ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 13, Issue, 02, pp. 61863-61869, February, 2023
https://doi.org/10.37118/ijdr.26422.02.2023

RESEARCH ARTICLE OPEN ACCESS

EFFECT OF POLYMER CONCENTRATIONON DRUG RELEASE IN THE FORMULATION CONTROLLED RELEASE TABLETS OF GLIPIZIDEUSING VARIOUS POLYMERS

N. Lavanya*[1], Dr. B. Majula[1], Dr. K. Balaji[2] and Dr. S. Ramya Sri[2]

[1]Department of Pharmaceutics, Avanthi Institute of Pharmaceutical Sciences, Jawarharlal Nehru Technological University, Hyderabad, Telangana, India
[2]Department of Pharmaceutics, Sura Pharma Labs, Hyderabad, Telangana, India

ARTICLE INFO

Article History:
Received 11th January, 2023
Received in revised form
26th January, 2023
Accepted 08th February, 2023
Published online 28th February, 2023

KeyWords:

Glipizide, Eudragit RSPO, Sodium alginate, Sodium CMC and Controlled release tablets.

Corresponding author: R. Lavanya,

ABSTRACT

The objective of the present study was to develop Controlled release tablets of Glipizide using different polymers. The tablets were prepared with different ratios of Eudragit RSPO, Sodium alginate and Sodium CMC by direct compression technique. The solubility study of the Glipizide was conducted to select a suitable dissolution media for in vitro drug release studies. FTIR study revealed no considerable changes in IR peak of Glipizide and Hence no interaction between drug and the excipients. In vitro release from the formulation F5 was found to be 99.31 %. From all the results of dissolution data fitted to various drug release Kinetic equations. It was observed that highest correlation was found for Higuchi release kinetics mechanism.

Citation: ***R. Lavanya, Dr. B. Majula, Dr. K. Balaji and Dr. S. Ramya Sri. 2023.*** "Effect of polymer concentrationon drug release in the formulation controlled release tablets of glipizideusing various polymers*", International Journal of Development Research*, 13, (02), 61863-61869.

INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral route is considered most natural, convenient and safe due to its ease of administration, patient acceptance, and cost effective manufacturing process. Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption.[1,2,3] Controlled release dosage form is a dosage form that release one or more drugs continuously in predetermined pattern for a fixed period of time, either systemically or locally to specified target organ. Greater attention is paid on development of oral controlled release drug delivery systems due to flexibility in designing of dosage form. The main challenges to oral drug delivery systems are to deliver a drug at therapeutically effective rate to desirable site, modulation of GI transit time and minimization of first pass elimination. Control release dosage form provides better maintenance of optimal and effective drug level for prolonged duration with less dosing frequency and side effects.[4,5]

Historically, oral drug administration has been the predominant route for drug delivery. It is known to be the most popular route of drug administration due to the fact the gastrointestinal physiology offers more flexibility in dosage form design than most other routes A major challenge for the pharmaceutical industry in drug development is to produce safe and efficient drugs, therefore properties of drugs and the way in which they are delivered must be optimised. A controlled release drug delivery system delivers the drug locally or systemically at a predetermined rate for a specified period of time. The goal of such systems is to provide desirable delivery profiles that can achieve therapeutic plasma levels. Drug release is dependent on polymer properties, thus the application of these properties can produce well characterised and reproducible dosage forms.[6] The basic rationale of a controlled release drug delivery system is to optimize the biopharmaceutics, pharmacokinetics, and pharmacodynamics properties of a drug in such a way that its utility is maximized through reduction in side effects and cure or control of disease condition in the shortest possible time by using smallest quantity of drug, administered by most suitable route. The immediate release drug delivery system lacks some features like dose maintenance, controlled release rate and site targeting. An ideal drug delivery system should deliver the drug at a rate dictated by the need of body over a specified period of treatment.

A controlled release drug delivery system is capable of achieving the following benefits over conventional dosage forms:[7]

- ✓ Total dose is low.
- ✓ Reduced GI side effects and other toxic effects.
- ✓ Reduced dosing frequency.
- ✓ Better patient acceptance and compliance.
- ✓ Less fluctuation in plasma drug levels.
- ✓ More uniform drug effect.
- ✓ Better stability of drug.

Advantages of Controlled Release Drug Delivery System

- Therapeutic advantage: Reduction in drug plasma level fluctuation, maintenance of a steady plasma level of the drug over a prolonged time period, ideally simulating an intravenous infusion of a drug.
- Reduction in adverse side effects and improvement in tolerability: Drug plasma levels are maintained within a narrow window with no sharp peaks and with AUC of plasma concentration Vs time curve comparable with total AUC from multiple dosing with immediate release dosage form.
- Patient comfort and compliance: Oral drug delivery is the most common and convenient for patient and a reduction in dosing frequency enhances compliance.
- Reduction in Health care cost: The total cost of therapy of the controlled release product could be comparable or lower than the immediate release product with reduction in side effects. The overall expense in disease management also would be reduced. This greatly reduces the possibility of side effects, as the scale of side effects increases as we approach the maximum safe concentration.

Avoid night time dosing: It also good for patients to avoid the at night time.[8,9,10]

MATERIALS

Glipizide Procured From Hetero Pharma, Hyderabad, India. Provided by SURA LABS, Dilsukhnagar, Hyderabad, Eudragit RSPO from Merck Specialities Pvt Ltd, Mumbai, India Sodium alginate from Merck Specialities Pvt Ltd, Mumbai, India Sodium CMC from Merck Specialities Pvt Ltd, Mumbai, India PVP-K 30 from Merck Specialities Pvt Ltd, Mumbai, India Aerosil from Merck Specialities Pvt Ltd, Mumbai, India. Magnesium Stearate from Merck Specialities Pvt Ltd, Mumbai, India. Micro crystalline cellulose from Merck Specialities Pvt Ltd, Mumbai, India.

METHODOLOGY

Analytical method development

Determination of absorption maxima: 10mg of Glipizide pure drug was dissolved in 10ml of Methanol (stock solution). 1ml of above solution was taken and made up to10ml by using 0.1 N HCl (100µg/ml). From this 1ml was taken and made up to 10 ml of 0.1 N HCl (10µg/ml) and the solution was scanned in the range of 200 – 400 nm. Similar procedure was repeated to pH 6.8 Phosphate buffer UV spectrum was taken using Double beam UV/VIS spectrophotometer.

Preparation calibration curve: 10mg of Glipizide pure drug was dissolved in 10ml of Methanol (stock solution). 1ml of above solution was taken and made up to10ml by using 0.1 N HCl (100µg/ml).From this 1ml was taken and made up to 10 ml of 0.1 N HCl (10µg/ml). The above solution was subsequently diluted with 0.1N HCl to obtain series of dilutions Containing 10,20,30,40 and 50 µg/ml of Glipized per ml of solution. The absorbance of the above dilutions was measured at 255nm by using UV-Spectrophotometer taking 0.1N HCl as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2)which determined by least-square linear regression analysis. The above procedure was repeated by using pH 6.8 phosphate buffer.

Preformulation parameters: The quality of tablet, once formulated by rule, is generally dictated by thequality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose: The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

$\tan \theta = h / r$ $\tan \theta$ = Angle of repose
h = Height of the cone, r = Radius of the cone base

RESULTS AND DISCUSSION

The present study was aimed to developing Controlled release tablets of Glipizide using various polymers. All the formulations were evaluated for physicochemical properties and in vitro drug release studies.

Analytical Method: Graphs of Glipizidewere taken in 0.1N HCl and in pH 6.8 phosphate buffer at255 nm and 260nm respectively.

Table 1. Formulation composition for tablets

All the quantities were in mg

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9
Glipizide	5	5	5	5	5	5	5	5	5
Eudragit RSPO	10	20	30	-	-	-	-	-	-
Sodium alginate	-	-	-	5	10	15	-	-	-
Sodium CMC	-	-	-	-	-	-	5	10	15
PVP-K 30	10	10	10	10	10	10	10	10	10
Aerosil	7	7	7	7	7	7	7	7	7
Magnesium Stearate	7	7	7	7	7	7	7	7	7
Micro crystalline cellulose	111	106	96	111	106	96	111	106	96
Total weight	150	150	150	150	150	150	150	150	150

Table 2. Observations for graph of Glipizide in 0.1N HCl (255nm)

Conc [µg/mL]	Abs
0	0
10	0.159
20	0.314
30	0.458
40	0.597
50	0.741

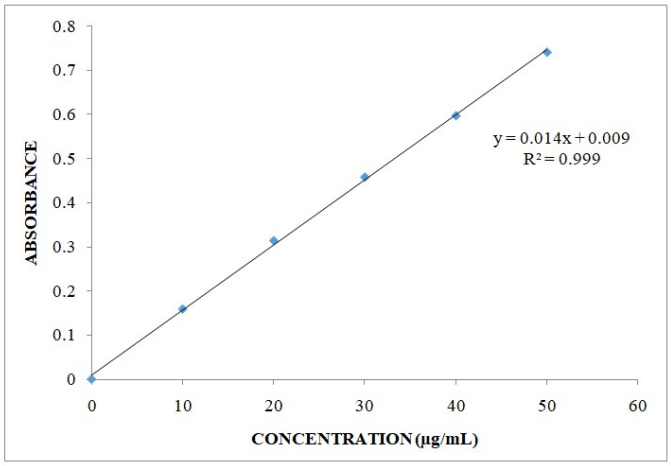

Figure 1. Standard graph of Glipizide in 0.1N HCl (255nm)

Table 3. Observations for graph of Glipized in p H 6.8 phosphate buffer (260nm)

Conc [µg/mL]	Abs
0	0
10	0.111
20	0.258
30	0.361
40	0.478
50	0.598

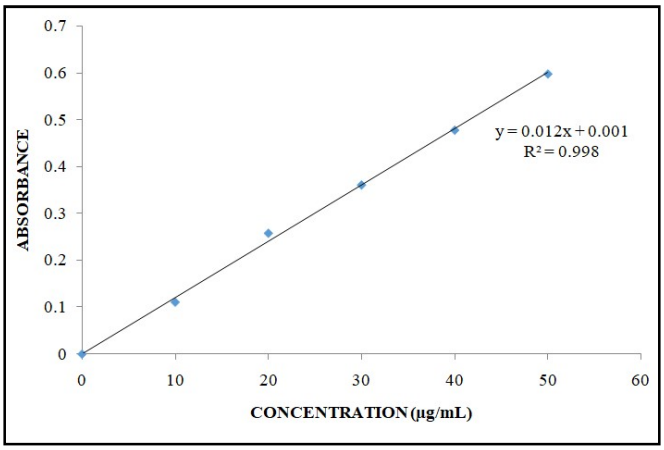

Figure 2. Standard graph of Glipizide pH 6.8 phosphate buffer (260nm)

Preformulation parameters of powder blend

Table 4. Pre-formulation parameters of Core blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	23.2 ± 0.2	0.434 ± 0.2	0.476 ± 0.3	8.695	1.095
F2	25.2 ± 0.1	0.277 ± 0.2	0.312 ± 0.2	11.11	1.333
F3	27.1 ± 0.1	0.588 ± 0.3	0.666 ± 0.4	11.76	1.333
F4	24.4 ± 0.4	0.521 ± 0.3	0.631 ± 0.3	17.39	1.121
F5	28.3 ± 0.4	0.625 ± 0.1	0.833 ± 0.1	25.00	1.333
F6	25.1 ± 0.1	0.476 ± 0.3	0.526 ± 0.2	9.52	1.105
F7	26.7 ± 0.4	0.416 ± 0.2	0.476 ± 0.3	12.50	1.142
F8	26.0 ± 0.3	0.384 ± 0.4	0.434 ± 0.3	11.53	1.130
F9	26.6 ± 0.2	0.555 ± 0.1	0.714 ± 0.1	22.22	1.285

All the values represent n=3

Quality control parameters for tablets

Table 5. *In vitro* quality control parameters for tablets

Formulation codes	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	148.52	3.24	0.48	2.54	98.35
F2	150.06	3.43	0.65	2.85	99.48
F3	148.56	3.38	0.72	2.68	99.16
F4	150.41	3.54	0.57	2.52	99.65
F5	146.35	3.18	0.45	2.74	100.48
F6	147.89	3.49	0.67	2.66	97.65
F7	149.88	3.33	0.68	2.81	97.76
F8	145.31	3.29	0.82	2.65	98.46
F9	149.40	3.43	0.59	2.72	99.79

***In Vitro* Drug Release Studies**

Table 6. Dissolution Data of Glipizide Tablets F1-F9

	CUMULATIVE PERCENT DRUG RELEASE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	8.92	4.78	6.70	26.15	24.90	18.72	18.17	16.90	11.49
1	13.27	8.90	10.22	35.70	32.67	22.39	26.12	22.45	18.63
2	16.75	12.83	15.93	41.38	40.79	29.56	36.64	30.02	29.55
3	22.41	17.94	18.51	56.33	45.52	32.20	45.20	38.31	35.84
4	26.39	19.30	23.74	64.38	53.96	41.71	59.56	46.82	40.39
5	29.56	22.46	29.93	76.45	58.83	52.98	65.43	54.47	46.71
6	32.81	25.62	34.45	83.11	64.30	59.23	73.01	60.74	54.05
7	38.40	32.76	38.60	89.82	71.91	65.45	85.57	66.05	61.87
8	42.52	37.61	45.91	97.37	78.29	72.39	97.28	71.93	67.02
9	48.75	45.85	47.59		84.50	79.63		78.26	75.12
10	56.16	50.96	56.75		89.91	82.72		85.45	82.21
11	73.39	62.35	60.32		94.72	89.90		96.25	89.50
12	85.54	78.14	66.83		99.31	91.83			98.14

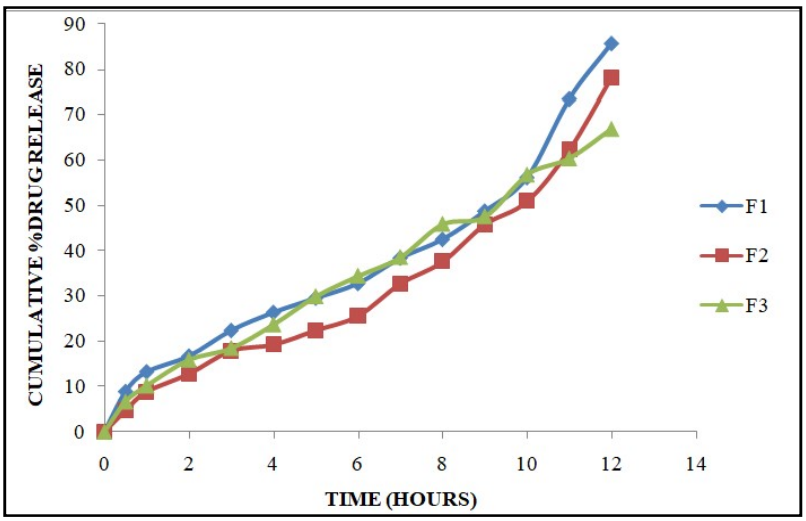

Figure 8.3. Dissolution profile of Glipizide (F1, F2, F3 formulations)

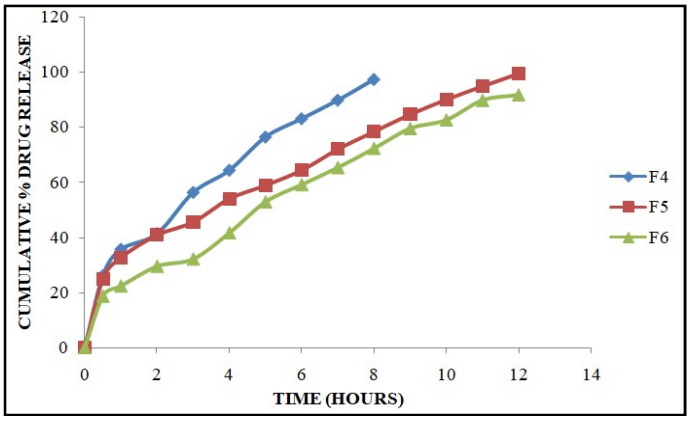

Figure 8.4. Dissolution profile of Glipizide (F4, F5, F6 formulations)

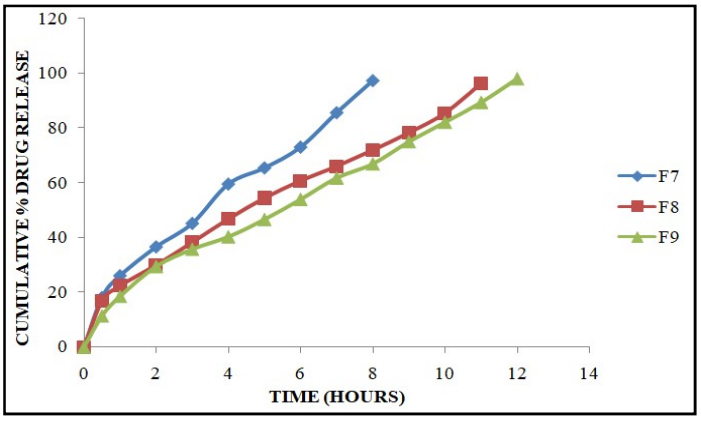

Figure 8.5. Dissolution profile of Glipizide (F7, F8, F9 formulations)

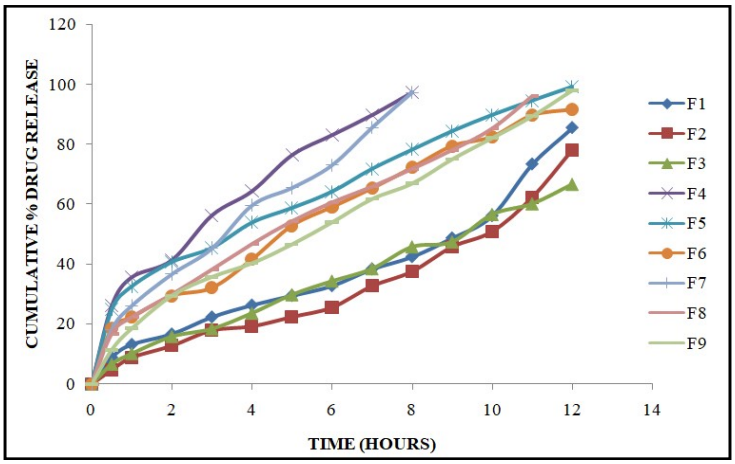

Figure 6. Dissolution profile of Glipizide (F1-F9 formulations)

Table 7. Release kinetics data for optimised formulation

Cumulative (%) release Q	Time (T)	Root (t)	Log(%) release	Log (t)	Log (%) remain	Release rate (cumulative % release / t)	1/cum% release	Peppas log q/100	% drug remaining	Q01/3	Qt1/3	Q01/3-qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
24.9	0.5	0.707	1.396	-0.301	1.876	49.800	0.0402	-0.604	75.1	4.642	4.219	0.423
32.67	1	1.000	1.514	0.000	1.828	32.670	0.0306	-0.486	67.33	4.642	4.068	0.573
40.79	2	1.414	1.611	0.301	1.772	20.395	0.0245	-0.389	59.21	4.642	3.898	0.744
45.52	3	1.732	1.658	0.477	1.736	15.173	0.0220	-0.342	54.48	4.642	3.791	0.851
53.96	4	2.000	1.732	0.602	1.663	13.490	0.0185	-0.268	46.04	4.642	3.584	1.058
58.83	5	2.236	1.770	0.699	1.615	11.766	0.0170	-0.230	41.17	4.642	3.453	1.189
64.3	6	2.449	1.808	0.778	1.553	10.717	0.0156	-0.192	35.7	4.642	3.293	1.349
71.91	7	2.646	1.857	0.845	1.449	10.273	0.0139	-0.143	28.09	4.642	3.040	1.602
78.29	8	2.828	1.894	0.903	1.337	9.786	0.0128	-0.106	21.71	4.642	2.790	1.852
84.5	9	3.000	1.927	0.954	1.190	9.389	0.0118	-0.073	15.5	4.642	2.493	2.148
89.91	10	3.162	1.954	1.000	1.004	8.991	0.0111	-0.046	10.09	4.642	2.161	2.481
94.72	11	3.317	1.976	1.041	0.723	8.611	0.0106	-0.024	5.28	4.642	1.741	2.900
99.31	12	3.464	1.997	1.079	-0.161	8.276	0.0101	-0.003	0.69	4.642	0.884	3.758

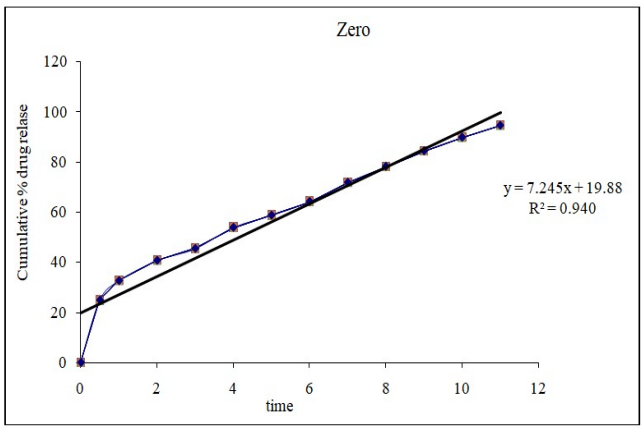

Figure 7. Zero order release kinetics graph

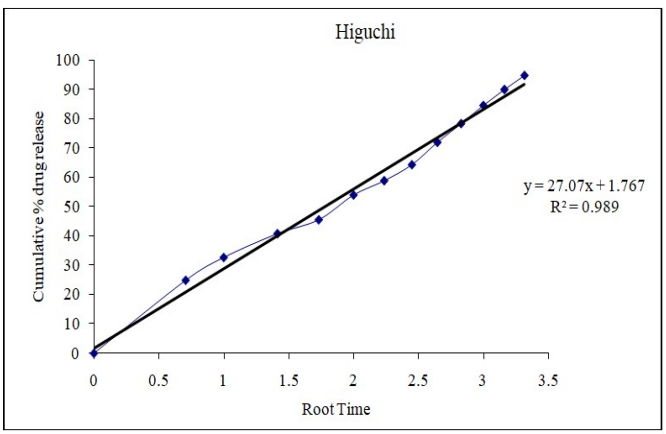

Figure 8. Higuchi release kinetics graph

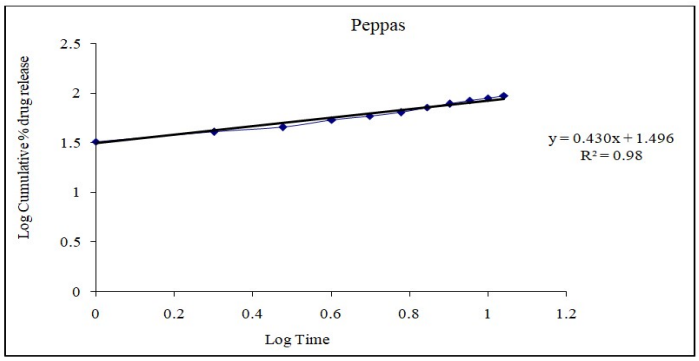

Figure 9. Karsmayer peppas graph

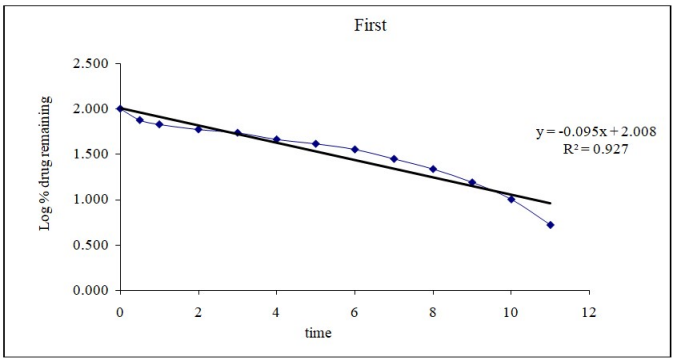

Figure 10. First order release kinetics graph

Drug – Excipient compatibility studies

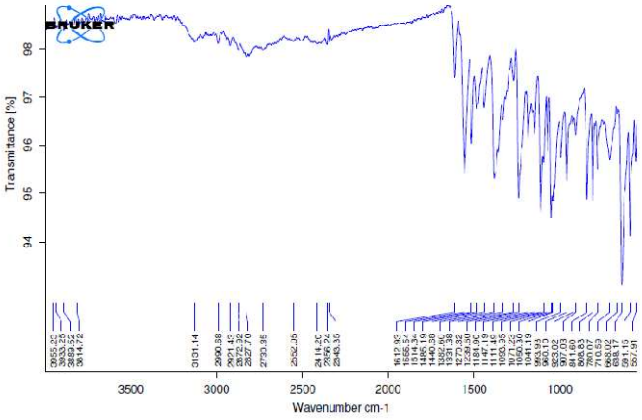

Figure 11. FT-TR Spectrum of Glipizide pure drug

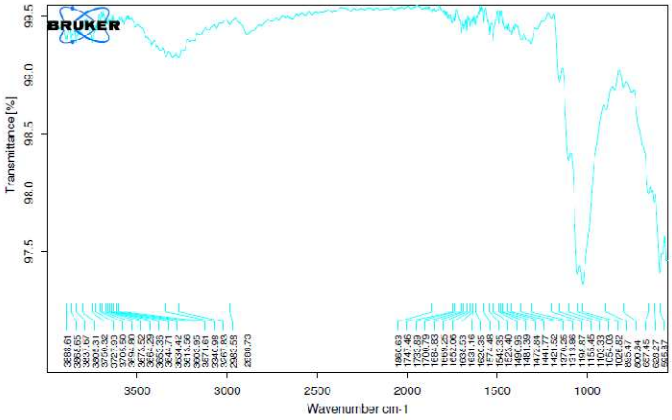

Figure 12. FT-IR Spectrum of Optimised Formulation

CONCLUSION

In this study an effort was made to study controlled release Glipizide which can provide controlled drug release for up to 12hrs. Glipizide controlled release tablets were formulated and evaluated. Glipizide controlled tablets were prepared with different polymers like Eudragit RSPO, Sodium alginate and Sodium CMC. The pre-compression and the post compression parameters are found to be within the limits. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation F5 were optimized by conducting various trails. F5 was showed good drug release 99.31 % was up to 12hrs. It followed Higuchi release kinetics mechanism.

REFERENCES

1. Sathish Ummadi, B. Shravani, N. G. Raghavendra Rao, M. Srikanth Reddy, B. Sanjeev Nayak. Overview on Controlled Release Dosage Form.International Journal of Pharma Sciences, (2013): Vol. 3, No. 4 258-269.
2. Brahmankar D.M. and Jaiswal S.B. (1995): “Biopharmaceutics and Pharmacokinetics” a Treatise. Vallabh Prakashan, First Edition; 336-337.
3. Lachman Leon, Lieberman Herbert A., Kanig Joseph L. (1996) “The theory and practice of industrial pharmacy” Second edition, Varghese publishing house; Bombay, 171-196.
4. Brahmankar DM, Jaiswal SB. Biopharmaceutics and Pharmacokinetics: Pharmacokinetics. 2nd ed. Vallabh Prakashan, Delhi: 2009; 399-401.
5. John C, Morten C, The Science of Dosage Form Design, Aulton: Modified release peroral dosage forms.. 2002; 2nd ed. Churchill Livingstone, 290-300.
6. Ali Nokhodchi, Shaista Raja, Pryia Patel, and Kofi Asare-Addo.The Role of Oral Controlled Release Matrix Tablets in Drug Delivery Systems.Bioimpacts. 2012; 2(4): 175–187.
7. John C, Morten C, The Science of Dosage Form Design, Aulton: Modified release peroral dosage forms. 2nd ed. Churchill Livingstone. 2002; 2nd ed, 290-300.
8. Sathish Ummadi, B. Shravani, N. G. Raghavendra Rao, M. Srikanth Reddy, B. Sanjeev Nayak.Overview on Controlled Release Dosage Form.International Journal of Pharma Sciences (2013): Vol. 3, No. 4, 258-269.
9. Vyas S, P, Khar RK.Controlled Drug delivery: Concepts and Advances .Concepts and Advances. vallabh prakashan,2002, 1st ed, p,156-189.
10. Shargel L, Yu ABC. Modified release drug products. In:Applied Biopharmaceutics and Pharmacokinetics.McGraw Hill.1999;4th ed 169-171.
11. Welling P. G. and Dobrinska M. R., Dosing consideration and bioavailability assessment of controlled drug delivery system, Chapter 7, Controlled drug delivery; fundamentals and applications, 2nd edition, Robinson J.R. and Lee V. H. L. (Eds.), Marcel Dekker Inc., New York, 1978, 29,p. 254, 373.
12. ManishaGahlyan, Saroj Jain.Oral Controlled Release Drug Delivery System- A Review.
13. Mamidala R, Ramana V, Lingam M, Gannu R, Rao MY. Review article factors influencing the design and performance of oral sustained/controlled release dosage form. Int. journal of pharmaceutical science and nanotechnology. 2009; 2:583.

14. Patel Nidh , Chaudhary Anamika, Soni Twinkle, SambyalMehul, Jain Hitesh,Upadhyay Umesh.Controlled Drug Delivery System: A Review.IAJPS 2016, 3 (3), 227-233.
15. Crank, J. (1975). The Mathematics of Diffusion. New York: Oxford Press.
16. Leon, L., & Herbert, L.A. Pharmaceutical Dosage Forms. (2002), New York: Marcel Dekker
17. Kar RK, Mohapatra S and Barik BB. Design and characterization of controlled release matrix tablets of Zidovudine. Asian J Pharm Cli 2009, Res, 2: 54.
18. Salsa T, Veiga F and Pina ME. Oral controlled release dosage form. I. Cellulose ether polymers in hydrophilic matrices. Drug Develop Ind Pharm, 1997; 23: 929-938.
19. Kumar S, Shashikant and Bharat P. Sustained release drug delivery system: a review. Int J Inst Pharm Life Sci, 2012, 2(3): 356-376.

****