Effect of Eudragit on Glimepiride Matrix Tablets

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Abstract: *Sustained Release Matrix Tablets of Glimeiride were prepared by using Different Rate controlling polymers like Eudragit RL and RS using different drug polymer ratios. Developed total six formulations by using Direct Compression method . The prepared sustained release matrix tablets were evaluated for different evaluation tests like weight variation, Hardness, thickness, friability, Content Uniformity and Invitro release studies. Out of all the six formulations F4 containing eudragit RL showed 100 % drug release within 10 hours with sustained release. So, Eudragit RL was selected as best formulation based on the invitroevaluation tests.*
Keywords: *Matrix tablets, sustained release dosage forms, Glimepiride, Eudragit RL*

I. Introduction

The important role of oral drug delivery system is to improve the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery and or targeting the drug to desired site. The aim of any drug delivery system is to provide a therapeutic amount of drug to a specific site in the body to achieve promptly and then maintain the desired drug concentration. [1]

Sustained Release dosage forms are most convenient dosage forms to improve the bioavailability of drugs. These dosage forms delay the release of drug by matrix formation there by allowing the drug to get soluble and absorbed completely from intestinal mucosa. These dosage forms are prepared by using rate retarding polymers which form network like matrix upon hydration. [2] The drugs which are sensitive to gastric environment can also be protected by formulating as matrix type dosage forms because of their ability to withstand the acidic environment. To get a successful sustained release product, the drug must be released from the dosage form at a predetermined rate and dissolve in the gastrointestinal fluids.[5]

The formulations of sustained-release drug delivery systems wish to achieve desired release rates, decrease the number of daily administrations, improve compliance and minimize side-effects. Among all the formulations of sustained release, matrix tablets are useful because of many advantages. [3]

Glimepiride is an Anti diabetic drug, used in treatment of diabetes mellitus type 2. Which acts as an insulin secretagogue. It lowers blood sugar by stimulating the release of insulin by pancreatic beta cells and by inducing increased activity of intracellular insulin receptors. Which is having a biological half life of 3-4 hrs[4,6].

II. Materials and Methods

Glimepiride was used as an active ingredient purchased from Hetero Labs, hyd, polymers like Eudragit RL and Rs were purchased from Hetero Labs, hyd, Starch was obtained from LOBA chemie , Mumbai, Talc and magnesium stearate were purchased from Accord labs, hyd.

Matrix tablets Preparation:

Glimepiride mixed manually in polybag with different ratios of Eudragit RLPO as rate controlling polymer and micro crystalline cellulose as diluent for 10 minutes and the blend was lubricated with magnesium stearate for 3-5mins and talc was added as glidant then compressed into tablets by direct compression method using 6mm diameter punches in a four station rotary tablet-punching machine. Similarly Glimepiride matrix tablets were prepared by using different concentrations of Eudragit RSPO as rate controlling polymer[8,9]. Compositions of matrix tablet formulations are given in table 1. Each tablet (400mg) contained 8mg of Glimepiride. The mass of tablets were determined using a digital balance (Shimadzu, India) and thickness with digital vernier calipers[10,11].

Table No: 1 Formulation of Glimepiride matrix tablets

INGREDIENTS	F1	F2	F3	F4	F5	F6
Glimepiride	8	8	8	8	8	8
Eudragit RL	2	4	8	-	-	-
Eudragit RS	-	-	-	2	4	8
MCC	378	376	372	378	376	372
Mg stereate	6	6	6	6	6	6
Talc	6	6	6	6	6	6

Evaluation of prepared tablets:

1. Hardness test: The tablets to be tested are held between a fixed and a moving jaw of hardness test apparatus (Monsanto) and reading of the indicator is adjusted to zero. The screw knob was moved forward until the tablet breaks and the force required breaking the tablet was noted[12,13].

2. Friability: Friability test was performed using Roche friabilator. Ten tablets were weighed and placed in the friabilator, which was then operated for 25 revolutions per minute. After 100 revolutions the tablets were dusted and reweighed. The percentage friability was determined using the formula [14,15]

Percentage friability = $\underline{\text{Initial weight - Final weight}} \times 100$
Initial weight

3. Weight Variation: For weight variation test, twenty tablets were selected at random and weighed individually. The individual weights were compared with average weight for determination of weight variation [16,17].

4. Drug Content Ten tablets were weighed and powdered. Powder equivalent to 200mg of Glimepiride was dissolved in 10ml of 0.1N HCl, then make upto 100ml with 0.1N HCl in 100ml standard flask. From this 10μg/ml, equivalent solution was prepared and analyzed at 226 nm using UV double beam spectrophotometer [18,19].

5. Dissolution Studies Invitro release study was performed using USP apparatus type II at 72rpm. The dissolution medium was 900ml of 0.1N HCl for 2 hrs. It was maintained at a temperature of 37 ± 0.5^o C. The drug release was evaluated by taking 5ml sample (which was replaced with fresh medium) every half- an-hour interval upto 2 hours and suitably diluted with 0.1N HCl and absorbance was measured at 226 nm using UV spectrophotometer. After 2 hrs 900 ml of 0.1N HCl was replaced with 900 ml of dist water and the dissolution was carried out up to 12 hours by taking 5ml of samples every time it replaced with fresh medium. The collected samples were analysed by UV spectrophotometer at 226nm [20,21].

6. Kinetic Analysis To analyze the mechanism of drug release rate kinetics of all the formulations, the results of invitro release profiles were fitted into first order kinetic model, Higuchi model, zero order kinetic model and Korsmeyer model. The results of invitro release profiles were plotted in models of data treatment as follows [22,23]:
1. Log cumulative percent drug remaining versus time (first order kinetic model) [28]
2. Cumulative percent drug release versus square root of time (Higuchi model) [29]
3. Log cumulative percent drug released versus time (zero order kinetic model) [30]
4. Log cumulative percent drug released versus log time (korsmeyers model).

7. Stability Studies Stability studies were carried out to assess the stability of all formulated controlled release Glimepiride tablets. The prepared tablets were kept at $45^o \pm 2^oC$, 75±5% RH for 45 days. At 15 days intervals the tablets were evaluated for all physical parameters. The percentage of Glimepiride content and invitro drug release studies were also determined [24,25].

III. Results And Discussion

Evaluation of Glimepiride powder mixture and matrix Tablets The powder prepared for compression of matrix tablets were evaluated for their flow properties (Table-2). These values indicate that the prepared granules exhibited good flow properties. From the above values the bulk density of granules were found to be in the range of 0.51 to 0.55g/ml. the tapped density of granules was found to be in the range of 0.55 to 0.62w/v. the flow characteristics of granules were assessed by determining their angle of repose which is found to be in the range of 30 to 34 degrees and the compressibility index was found to be in the range of 11.2 to 13.33. the hausners ration was found be in the range of 1.12 to 1.15.

Table no:2 Physical Properties of powder blends

Formulation code	Bulk density (g/cm³)	Tapped density(g/cm³)	Cars index (C.I)	Hausner's ratio	Angle of repose (θ)
F1	0.53	0.61	13.11475	1.150943	32.22
F2	0.51	0.58	12.06897	1.137255	30.84
F3	0.54	0.55	12.90323	1.148148	33.95
F4	0.52	0.6	13.33333	1.153846	32.55
F5	0.53	0.61	13.11475	1.150943	33.92
F6	0.55	0.62	11.29032	1.127273	34.13

Table no: 3 Physical properties of prepared tablets

| Formulation	Weight variation test	Hardness (kg/cm2)	Friability (%)	Assay (%)
F1	401.6	5.1	0.50	98.46
F2	400.70	5.2	0.29	101.25
F3	399.10	4.9	0.32	99.25
F4	400.40	5.0	0.78	110
F5	401.40	5.3	0.66	91.3
F6	398.00	5.1	0.51	102

The prepared tablets were evaluated for their weight variation, hardness, friability, drug content uniformity. All the prepared tablets showed good elegance in appearance. The hardness of the tablets of all formulations was within the range of 5.1 to 5.6 kg/cm² , indicating good mechanical resistance of the tablets. The variation in weight was within the range of ±1.5% complying with Pharmacopoeial specifications. The percentage of Glimepiride in all formulations was ranging from 91.3 to 110 % indicating content uniformity was within the limits (±10%).The thickness and diameter of Glimepirede tablets was found to be in the range of 3.74 to 4.14mm and 6.1 to 6.2 mm respectively, which showed uniform thickness and diameter. (Table-3). The particle loss in the friability test was below 1% for all the formulations, which is an indication of good mechanical resistance of tablets.

Dissolution Studies Invitro release studies were performed to determine the percentage of drug released from Glimepiride matrix tablet formulations with polymer. Results of the invitro release studies of Glimepiride matrix tablet formulations with polymer are presented in (Table 4). The percentage drug release of Glimepiride matrix tablets was found to be 149% in F2, 78% in F1, 96% in F3, 89% F4, 68% in F5, 55% in F6 within 8hrs.based on all the evaluations F3 formulation containing Eudragit showed sustained release. The cumulative percentage of drug release in the formulation F3 showed controlled release than other formulations. The type of polymer concentration played a major role in drug release with eudragit, the drug release was prolonged. The graphical representation data of the Glimepiride matrix tablet formulations with polymer is shown in (Figure I).

Table 4 : Cumulative % drug release of all the formulations

Time (hrs)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	26.1	51.2	28.8	25.65	23.4	19.8
2	40.95	79.9	57.15	55.8	31.5	24.75
4	54	104	74.25	69.75	45.9	33.3
6	75	144	83.25	80.55	57.15	45
8	78.75	149.5	96.3	89.1	68.85	55.8

Figure 1: % drug release of Glimepiride matrix tablets
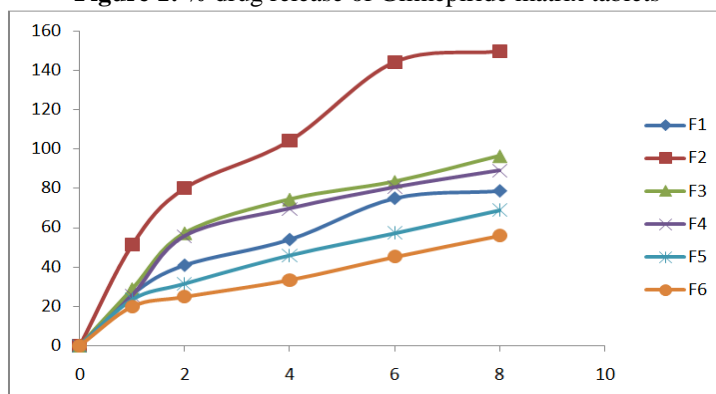
Kinetic Analysis The release rate kinetic data for all the formulations were shown in Table-5. When the data were plotted according to zero order, the formulations showed a high linearity, with regression coefficient values (r^2) between 0.91-0.97. Diffusion is related to transport of drug from the dosage matrix into the invitro study fluid depending on the concentration. This is explained by Higuchi's model. The release profiles of drug from all the formulations could be best expressed by Higuchi's equations, as the plot showed high linearity with regression co-efficient values (r^2) between 0.97-0.64.By using korsmeyer model, if n = less than 0.45 it is Fickian diffusion, if n = 0.45-0.89 it is non-Fickian transport. The result of all the formulations showed 'n' values between 0.611-0.843. It showed that all the formulations follow non- Fickian transport mechanism and also follow the mechanism of both diffusion and erosion (Table-5) [26, 27].

Table no:5 Mechanism of drug release from zidovudine matrix tablets

Formulation	Zero order r^2	First order r^2	Higuchi r^2	Korsmeyer r^2	Hixoncrowel r^2	N
F1	0.916	0.368	0.649	0.482	0.362	0.46
F2	0.941	0.674	0.953	0.775	0.980	0.57
F3	0.945	0.674	0.979	0.965	0.149	0.84
F4	0.973	0.037	0.951	0.169	0.165	0.64

Stability Studies zidovudine matrix tablets from all the formulations were stored at $45^o \pm 2^oC$, $75 \pm 5\%$ RH upto 30 days. Tablet evaluation tests were carried out at every 15 days intervals. All the formulations are physically stable. There were no deviations found in the tests and all are within the limits. There were no significant change in the drug content and invitro drug release profiles. It showed that all the formulations are chemically stable.

IV. Conclusion

The results of experimental studies of Glimepiride matrix tablets proved that the powder of Glimepiride showed good flow properties, tablet evaluation tests are within the acceptable limits, the kinetic studies revealed that all the formulations followed zero order drug release and stability studies revealed that all the formulations were found to be stable after storing at $45^o \pm 2^oC$, $75 \pm 5\%$ RH for 30 days. The drawbacks of the conventional dosage forms of Glimepiride can be minimized by Glimepiride matrix tablets. Thus the results of the above study clearly indicated that Glimepiride may be formulated as sustained release tablets using eudragit RLPO as rate controlling polymer using direct compression method, which will provide continuous release of drug at a predetermined rate and for a predetermined time.

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