Preparation and Evaluation of Gastroretentive drug delivery system of Gliclazide

[1]Diksha Ghorpade, [2]Shivani Kotamkar, [3]Samiksha Burange, [4]Gauri Rathod

Department of Pharmaceutics,
P.R.Pote Patil College of Pharmacy, Amravati-444604

Corresponding Author: Diksha Ghorpade
Address: Department of Pharmaceutics, P.R.Pote Patil College of Pharmacy, Amravati-444604

***Abstract*: In the conventional drug delivery system achieving and maintaining concentration of drug within the therapeutic range, frequent dosing is required which results into see - saw pattern of the drug levels. To overcome these problems, controlled drug delivery systems were introduced. The objective of the present study was to develop Gliclazide gastroretentive drug delivery system in order to achieve an extended retention in the upper GIT which may result in enhance the absorption and improve the bioavailability. The tablets were prepared by applying polymers like carbopol974P, eudragit RSPO, eudragit RLPO, eudragit RS100 and combination formulations like of HPMCK100LV with EC and HPMCK100LV with HPMCK4M. The results were satisfactory which clearly manifests the necessity of combining different class of polymers to get an acceptable release profile. It can be suggested that formulations containing combinations of HPMCK100LV and EC (B10), HPMCK100LV and HPMCK4M (B25) can be employed successfully for the development of sustained release tablets of gliclazide. The formulations containing combinations of HPMCK100LV and EC (B10), HPMCK100LV and HPMCK4M (B25) can be employed successfully for the development of sustained release tablets of gliclazide. Also these formulations showed comparable release with that of marketed product M_1. Formulations B10 and B25 were found to be stable when short-term stability study was carried out at 40^0C/75%RH.**

***Keywords*: Gliclazide, Anti-Diabetic, HPMC, Eudragit, Carbopol, Matrix tablet, Sustained release tablet, gastroretentive drug delivery.**

Introduction: The conventional type of dosage forms has many type of problems related to bioavailability, gastric irritation, absorption, metabolism of drug and etc. therefore, to overcome these problems, controlled drug delivery systems were introduced three decades ago. These delivery systems have a number of advantages over traditional systems such as improved efficiency, reduced toxicity, and improved patient convenience. The main goal of controlled drug delivery systems is to improve the effectiveness of drug therapies. Controlled drug delivery is drug delivery at a rate or at a location determined by needs of body or disease state over a specified period of time. The basic motive for developing controlled drug delivery is to alter the pharmacokinetics and pharmacodynamics of pharmacologically active moieties by using novel drug delivery system or by modifying the molecular structure and / or physiological parameters inherent in a selected route of administration [1-5].
Gliclazide is a sulfonylurea with hypoglycaemic activity. It is given orally in treatment of NIDDM. It has attracted attention because in addition to hypoglycemic effect it has antiplatelet properties. It has biological half-life of 10-12 hr. It is absorbed by whole GIT. Usual initial dose of gliclazide is 40 to 80 mg daily, gradually increased if necessary up to 320 mg depending on blood glucose result. The usual average prescription is two tablets per day in two administrations, but may vary from 1 to 4 tablets per day in several administrations depending on severity of diabetes. Therefore to reduce frequency of dosing and enable better compliance, formulating sustained release dosage form is necessary [6].

Materials and Methods: Gliclazide was procured from Yarrow Chem, Pvt.Ltd, Mumbai. Eudragit of various grades were obtained as a gift sample from Evonik India, Mumbai. HPMC of various grades were obtained as a gift sample from Colorcon India, Goa, Carbopol and Ethyl cellulose was procured from S.D. Fine Chem, Mumbai. All other chemicals and reagents used were of analytical grade.

Methods:
Standard Calibration Curve: A stock solution of 100mg/ml was prepared by dissolving 100 mg of drug in 20 ml of methanol and diluting with distilled water up to 100 ml. Second stock solution of 100µg /ml was prepared by appropriately diluting the above stock solution with distilled water and from these second stock, further standard solutions in concentration range of 10-40 µg /ml were prepared by diluting with water. The absorbance of each of the standard solution was recorded by Shimadzu-1800 double beam spectrometer, at the wavelength of maximum absorbance (λ max) 226 nm using blank in the reference cell [7-9].

Drug-Excipients Interaction: Infra red spectra matching approach was used for the detection of any possible chemical and physical interaction between the drug and the excipients. A physical mixture (1:1) of drug and polymer was prepared and mixed with suitable quantity of potassium bromide. About 100mg of this mixture was compressed to form a transparent pellet using a hydraulic press at 2 tons' pressure. It was scanned from 4000 to 150 cm^{-1} in FT-IR spectrophotometer [10]. The

IR spectrum of the physical mixture was compared with the standard value of pure drug and excipients and it was matched for any disappearance of any peak to detect any of interaction between the drug and excipient.

Preparation of Matrix Tablet: Matrix tablets containing 60mg of gliclazide along with various amounts of polymers such as HPMC'S, EC, Carbopol, Eudragit and other inactive ingredients (such as DCP, lactose, aerosil and magnesium stearate) were prepared by direct compression technique. In the first step, active and inactive ingredients weighed accurately and were screened through a 60-mesh sieve. Required materials except lubricant were then combined and passed through 60-mesh sieve 10 times, following the addition of given amount of lubricant and again mixing, the powder was passed through 60-mesh sieve 5 times. Then desired amount of blend was compressed into tablets using rotary tablet compression machine equipped with 7mm tooling of plain face on lower punch and a central break line on upper punch. Before compression, the surfaces of the die and punch were lubricated with magnesium stearate [11]. All the preparations were stored in airtight containers at room temperature for further study.

Table 1: Formulation Table of Gliclazide Matrix Tablets

Batch	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11	B12	B13	B14
Gliclazide	60	60	60	60	60	60	60	60	60	60	60	60	60	60
DCP	63	61	58	53	46	63	54	49	44	34	63	43	37	73
Lactose	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mg. stearate	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Aerosil	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
HPMC K4M	25	27	30	35	27	----	---	---	----	----	---	---	----	----
HPMC K100LV	---	---	---	---	---	25	34	34	34	34	---	---	----	----
EC	---	---	---	---	15	---	---	5	10	20	---	20	---	---
HPMC K15M	---	---	---	---	---	---	---	---	---	---	25	20	----	----
HPMC K100M	---	---	---	---	---	---	---	---	---	---	---	---	25	15
Total weight	160	160	160	160	160	160	160	160	160	160	160	160	160	160

Table 2: Formulation Table of Gliclazide Matrix Tablets

Batch	B15	B16	B17	B18	B19	B20	B21	B22	B23	B24	B25	B26
Gliclazide	60	60	60	60	60	60	60	60	60	60	60	60
DCP	63	43	63	63	63	48	63	43	37	73	63	43
Lactose	11	11	11	11	11	11	11	11	11	11	11	11
Mg. stearate	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Aerosil	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
EC	--	20	---	---	---	---	---	---	---	---	---	---
Carbopol 974P	25	25	---	---	---	---	---	---	---	---	---	---
Carbopol 971P	---	---	25	---	---	---	---	---	---	---	---	---
Eudragit RLPO	---	---	---	25	---	---	---	---	---	---	---	---
Eudragit RSPO	---	---	---	---	25	15	---	---	---	---	---	---
Eudragit RL100	---	---	---	---	---	---	25	---	---	---	---	---
Eudragit RS100	---	---	---	---	---	---	---	25	---	---	---	---
HPMC K4M	---	---	---	---	---	---	---	---	24	17	10	8
HPMC K100LV	---	---	---	---	---	---	---	---	10	17	24	26
Total weight	160	160	160	160	160	160	160	160	160	160	160	160

Evaluation Parameters: [12-15]

1] Thickness: The thickness of the tablets was determined using Vernier Caliper. Five tablets from each batch were used and average values were calculated.

2] Weight Variation: To study weight variation, 20 tablets of each formulation were weighed using an electric balance, and the test was performed according to official method.

3] Hardness: For each formulation, the hardness of 5 tablets was determined using the Monsanto hardness tester.

4] Friability: Twenty tablets for each formulation were weighed and placed into a Roche friabilator (Remi Electronics, Mumbai, India). The samples underwent 25 rotations per minute, for 4 min, and were then re-weighed. This process was repeated for all formulations and the percentage friability was calculated.

5] Drug content: The % drug content was calculated by crushing the tablet in a mortar pestle and dissolving the powdered contents into methanol and sonicate it for 20 minutes. Filter the solution and allow cooling down at room temperature. The resultant solution was then scanned on UV-spectrophotometer at 226 nm.

6] In-vitro Drug Release: In-vitro drug release studies of the prepared matrix tablets were conducted for a period of 8 hrs using USP XXIV type 2 apparatus at 37± 0.5° C and 50 rpm speed. The dissolution studies were carried out in triplicate for 8 hrs (initial 2 hours with 0.1N hydrochloric acid and rest 6 hours in phosphate buffer of pH 7.4) under sink conditions. At every 1-hour interval samples of 10 ml were withdrawn from the dissolution medium and replaced with fresh medium to maintain the sink conditions. After filtration and appropriate dilution, the samples were analyzed by a UV spectrophotometer at 226 nm [16-18].

7] Drug Kinetics: The dissolution data obtained was fitted to various kinetic models like Zero Order, First Order, Higuchi, Hixson Crowell and Korsmeyer Peppas [19-20].

Results and Discussion:

Standard Calibration Curve: The standard calibration curve was plotted concentration Vs absorbance according to the absorbance reading and the obtained equation was found to be y = 0.0248x - 0.07and the r2 value was found to 0.9866.

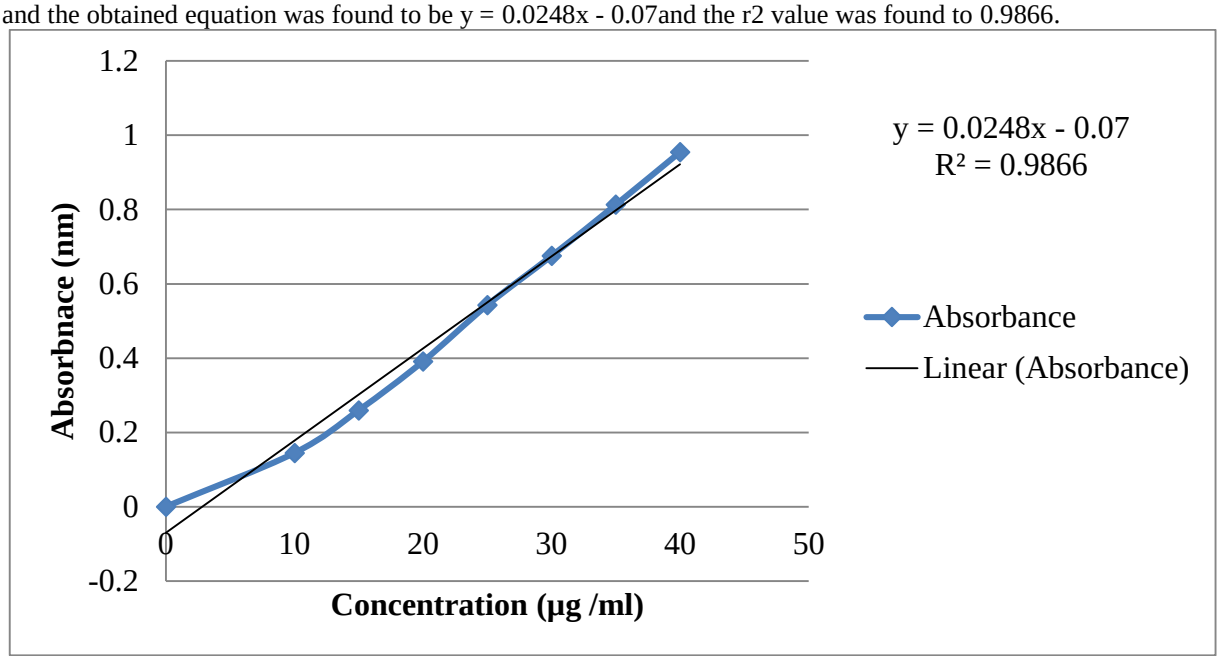

Figure 1: Standard Calibration Curve of Gliclazide

Drug-Excipients Interaction Study: From the figures obtained of the FT-IR spectrum it was seen that there was no disappearance of any peak which concludes that there was no physical and chemical interaction between the drug and excipients.

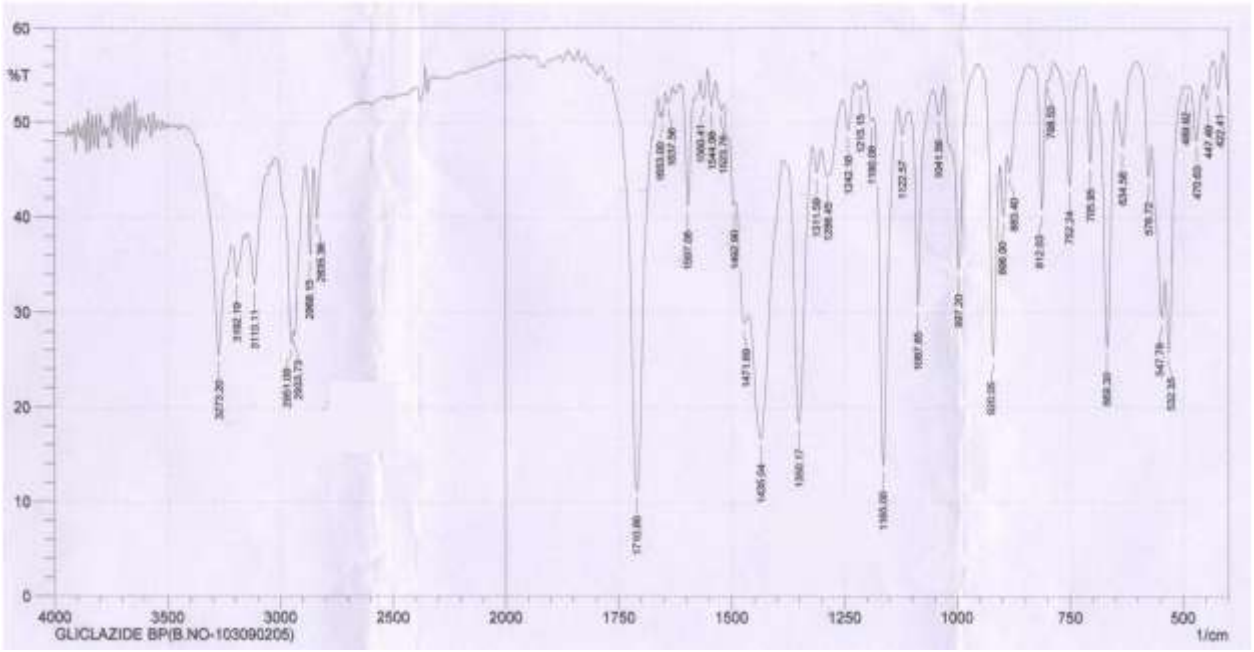

Figure 2: FT-IR of Pure Drug Gliclazide

Evaluation Parameters: The physical characteristics of the prepared gliclazide matrix tablets were found to be satisfactory giving the good results in the range of thickness of 3.09-3.18mm, hardness in the range of 5-6 kg/cm^2, % friability in the range of 0.09-18 %, the average weight of the prepared tablets was found to be in the range of 159.06-161.73 mg and lastly the % drug content in the prepared tablets was found to be in the range of 98.05±0.23-100.61±0.31.

Table 3: Physical Characteristics of Gliclazide Matrix Tablets

Batch	Thickness (mm)	Hardness (Kg/cm^2)	% Friability	Weight variation			% Drug Content ±SD
				Av. w t. (mg)	Max. % Deviation (+ve)	Max. % Deviation (-ve)	
B1	3.15	5.5	0.21	160.50	0.93	0.37	98.95± 0.44
B2	3.13	5.0	0.13	160.18	0.63	0.69	100.38±0.18
B3	3.11	5.0	0.11	161.55	0.59	0.9	99.14±0.52
B4	3.09	6.0	0.15	159.72	0.73	0.81	98.79±0.30
B5	3.12	5.0	0.13	159.86	0.41	0.69	99.27±0.55
B6	3.15	6.0	0.16	160.09	0.87	0.46	100.61±0.31
B7	3.11	5.5	0.09	159.45	0.32	0.53	98.53±0.11
B8	3.09	5.0	0.18	160.77	0.88	0.49	99.25±0.64
B9	3.15	5.0	0.12	160.36	0.57	0.96	99.16±0.41
B10	3.12	6.0	0.14	159.47	0.38	0.57	98.05±0.23
B11	3.17	5.0	0.17	160.88	0.61	0.55	100.09±0.33
B12	3.07	6.0	0.12	160.06	0.34	0.43	100.55±0.12
B13	3.12	5.5	0.11	159.58	0.60	0.75	100.31±0.47
B14	3.14	5.0	0.18	159.66	0.91	0.44	98.18±0.51
B15	3.09	5.5	0.15	159.91	0.52	0.80	99.22±0.33
B16	3.16	5.0	0.18	161.13	0.72	0.62	99.95±0.18
B17	3.17	5.0	0.16	161.78	0.45	0.83	99.16±0.57
B18	3.13	6.0	0.14	160.10	0.56	0.33	98.05±0.23
B19	3.17	5.0	0.17	161.64	0.37	0.46	100.06±0.14
B20	3.11	6.0	0.11	159.99	0.61	0.79	98.45±0.39
B21	3.18	5.5	0.17	159.06	0.48	0.35	100.13±0.42
B22	3.13	6.0	0.13	160.49	0.36	0.66	99.35±0.75
B23	3.16	5.0	0.11	161.07	0.69	0.58	98.88±0.50
B24	3.08	6.0	0.15	161.73	0.42	0.92	99.88±0.16
B25	3.16	5.5	0.13	161.22	0.77	0.67	100.06±0.66
B26	3.10	5.0	0.14	161.04	0.86	0.51	98.75±0.13

In-vitro Drug Release: The in-vitro drug release of the prepared matrix gliclazide tablets showed tablets containing HPMC of various viscosities. Prepared tablets did not disintegrate, however a gel layer was formed on surface of the tablet due to swelling of HPMC in presence of water. Here concentration of each type of HPMC (K4M, K100LV, K15M and K100M) was kept constant (15.6%). Formulations containing HPMCK15M and HPMCK100M (B11 and B13) showed delayed release as compared to those containing HPMCK4M and HPMCK100LV (g1A and B6). This revealed that as viscosity of HPMC increased release rate of drug was decreased. In subsequent studies, effect of increasing concentrations of HPMCK4M alone and with that of EC on in-vitro release of drug was studied. The result showed (Fig .16) that for formulations g1A, B2, B3 and B4 % drug released was 79.14%, 69.54%, 27.83% and 21.14% respectively at the end of 4 hr. In case of formulation B2 and B5 containing HPMC alone and in combination with 9.38% EC, release was same at the end of 4hr i.e. 69.54%. But comparatively, cumulative % drug release was more initially in case of B2 and afterwards it became more sustained, which might be due to complete swelling of the polymer that in turn retarded the drug release. In case of B5 more sustained effect was observed initially and then drug released rate increased as compared to B2. This may be attributed to hydrophobicity of EC initially, and then erosion-diffusion both might be playing dominant role in drug release. Effect of HPMCK100LV alone and in combination with EC on in-vitro release profile. For formulation B6 and B7 containing 15.6% and 21.25% of HPMCK100LV respectively, %drug release was found to be 83.11 % and

58.94 % at the end of 4 hr. Addition of increasing concentrations of EC led to decrease in drug release to 57.77%, 55.28% and 48.9% for formulation B8, B9 and B10 respectively. A further study was done to check the effect of different proportions 0f HPMCK4M and HPMCK100LV on release profile of drug (Fig.18). As the concentration of HPMCK4M decreased and that of HPMCK100LV increased, the % drug released was increased. For formulations B23, B24, B25 and B26 drug release was increased to 28.74%, 41.22%, 48.91% and 52.91% respectively at the end of 4 hr.Effect of HPMCK15 (B11) and HPMCK100M (B13) where at concentration of 15.6%, both grades showed more sustained effect as compared to marketed products i.e. 27.84% 29.35% at the end of 4 hr. Decrease in concentration of both grades to 9.4% did not give satisfactory release. Combination of 12.5% EC with 12.5% of HPMCK15 (B12) showed 55.86% drug release, which was near to the marketed products. The study also shows effect of acrylic acid based polymers i.e. carbopol971P and carbopol974P on release rate of gliclazide. Release profiles revealed that with the same concentration (15.6%) of polymers, release was more delayed for carbopol971P (g6 A) i.e. 24.54% as compared to carbopol974P (B15) i.e. 60.9% at the end of 4 hr. Addition of 12.5% of EC to carbopol974P (B16) made the release somewhat uniform. In-vitro dissolution studies were performed on formulations containing different types of eudragit like RLPO, RSPO, RL100 and RS100 (Fig.21). For formulation B18 containing eudragit RLPO, release was 52.78% i.e. near to the marketed preparation at the end of 4 hr, while release was retarded more in case of formulation B19 containing eudragit RSPO. In case of formulation B22 containing eudragit RS100, sustained effect was found and in case of formulation B21 containing eudragit RL100, almost all drug was released at the end of 4 hr.

Table 4: % Cumulative Drug Release

Time (hr)	% Cumulative Release (± SD)													
	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11	B12	B13	B14
1	26.99 (± 0.44)	26.59 (± 0.72)	14.30 (±0.21)	6.05 (± 0.10)	22.48 (± 0.32)	30.05 (± 0.66)	12.90 (± 0.13)	10.63 (±0.24)	12.00 (±0.29)	11.42 (±0.28)	13.70 (±0.85)	28.58 (±0.06)	3.06 (±0.19)	52.46 (±0.31)
2	47.44 (± 0.16)	44.66 (± 0.19)	18.24 (±0.59)	10.78 (± 0.33)	31.12 (± 0.18)	52.94 (± 0.77)	29.95 (± 0.28)	27.73 (±0.78)	25.51 (±0.17)	21.58 (±0.19)	19.30 (±0.92)	41.21 (±0.22)	10.88 (±0.39)	79.82 (±0.36)
3	68.99 (± 0.88)	64.75 (± 0.15)	25.21 (±0.88)	15.23 (± 0.14)	60.90 (± 0.07)	75.17 (± 0.43)	48.56 (± 0.35)	45.95 (±0.71)	45.63 (±0.55)	38.12 (±0.43)	25.48 (±0.44)	55.86 (±0.14)	21.12 (±0.20)	93.21 (±0.57)
4	79.14 (± 0.55)	69.83 (± 0.08)	27.83 (±0.65)	21.14 (± 0.53)	69.54 (± 0.41)	83.11 (± 0.05)	58.94 (± 0.75)	57.77 (±0.33)	55.28 (±0.77)	48.90 (±0.54)	29.35 (±0.72)	70.85 (±0.09)	27.84 (±0.27)	96.05 (±0.83)
5	82.01 (± 0.08)	71.50 (± 0.13)	32.59 (±0.19)	24.61 (± 0.05)	81.2 (± 0.57)	88.25 (± 0.36)	71.57 (± 0.59)	68.02 (±0.09)	67.49 (±0.15)	60.00 (±0.76)	30.35 (±0.88)	74.76 (±0.77)	28.14 (±0.17)	99.02 (±0.42)
6	87.64 (0.24)	74.56 (± 0.66)	37.14 (±0.49)	28.11 (± 0.78)	89.00 (± 0.27)	92.43 (± 0.68)	81.74 (± 0.22)	79.20 (±0.19)	80.20 (±0.22)	76.05 (±0.37)	30.87 (±0.99)	81.64 (±0.78)	28.47 (±0.13)	----
7	90.90 (± 0.11)	76.73 (± 0.71)	45.45 (±0.35)	31.09 (± 0.58)	92.24 (± 0.14)	98.36 (± 0.16)	89.46 (± 0.13)	88.45 (±0.16)	87.14 (±0.49)	86.11 (±0.11)	32.35 (±0.17)	85.80 (±0.38)	30.13 (±0.16)	----
8	97.01 (± 0.05)	81.67 (± 0.41)	51.35 (±0.32)	32.87 (± 0.73)	97.61 (± 0.16)	100.10 (± 0.39)	97.33 (± 0.06)	96.76 (±0.83)	95.92 (±0.33)	94.62 (±0.18)	35.79 (±0.08)	95.34 (±0.03)	30.99 (±0.25)	----

Time (hr)	% Cumulative Release (± SD)											
	B15	B16	B17	B18	B19	B20	B21	B22	B23	B24	B25	B26
1	4.07 (±0.21)	4.00 (±0.49)	8.37 (±0.47)	10.05 (±0.31)	7.50 (±0.24)	10.85 (±0.04)	3.84 (±0.13)	8.76 (±0.66)	11.40 (±0.22)	12.34 (±0.55)	13.40 (±0.26)	12.02 (±0.08)
2	7.36 (±0.18)	13.20 (±0.19)	12.25 (±0.01)	28.49 (±0.12)	12.50 (±0.81)	15.17 (±0.17)	9.86 (±0.53)	43.02 (±0.32)	16.83 (±0.14)	21.99 (±0.77)	24.57 (±0.12)	28.56 (±0.05)
3	60.69 (±0.45)	57.89 (±0.36)	19.34 (±0.89)	40.91 (±0.78)	17.05 (±0.31)	18.55 (±0.61)	14.36 (±0.03)	98.03 (±0.53)	27.00 (±0.28)	37.36 (±0.07)	38.50 (±0.15)	43.68 (±0.57)
4	60.90 (±0.02)	72.78 (±0.93)	24.54 (±0.46)	52.78 (±0.61)	19.29 (±0.56)	24.28 (±0.95)	18.22 (±0.52)	98.35 (±0.53)	28.74 (±0.15)	41.22 (±0.12)	48.91 (±0.65)	52.61 (±0.02)
5	61.96 (±0.81)	77.10 (±0.11)	36.55 (±0.03)	66.63 (±0.18)	28.8 (±0.05)	35.35 (±0.1)	23.2 (±0.4)	99.69 (±0.26)	32.96 (±0.38)	45.34 (±0.77)	61.00 (±0.24)	64.36 ±0.17)
6	76.79 (±0.33)	83.17 (±0.54)	38.76 (±0.29)	76.22 (±0.75)	33.91 (±0.3)	45.39 (±0.06)	27.51 (±0.7)	99.77 (±0.39)	39.75 (±0.56)	58.70 (±0.29)	76.06 (±0.85)	80.24 (±0.41)
7	93.70 (±0.46)	88.43 (±0.22)	45.90 (±0.07)	85.14 (±0.66)	38.16 (±0.01)	48.64 (±0.44)	32.59 (±0.14)	99.89 (±0.22)	42.70 (±0.06)	61.86 (±0.61)	85.09 (±0.38)	87.47 (±0.96)
8	97.85 (±0.32)	96.76 (±0.46)	52.10 (±0.44)	92.58 (±0.09)	39.46 (±0.11)	52.84 (±0.58)	38.92 (±0.73)	99.92 (±0.19)	47.06 (±0.44)	68.26 (±0.67)	93.57 (±0.05)	95.39 (±0.36)

Table 5: % Cumulative Drug Release

Kinetics Study: Different kinetic models (Zero order, First order, Higuchi, Hixson Crowell and Korsmeyer-Peppas) were applied to the dissolution data to interpret the release kinetics and mechanism of drug release. The coefficient of determination was considered as main parameter for interpreting the results. All formulations containing HPMCK4M alone and in combination with EC were not fitting to a specific model. Formulation B6 containing HPMCK100LV alone follows Higuchi's release kinetics with R^2 value 0.9714, while addition of EC to HPMCK100LV (B5) shows zero order release and linearity of plot was found to be increase as the amount of EC in the formulation increased. R^2 values for formulation B7 to B10 ranged from 0.9806 to 0.994. Formulation containing HPMCK15M alone (B11), in combination with EC (B12) and HPMCK100M alone (B13) in low concentration followed Higuchi's release kinetics with R^2 values 0.9764, 0.9909 and 0.9036 respectively, while decrease in concentration of HPMCK100M (B13) followed Hixson Crowell release kinetics. As well as formulations B15 and B16 containing carbopol 971P R^2 values are 0.9202 and 0.9507 also follows Hixson Crowell kinetic release. Other formulations containing carbopol974P, eudragit RSPO, eudragit RLPO, eudragit RS100 showed best fit to zero order release kinetics with R^2 values ranging from 0.981 to 0.9975. While eudragit RL100 fits into first order release. Formulations containing combination of low concentration of HPMCK100LV and high concentration of HPMCK4M i.e. B23 and B24 followed first order release kinetic with R^2 values 0.99 and 0.9870 respectively while with increasing concentration of HPMCK100LV and decreasing concentration of HPMCK4M i.e. B25 and B26, best fit was found to zero order release kinetics with R^2 values 0.9949 and 0.9908 respectively. The drug release mechanism from the polymer matrices is complex and is not yet completely understood. Although some processes are classified as either purely diffusion or purely erosion controlled, many others can be interpreted as being governed by both. The analysis of dissolution data involves interpretation of corresponding release exponent values (n), which leads to better understanding of the balance between two mechanisms. This kind of analysis was performed on all. For formulations containing HPMCK4M, g_1A to B5, n values ranged from 0.5178 to 0.8393 indicating that the release mechanism from these systems was anomalous type (Non

Fickian transport), which refers to a combination of both diffusion and erosion controlled-drug release. For formulations containing HPMCK100LV alone and in combination with EC, n values ranged from 0.5682 to 1.0535 indicating that these systems released the drug with Non Fickian mechanism. Formulations containing HPMCK100LV alone (B6) and in combination with EC (B8 to B10) showed super case II type of transport mechanism. In case of B11 containing HPMCK15M transport mechanism was Fickian diffusion (n=0.4476) and with addition of EC (B12) it showed anomalous behavior (n=0.5844). HPMCK100M at low concentration (B14) showed case I transport and with increase in concentration (B13) showed Super Case II transport mechanism. Formulations containing combination of HPMCK100LV and HPMCK4M showed Non Fickian release mechanism. For formulations containing carbopol and eudragit major mechanism of release was Anomalous or Super Case II type.

Conclusion: Sustained released matrix tablets of gliclazide were successfully prepared using different hydrophilic and plastic polymers as the release retarding materials by direct compression method. For all the prepared formulations evaluation parameters like thickness, hardness, friability, weight variation and drug content were found to be satisfactory. The result generated in this study showed that the profile and kinetics of drug release were function of polymer type, polymer grade and polymer concentration. Drug release from HPMC matrices showed that viscosity of polymer plays important role.

References:

[1] Wai-Yip Lee T, Robinson JR. Controlled/Release Drug-Delivery Systems, Chapter 47 dalam Remington's Pharmaceutical Sciences.

[2] Ummadi S, Shravani B, Rao NR, Reddy MS, Sanjeev B. Overview on controlled release dosage form. System. 2013;7(8):51-60.

[3] Reynolds JE. Martindale: the extra pharmacopoeia. London, UK; The Pharmaceutical Press; 1982.

[4] Patil R, Jat RK. Formulation and Evaluation of Matrix tablets containing Chitosan Based Polyelectrolyte Complex with Natural Gum for Prolonged Release of Diltiazem HCl. Journal of Drug Delivery and Therapeutics. 2019 Aug 15;9(4-s):22-31.

[5] Verma PR. Sustained release of theophylline from Eudragit RLPO and RSPO tablets. Drug development and industrial pharmacy. 1996 Jan 1;22(12):1243-7.

[6] Malviya VR, Tawar MG. Preparation and Evaluation of Oral Dispersible Strips of Teneligliptin Hydrobromide for Treatment of Diabetes Mellitus. International Journal of Pharmaceutical Sciences and Nanotechnology. 2020 Jan 31;13(1):4745-52.

[7] Gao P, Skoug JW, Nixon PR, Ju TR, Stemm NL, Sung KC. Swelling of hydroxypropyl methylcellulose matrix tablets. 2. Mechanistic study of the influence of formulation variables on matrix performance and drug release. Journal of pharmaceutical sciences. 1996 Jul 1;85(7):732-40.

[8] V.R. Malviya 1 *, S.D. Pande 2. (2019). PREPARATION AND EVALUATION OF ZOLMITRIPTAN HYDROCHLORIDE LOZENGES. Journal of Pharma Research, 8(8), 624–629.

[9] Nasseri AA, Aboofazeli R, Zia H, Needham TE. An Investigation into the Optimization of Release Profile of Lithium Carbonate from Matrix-type Tablets Containing Carbopols, Pemulen and Eudragits. Iranian Journal of Pharmaceutical Research.;2(1):59-63.

[10] Malviya V, Ladhake V, Gajbiye K, Satao J, Tawar M. Design and Characterization of Phase Transition System of Zolmitriptan Hydrochloride for Nasal Drug Delivery System. International Journal of Pharmaceutical Sciences and Nanotechnology. 2020 May 31;13(3):4942-51.

[11] Lee BJ, Ryu SG, Cui JH. Formulation and release characteristics of hydroxypropyl methylcellulose matrix tablet containing melatonin. Drug development and industrial pharmacy. 1999 Jan 1;25(4):493-501.

[12] Ludwig JS, Bass Jr WL, Sutton Jr JE, inventors; Burroughs Wellcome and Co Inc, assignee. Controlled sustained release tablets containing Bupropion. United States patent US 5,427,798. 1995 Jun 27.

[13] Abbaspour MR, Sadeghi F, Garekani HA. Design and study of ibuprofen disintegrating sustained-release tablets comprising coated pellets. European journal of pharmaceutics and biopharmaceutics. 2008 Mar 1;68(3):747-59.

[14] Malviya VR, Pande SD, Bobade NN. Preparation and Evaluation of Sustained Release Beads of Zolmitriptan Hydrochloride. Research Journal of Pharmacy and Technology. 2019;12(12):5972-6.

[15] Ford JL, Rubinstein MH, Hogan JE. Formulation of sustained release promethazine hydrochloride tablets using hydroxypropyl-methylcellulose matrices. International Journal of Pharmaceutics. 1985 May 1;24(2-3):327-38.

[16] Taylan B, Capan Y, Güven O, Kes S, Hincal AA. Design and evaluation of sustained-release and buccal adhesive propranolol hydrochloride tablets. Journal of Controlled Release. 1996 Jan 1;38(1):11-20.

[17] Varshosaz J, Tavakoli N, Kheirolahi F. Use of hydrophilic natural gums in formulation of sustained-release matrix tablets of tramadol hydrochloride. Aaps Pharmscitech. 2006 Mar 1;7(1):E168-74.

[18] Malviya V, Thakur Y, Gudadhe SS, Tawar M. Formulation and evaluation of natural gum based fast dissolving tablet of Meclizine hydrochloride by using 3 factorial design 2. Asian Journal of Pharmacy and Pharmacology. 2020;6(2):94-100.

[19] Mutalik S, Naha A, Usha AN, Ranjith AK, Musmade P, Manoj K, Anju P, Prasanna S. Preparation, in vitro, preclinical and clinical evaluations of once daily sustained release tablets of aceclofenac. Archives of pharmacal research. 2007 Feb 1;30(2):222-34.

[20] Amaral MH, Lobo JS, Ferreira DC. Effect of hydroxypropyl methylcellulose and hydrogenated castor oil on naproxen release from sustained-release tablets. AAPS PharmSciTech. 2001 Jun 1;2(2):14-21.