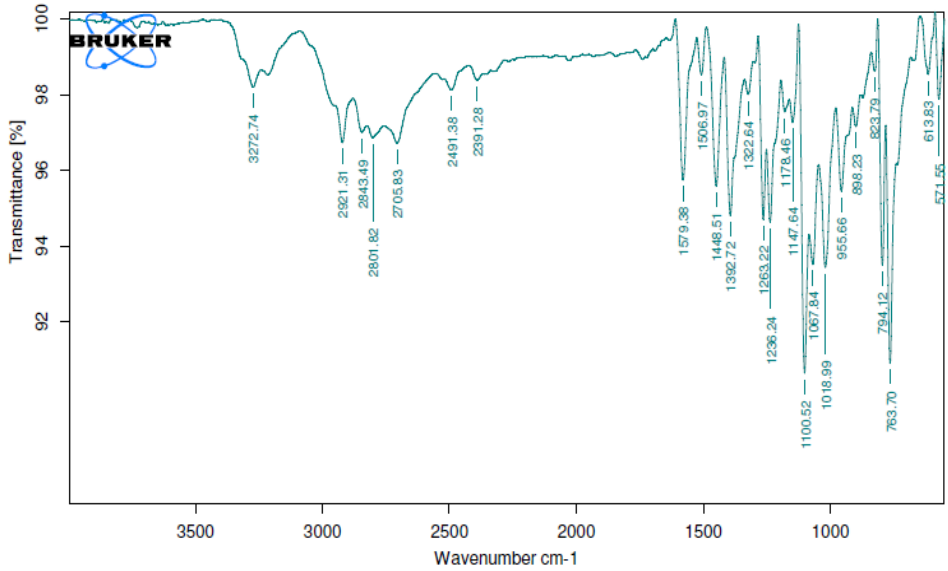

Fig 4: IR spectra of Glibenclamide.

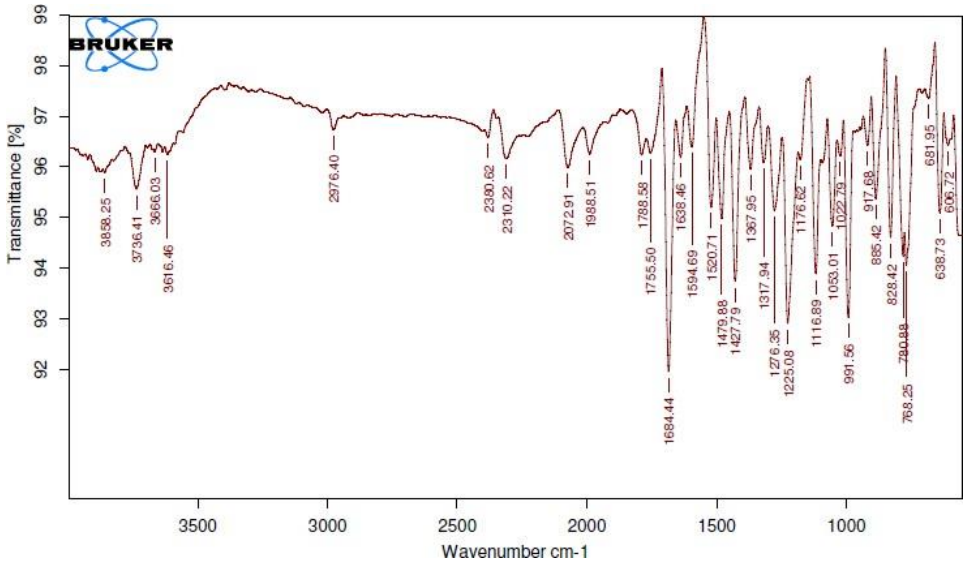

Fig 5: IR spectra of optimized formulation (F3).

Evaluation Studies

Characterization of blend

Table 4: Pre-Compression parameters.

Formulation code	Angle ofRepose	Bulk Density	TappedDensity	Carr's Index	Hausner'sRatio
F1	32.97	0.59	0.67	10.24	1.11
F2	31.54	0.61	0.71	9.56	1.09
F3	33.49	0.59	0.69	13.57	1.19
F4	32.53	0.63	0.75	11.64	1.09
F5	27.58	0.61	0.67	11.53	1.16
F6	31.46	0.65	0.68	8.99	1.17
F7	32.92	0.68	0.76	12.55	1.15
F8	30.88	0.62	0.74	11.34	1.18

Characterization of tablets

Post Compression parameters

All the batches of tablet formulations were characterized for official evaluation parameters like Weight variation, Hardness, Friability, Tablet thickness and drug content and results are shown in the table 5.

Table 5: Characterization of Glibenclamide of matrix tablets.

Formulation	Weight variation(mg)	Thickness(mm)	Hardness(kp)	Friability(%)	Drug content (%)
F1	301	4.43	5-7	0.55	98.24
F2	298	4.45	5-7	0.46	99.41
F3	301	4.40	5-7	0.83	100.36
F4	298	4.39	5-7	0.53	99.55
F5	300	4.39	5-7	0.25	99.70
F6	302	4.40	5-7	0.78	97.82
F7	300	4.46	5-7	0.78	100.29
F8	301	4.40	5-7	0.28	99.97

In vitro dissolution studies

Dissolution profile for Glibenclamide extended release tablets: (Glibenclamide REFERENCE)

Table 6: % Cumulative drug release of Marketed product.

Time(hr)	Mean % drug release
	MP
1	18.67
2	26.26
4	40.24
6	53.89
8	68.23
10	81.92
12	96.41

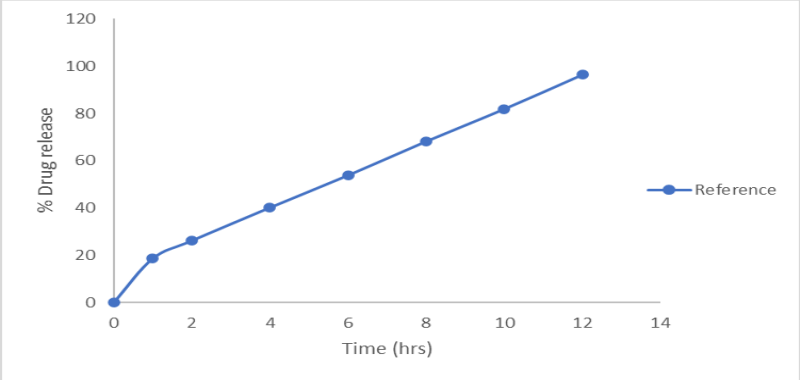

Fig 6: Dissolution study of Reference Drug.

Dissolution studies

Table 7: % Cumulative drug release of formulations F1-F4.

Time(hr)	% drug release			
	F1	F2	F3	F4
0	0	0	0	0
1	28.14	31.26	40.14	37.23
2	39.38	40.52	54.38	51.62
4	58.23	55.34	78.23	75.24
6	77.84	70.25	99.84	97.58
8	98.16	85.67		
10		100.37		
12				

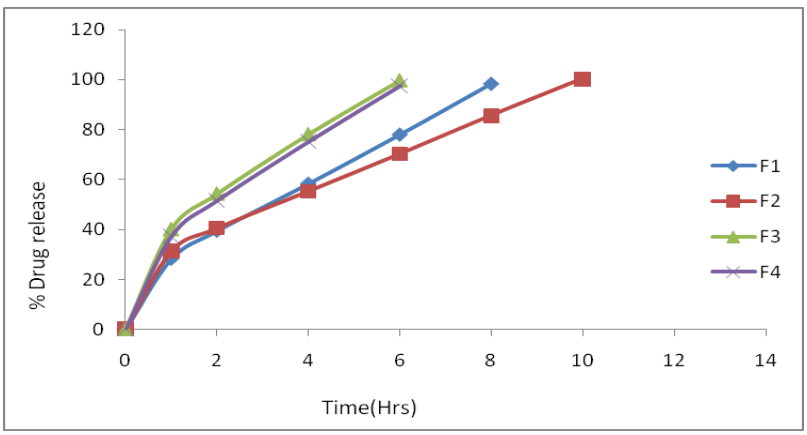

Fig 7: In Vitro Drug release study of F1 - F4.

Table 7: % Cumulative drug release of formulations F5-F8.

Time(hr)	% drug release			
	F5	F6	F7	F8
0	**0**	**0**	**0**	**0**
1	20.1	**22.26**	50.13	36.27
2	27.36	**29.97**	62.38	47.62
4	41.73	**43.88**	81.23	64.98
6	56.08	**58.3**	99.18	81.58
8	70.16	**72.6**		98.86
10	84.34	**86.96**		
12	97.23	**99.4**		

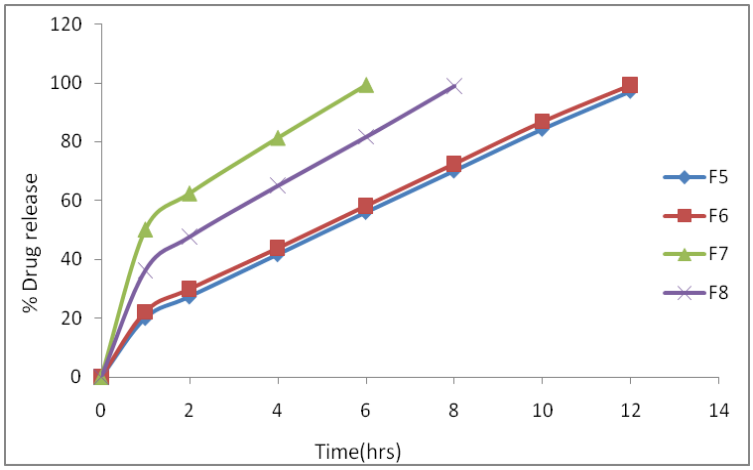

Fig 8: In vitro drug release study of F5 - F8.

Table 8: % Cumulative drug release of formulations F1-F8.

Time(hr)	% drug release							
	F1	F2	F3	F4	F5	F6	F7	F8
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1	28.14	31.26	40.14	37.23	20.1	**22.26**	50.13	36.27
2	39.38	40.52	54.38	51.62	27.36	**29.97**	62.38	47.62
4	58.23	55.34	78.23	75.24	41.73	**43.88**	81.23	64.98
6	77.84	70.25	99.84	97.58	56.08	**58.3**	99.18	81.58
8	98.16	85.67			70.16	**72.6**		98.86
10		100.37			84.34	**86.96**		
12					97.23	**99.4**		

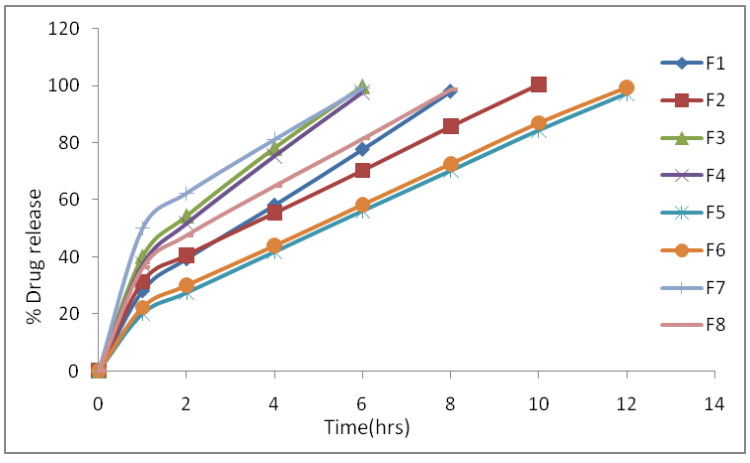

Fig 9: In vitro drug release study of F1 - F8.

Evaluation of drug release kinetics

Release kinetic study: The kinetic release data was computed from the release data obtained from the *in-vitro* dissolution study of the best formulation F6 and reference and fitted to the mathematical models; Zero order equation, First order, Higuchi release and Korsmeyer- Peppas models.

Table 9: In Vitro Drug Release kinetics for optimized formulation.

	R^2 values				n values
Formulation	**Zero order**	**First order**	**Higuchi**	**Korsmeyer-Peppas**	**Korsmeyer-Peppas (n)**
Reference	0.988	0.850	0.966	0.670	1.210
F-06	0.980	0.784	0.976	0.636	1.189

The *invitro* dissolution data for best formulation F14were fitted in different kinetic models i.e., zero order, first order, Higuchi and korsemeyer-peppas equation. Optimized formulation F14shows R^2 value 0.980. As its value nearer to the '1' it is conformed as it follows the First order release. The mechanism of drug release is further confirmed by the korsmeyer and peppas plot, if n = 0.45 it is called Case I or Fickian diffusion, 0.45 < n < 0.89 is for anomalous behavioror non-Fickian transport, n = 0.89 for case II transport and n > 0.89 for Super case II transport.

The 'n' value is 0.89 for the optimised formulation (F 06) i.e., n value was between 0.45 and 0.89 this indicates anomalous transport (non fickian diffusion).

Kinetic modelsgraph's for Glibenclamide (Reference) Sample

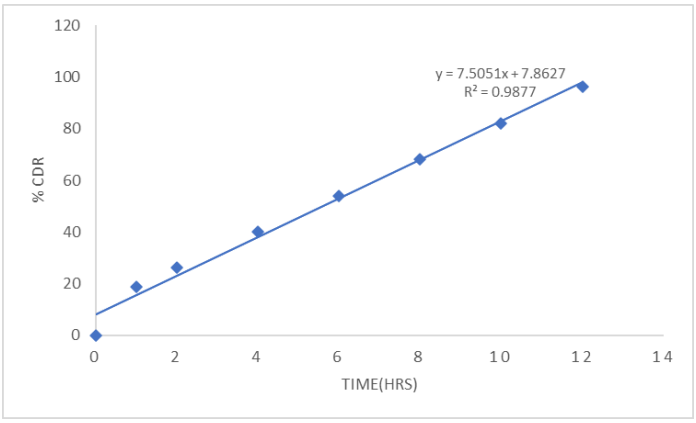

Fig. 10: Zero order plot of Glibenclamide (Reference) Sample.

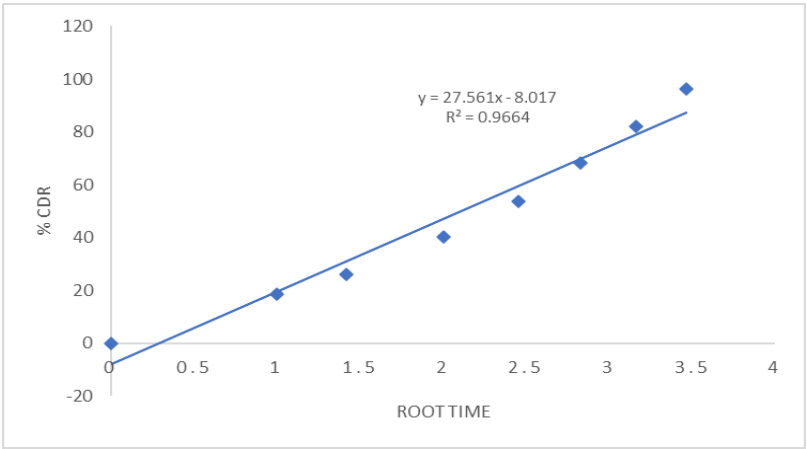

Figure 11: Higuchi plot of Glibenclamide (Reference) Sample.

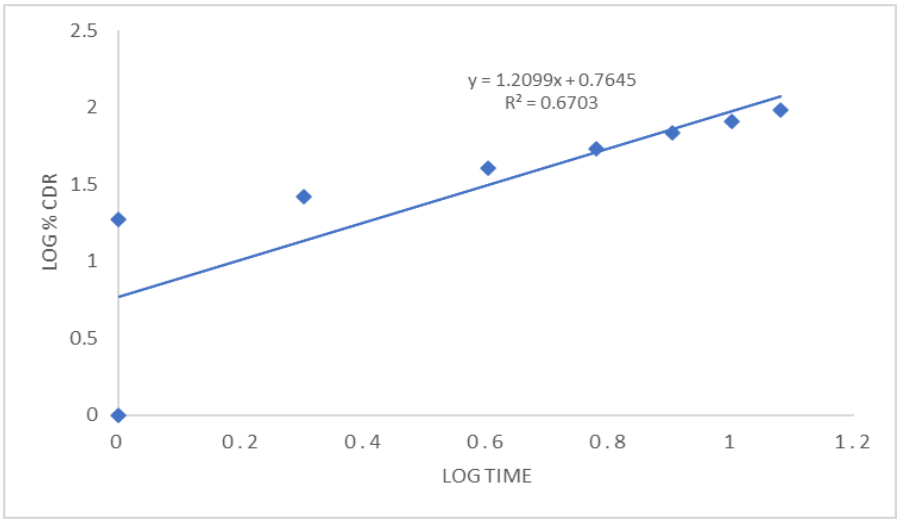

Fig. 12: Korsmeyer-peppas plot of Glibenclamide (Reference) Sample.

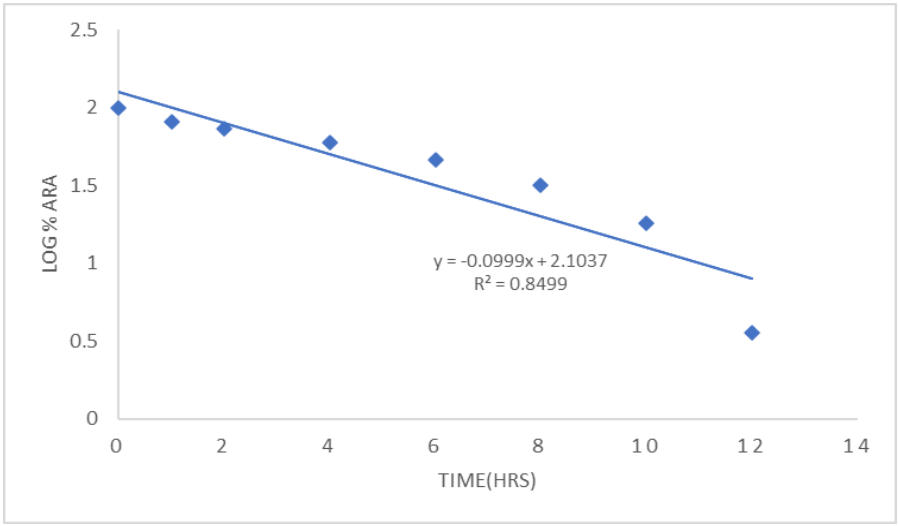

Fig. 13: First order plot of Glibenclamide (Reference) Sample.

Kinetic models for optimized formulation F6

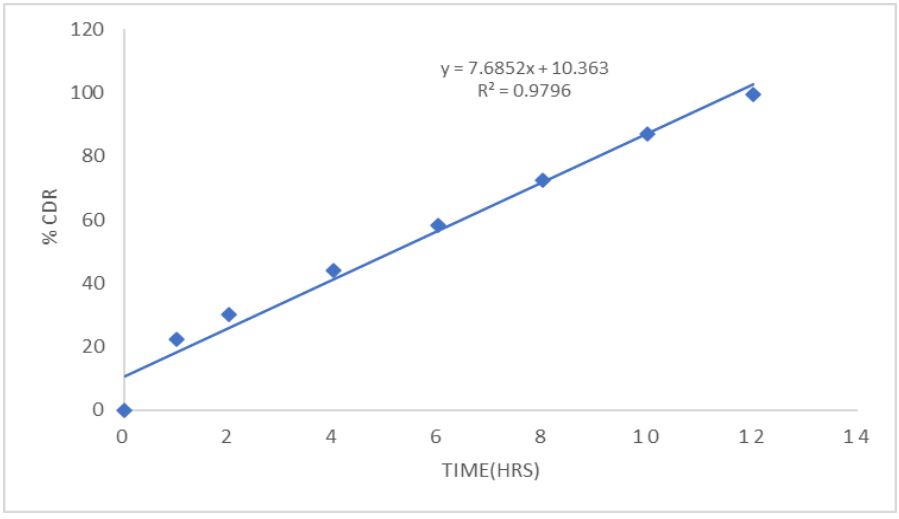

Fig. 14: Zero order plot of F6.

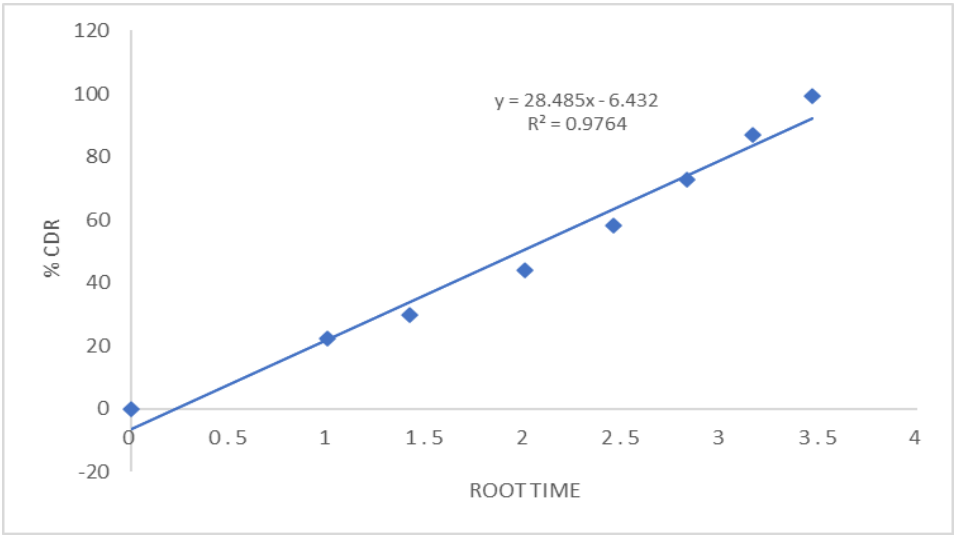

Fig. 15: Higuchi plot of F6.

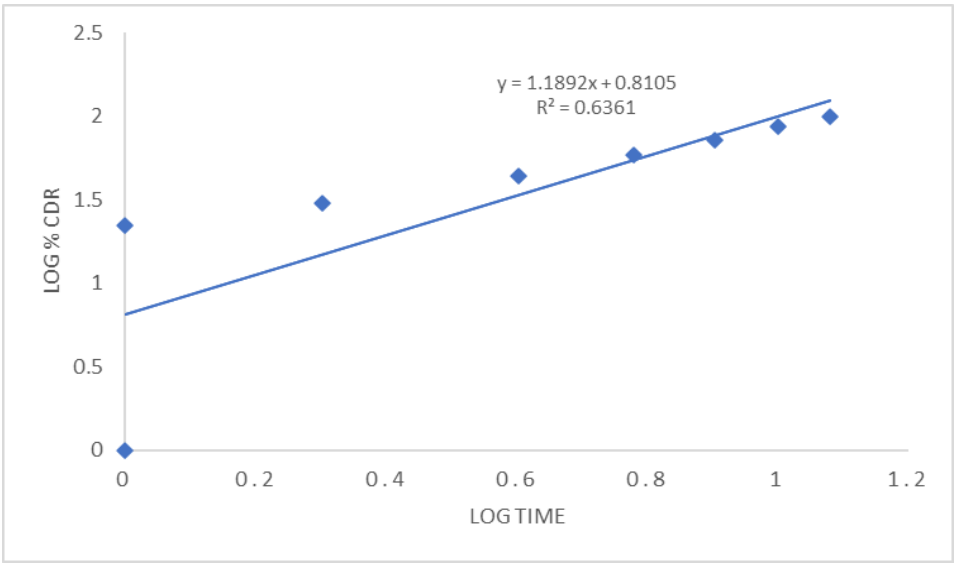

Fig. 16: Korsmeyer-peppas plot of F6.

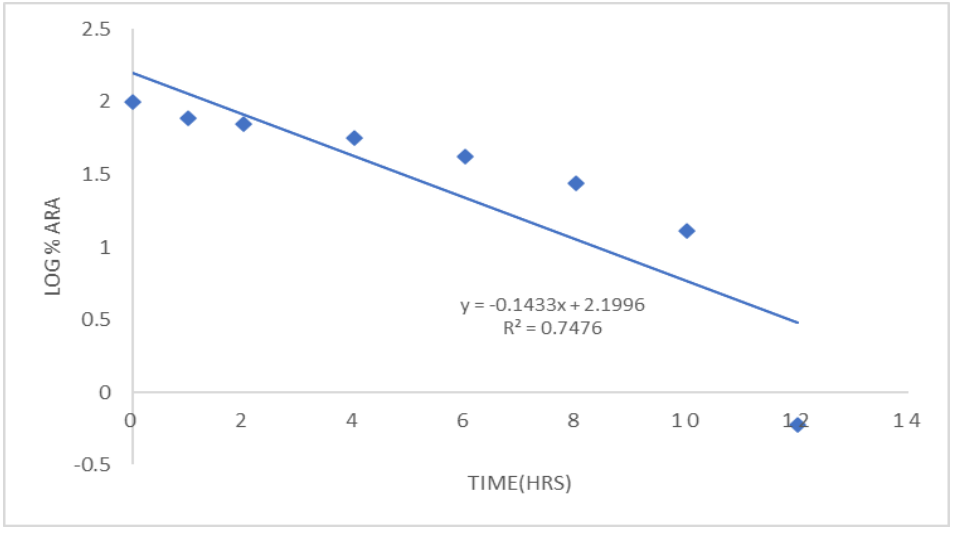

Fig. 17: First order plot of F6.

Stability data of formulation (F6)

The tablets were stored at 40 ± 2˚C/75 ± 5% RH for three months to assess their stability. At the end of three months, tablets were withdrawn, evaluated for tablet characteristics and *invitro* drug release and results were shown in table 10.

Dissolution studies of formulation F6 after 12weeks at 40^0 c /75% RH

Table 10: Dissolution studies of formulation F 06 after 12weeks at 40^0 c /75% RH.

Time(hrs)	% drug release
	F6
1	22.26
2	29.97
4	43.88
6	58.3
8	72.6
10	86.96
12	99.4

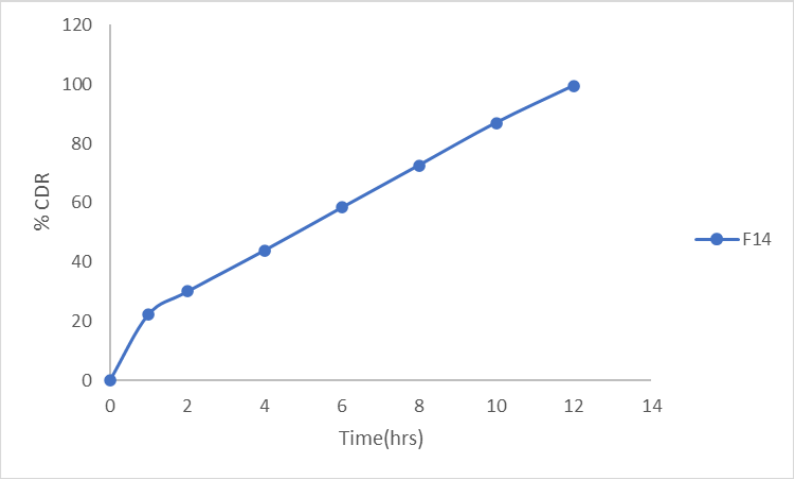

Fig. 18: Accelerated stability graph of F6.

INFERENCE AND DISCUSSION

Information from Table 2 gives the solubility of glibenclamide was occurs more in 0.1N HCl when compared with 6.8 pH phosphate buffer and distilled water.

Form the fig 2 Based upon the solubility studies 0.1N HCL was selected for the determination of UV spectra at a concentration of 25µg/ml solution, and the maximum absorption was found to be240nm.

From table 4 The angle of repose of different formulations was ≤ 33.49 which indicates that material had goodflow property. So it was confirmed that the flow property of blends were free flowing.The bulk density of blend was found between 0.59g/cm^3 to 0.68 g/cm^3.Tapped density was foundbetween 0.67g/cm^3 to 0.76 g/cm^3.These values indicate that the blends had good flow property.Carr's index for all the formulations was found to be between 8.95-13.57 and Hausner's ratiofrom 1.09-1.19 which reveals that the blends have good flow character.

From table 5 The hardness of the tablet was acceptable and uniform from batch-to-batch variation, which was found to be 5 - 7 kg/cm2.All the formulations passed the weight variation test as the % weight variation was within the pharmacopeial limits of ±7.5% of the tablet weight.Friability values were found to be less than 1% in all the

formulations F1 – F24 and considered tobe satisfactory ensuring that all the formulations are mechanically stable.The % drug content for all the formulations were close to 100 and varied between 97.82 to 100.37%.

From the fig 7 dissolution, studies indicate that Formulation F2 containing HPMC K4M as 10% of the polymer has extended the model drug release up to 10 hours. But formulations F3, F4 containing 5%, 10% concentrations of Metolose as the polymer showed faster drug release and they released drug within 6 hours only.

From the fig 8 Above dissolution studies indicate that Formulation F13&F14 containing Carbopol 934P as 10%, 15% concentration of the polymer has extended the model drug release up to 12hours. Whereas the formulations F21 and F22 containing Sodium alginate as the polymer has showed faster drug release and they released drug within 6 to 8 hours only.

From fig 9 By comparing with all dissolution studies from F1-F8, formulation F6 shows maximum extended drug release with the end of 12 hr as 99.4%.

From fig 18 The controlled stability samples showed comparable dissolution profile with the initial release. And also, there was no change in the physical characteristics. Hence, we may conclude that Model drug extended-release formulation had good stability's formulation had good stability.

The conclusion of the study is as follows

This study involved preformulation studies, formulation, evaluation, and stability studies of prepared matrix tablets, revealing compatibility between the API and excipients through physical evaluation and FTIR studies. Sustained-release tablets of a model drug, Glibenclamide, were formulated and evaluated using different polymers, including HPMC K4M, metalose, Carbopol 934P NF, and sodium alginate, with formulations F1-F8 demonstrating sustained release up to 10-12 hours. Among these, F6, containing 10% Carbapol 971P, was identified as the optimized formulation, releasing 99.4% of the drug at the end of 12 hours. Dissolution profiles and kinetic studies indicated that the release of Glibenclamide can be effectively controlled using hydrophilic matrix systems, following zero-order, first-order, Higuchi's equation, and Korsmeyer-Peppas equation kinetics.

Different kinetic models were applied to the formulation optimized and observed that formulation (F6) followed first order kinetic model and it was complied with (Reference sample). The best linearity was found in Korsmeyer-peppas model (where n=1.189 is the release exponent). Applicability of data indicating Non Fickian diffusion (or) Anomalous Transport as mechanism of drug release. Non Fickian diffusional release occurs by the usual molecular diffusion of the drug due to a chemical potential gradient. (Peppas model indicates the mechanism of drug release i.e., release of drug from the formulation is by diffusion, erosion, swelling and may by the combination of diffusion and swelling).

REFERENCES

1. John C, Morten C. The Science of Dosage Form Design, Aulton: Modified release peroral dosage forms. 2nd ed. Churchill Livingstone, 2002; 290-300.
2. Mandal S, Ratan GN, Mulla JS, Thimmasetty J, Kaneriya A, "Design and In Vitro Evaluation of Gastro Retentive Sustained Release Tablets of Tizanidine Hydrochloride", Indian Journal of Novel Drug delivery, 2010; 2(4): 144-152.
3. Chien Y. W. Novel Drug Delivery System, 1992; 2: 139 – 140.

4. Dixit Navin, Sheo, DM. Bhanu, Sagar PS. Sustained Release Drug Delivery System. Indian Journal of Research in Pharmacy and Biotechnology, 2013; 1(3): 305.
5. Chugh I, Seth N, Rana AC, Gupta S. Oral sustained release drug delivery system: an overview. International research journal of pharmacy, 2012; 3(5): 57-62.
6. Jantez GM, Robinson JR. Sustained and controlled release drug delivery systems. In: Banker GS, Rhodes CT, editors. Modern pharmaceutics. 3rd edition. New York: marcel dekker inc, 1996.
7. Brahmankar D. M. and Jaiswal S. B. in “Biopharmaceutics and Pharmacokinetics”, "A Treatise,” Vallabh Prakashan, 1st Edition, 1995; 347-352.
8. Kar RK, Mohapatra S, Barik BB. Design and characterization of controlled release matrix tablets of Zidovudine. Asian J Pharm Cli Res, 2009; 2: 54-6.