INTERNATIONAL JOURNAL OF DRUG DISCOVERY AND HERBAL RESEARCH (IJDDHR)
3(1): Jan.-March.: (2013), 573-578
ISSN: 2231-6078

Research Article

Design and Characterization of Sustained Release Matrix Tablets of Glimepiride By Using Synthetic and Natural Polymers

Jekku Naga Subba Reddy[1*], T.S Nagaraja[1], N. Raghavendra Naveen[1], M. Devi Reddy[2]

1.Department of Pharmaceutics, SJM College of Pharmacy, JMIT Campus, Chitradurga, Karnataka-577502
2.Department of Pharmaceutics, Krishna Teja College of Pharmacy, Chadalavada Nagar, Thirupathi, Andhra Pradesh-517501.

Abstract

The objective of this study was to develop sustained release tablets of Glimepiride by wet granulation method based on various concentrations of Synthetic polymers (HPMC K 15M & HPMC K 4M) and Natural polymer (Starch acetate & Starch urea) polymers. Glimepiride is a FDA approved sulfonayl urea oral anti-diabetic drug, which has rapid and complete absorption after oral administration. Diseased state (diabetes) influences the gastric emptying rate. Modulated gastric emptying rate affects the absorption of the drug. Incomplete absorption of the drug is often accompanied by lesser bioavailability. Enhanced gastric retention would enable extended the absorption phase of the drug. From the present work, it is concluded that the using various concentrations of Natural polymers (Starch acetate & Starch urea) will sustain the drug release when compare to Synthetic polymers (HPMC K 15M & HPMC K 4M). Among all the formulations F-12 formulation with starch urea at 30% have more sustain action when compare to other formulation and it shows drug release of 49.70 % at the end of 7 hrs.

Key words: Sustained release matrix tablets, Glimepiride, HPMC K15 M, HPMC K4 M, Sodium acetate, Starch urea.

Introduction

Matrix tablets composed of drug and polymer as release retarding material offer the simplest approach in designing a sustained release system. Sustained release systems include any drug delivery system that achieves slow release of drug over an extended period of time[1,2]. If the system is successful in maintaining constant drug levels in the blood or target tissue, it is considered as a controlled-release system. If it is unsuccessful at this but nevertheless extends the duration of action over that achieved by conventional delivery, it is considered as a prolonged release system. The oral route of administration for sustained release systems has received greater attention because of more flexibility in dosage form design. The design of oral sustained release delivery systems is subjected to several interrelated variables of considerable importance such as the type of delivery system, the disease being treated, the patient, and the length of therapy and the properties of the drug[3, 4, 5].

*** Corresponding Author**
E.mail: : subbu.naga14@gmail.com
Phone no : +919738331421

The present study aims to develop sustained release matrix tablets using hydrophilic matrix materials, such as HPMC- K15 M, HPMC- K4 M, Sodium acetate and Starch urea along with drug in varying proportions by wet granulation method. Sustained drug delivery system can improve patient compliance and provide extended periods of effective blood levels. In an approach, polymers and their blend are used in various formulations to achieve sustained drug release[6, 7]. Diabetes mellitus is a group of metabolic disease characterized by hyperglycaemia resulting from defects in insulin secretion, action or both. In 1990, 23.4 million of oral ant diabetic agents were dispensed. By 2001, this number had increased to 91.8 million prescriptions. Consistent with the reported increase in the prevalence of type II diabetes, the number of dispensed outpatient prescription of oral anti-diabetic drug increased rapidly between 1990 to 2001.Glimepiride is used with diet to lower blood glucose by increasing the secretion of insulin from pancreas and increasing the sensitivity of peripheral tissues to insulin. The mechanism of action of Glimepiride in lowering blood glucose appears to be dependent on stimulating the release of insulin from functioning pancreatic beta cells, and increasing sensitivity of peripheral tissues to insulin[8, 9].

OBJECTIVE:

The aim of the present work was to prepare sustained release matrix tablets of Glimepiride by using various concentrations of synthetic polymers (HPMC K15M & HPMC K4 M) and natural polymer (Starch acetate & Starch urea) by wet granulation method. Based on this, an attempt was made to formulate floating matrix tablet of Glimepiride using different Synthetic and Natural polymers. The prepared tablets were evaluated for physical characteristics such as hardness, thickness, %friability, weight variation. All the tablets were evaluated for *in vitro* drug release profile.

MATERIALS AND METHODS

Materials

Glimepiride was obtained as gift sample from Dr. Reddy's laboratories limited, Hyderabad,, India. HPMC K 4 M, HPMC K 15 M, Talc and Magnesium stearate were procured from Loba Chemie Pvt Ltd; Mumbai, India. MCC, Mannitol are procured from S.d fine chem. Pvt Ltd; Mumbai, India. All other chemicals and reagents used were of analytical grade.

FORMULATION OF TABLETS[10, 11]

Accurately weighed quantity of Glimepiride, polymer, and mannitol were taken in mortar and mixed. Mixture of water: isopropyl alcohol (1:1) was added to dry blend

gradually with constant kneading to ensure a homogenous mass. The dough mass was passed through a #12 mesh sieve. Then granules were dried at 60°C for 2hrs and dried granules were lubricated with magnesium Stearate and compressed into tablets using 8 mm punches. Each tablet contains 10 mg of Glimepiride.

EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF GLIMEPIRIDE.

PRE COMPRESSION PARAMETERS:

Bulk density[12]:

Apparent bulk density was determined by placing pre-sieved drug excipient blend in to a graduated cylinder and measuring the volume and weight as it is.

$$Db = M/Vb$$

Where, M = Weight of powder taken; Vt= tapped volume.

Tapped density[13]:

Tapped density was determined by USP method II tablet blend was filled in 100 ml graduated cylinder of tap density tester which was operated for fixed number of taps until the powder bed volume has reached a minimum, thus was calculated by formula

$$Dt = M/Vt$$

Where, M = Weight of powder taken; Vt= tapped volume.

Angle of Repose[14]:

Angle of repose was determined by using funnel method. Tablet blend were poured from funnel, that can be raised vertically until a maximum cone height h was obtained diameter heap r, was measured. The repose angle θ was calculated by formula

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

Where, θ is the angle of repose, h is height of pile; r is radius of the base of pile.

Compressibility index and Hausner ratio [15, 16]**:**

This was measured for the property of a powder to becompressed; as such they are measured for relative importance of interparticulate interactions.

Compressibility index was calculated by following equation

$$\text{Compressibility index} = \{(Dt - Db)/ Dt\} \times 100$$

Where, Dt= tapped density; Db= bulk density;

Hausner ratio was calculated by following equation

$$\text{Hausner ratio} = Dt/ Db$$

Where, Dt= tapped density; Db= bulk density

POST COMPRESSION PARAMETERS:

All prepared Glimepiride tablets were evaluated for its uniformity of weight, hardness, friability and thickness, *in vitro* drug release according to official methods shown in Table 3.

Weight variation[17]:

Twenty tablets were randomly selected from each batch weighed individually and compared with average weight and calculate the standard deviation.

Thickness[17]**:**

The thickness of the tablet was measured by using digital vernier caliper, twenty tablet from each batch were randomly selected and thickness were measured.

Hardness[18]**:**

Hardness was measured using Pfizer hardness tester, for each batch three tablet were tested.

Friability [19]

Ten tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was measured as per the following formula,

Percentage friability =

$$\frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Dissolution studies [20]**:**

In Vitro dissolution studies for all the prepared tablets were carried out using USP paddle method at 50 rpm using 900 ml of 7.4 pH phosphate buffer as dissolution media, maintained at 37 ± 0.5º. 5 ml of samples were withdrawn from the dissolution medium at the specified regular intervals, filtered through Whatmann filter paper and release of the drug was determined spectrophotometrically at 230 nm. An equal volume of pre warmed (37ºC) fresh medium was replaced into the dissolution medium after each sampling, to maintain the constant volume of the dissolution medium throughout the test. Then the cumulative percentage of drug release was calculated and represented graphically(Figure-1& 2).

RESULTS AND DISCUSSION

Pre compressional parameters of granules shows (Table 2), bulk density (0.3649 to 0.4282), tapped density (0.4255 to 0.4944),angle of repose (26.43 to30.28), % compressibility (9.60 to 17.80%),and Hausner's ratio (1.071 to 1.35) are in the range given in official standards.

Table 3 shows post compressional parameters i.e. hardness (6.3 to 8.2 kg/cm^2), friability(0.54 to 0.70%), weight variation (198.33 to 200.80) and thickness (2.54 to 5.12 mm) within the acceptable official limits.

Dissolution study of all the formulations was carried out using phosphate buffer pH 7.4 up to 8 hrs. Formulations F1, F2, and F3 containing drug: polymer ratio1:2, 1:4, and1:6 prepared with HPMC K15 M 96.15%, 82.43%, and 67.38% of drug release in 8hrs respectively and the drug release profiles are shown in Figure 1 & 2. Formulations F4, F5, and F6 containing drug: polymer ratio1:2, 1:4, and1:6 prepared with HPMC K4 M,

98.28%, 89.77%, and 75.44% of drug release in 8 hrs respectively and the drug release profiles are shown in Figure 1.Formulations F7, F8, and F9 containing drug: polymer ratio1:2, 1:4, and1:6 prepared with Sodium acetate, 95.56%, 91.12% and 74.07% of drug release in 8 hrs respectively and the drug release profiles are shown in Figure 2. Formulations F10, F11, and F12 containing drug: polymer ratio1:2, 1:4, and1:6 prepared with Starch urea, 68.32%, 62.92% and 49.70% of drug release in 8 hrs respectively and the drug release profiles are shown in Figure 2.

In the above results, it was observed that as the concentration of the polymer increased and there is a decrease in the drug release rates. From the present work, it is concluded that the using various concentrations of Natural polymers (Starch acetate & Starch urea) will sustain the drug release when compare to Synthetic polymers (HPMC K15 M & HPMC K4M). Among all the formulations F-12 formulation with starch urea at 30% have more sustain action when compare to other polymers and it shows drug release of 49.70 % at the end of 8 hrs.

CONCLUSION

The main objective of the present study was to develop sustained release matrix tablet formulation containing 10 mg of Glimepiride for once daily therapy. In the present work it has been observed that using of Starch urea natural polymer retarded the drug release up to 7hrssatisfactorily. When compared with same concentrations of other polymers. When compared with all the formulations F12 was sufficiently sustained the release of the drug was observed.

AKNOWLEDGEMENT

The authors are thankful to Dr. Shivamurthy Murugha Sharanaru, President, S.J.M VidyaPeetha for providing all necessary facilities through the Principal and HOD, Dept. of pharmaceutics, S.J.M college of Pharmacy, Chitradurga and also thankful to Dr. Reddy's laboratories limited, Hyderabad,for providing the gift sample of Glimepiride.

REFERENCE

1) Goodrich BF. Controlled Release Tablets and Capsules.Bulletin no. 17, Brecksville OH. Ed 1995.
2) Patrick JS. Martin's Physical Pharmacy and Pharmaceutical Sciences, (3rd ed), Varghese Publishing House, Bombay. 1991: 512-19.
3) Kar RK, Mohapatra S, Barik BB. Design and characterization of controlled release matrix tablets of Zidovudine. *Asian J Pharm Cli Res*. 2009; 2: 54-61.
4) Higuchi T. Mechanism of sustained-action medication: theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *J Pharm Sci.*1963; 52: 1145-49.
5) Robinson JR, Lee HL (Ed). Controlled Drug Delivery: Fundamentals & Applications, 2nd Edition, Marcel Dekker Inc: New York: 1987; 373.
6) Gennaro AR (Ed.) Remington. The Science & Practice of Pharmacy. 19th Edition, Vol. II; 1995: 1662.
7) Herbert A, Lieberman & Leon Lachman. Pharmaceutical Dosage Forms. Tablets, Vol. III, Marcel Dekker Inc., New York; 9-10.
8) 8.Rother KI (April 2007). "Diabetes treatment – bridging the divide". The New England Journal of Medicine 356; 15: 1499-501.
9) American Diabetes Association. Economic cost of diabetes in the US in 2002. Diabetes Care.2003; 26: 917-932.
10) Hindustan AA, Sreeramulu J, Hima BV, Guru P, Sravanthi M: Fabrication of glimepiride aloe barbadensis miller leaves mucilage and povidone sustained release matrix tablets:in vitro and in vivo evaluation. *J Pharm Res:* 2011; 4(3): 748-52.
11) Hindustan AA, Anand B U, Nagesh K, SaiKD,BinduMK: Fabrication of glimepiride datura stramonium leaves mucilage and poly vinyl pyrrolidone sustained release matrix tablets:in vitro evaluation: *Kathmandu Uni J of Sci, Eng Tech*: 2012; 8(1): 63-72
12) Martin A, Micro meritics. In: physical pharmacy. 4th ed. Philadelphia: Lippincott Williams & wilkins, 2001: 423-52.
13) Rajiv G. Pre-formulation: A need for dosage form design. Pharmainfo. Net; 2008; 6.
14) Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. Philadelphia, pa: lea and febiger, 1987; 317-318.
15) Bhanja S, Ellaiah P, Martha SK, Singh P, Panigrahi, Bibhuti B, Das D. Design and in-vitro evaluation of Sustained release matrix tablets of repaglinide. *Int J PharmaSci Tech*: 4(1), 2010; 42-53.
16) Mahalaxmi D, Senthil A, Prasad V, Sudhakar B, Mohideen S,Formulation and evaluation of Sustained release matrix tablets tablets of glipizide: *Int J Biopharm*. 1; 2010:100-07.
17) Chowdary KPR, AreefullaS. Formulation and evaluation of floating tablets of gliclazide employing hpmc k100m, starch acetate and carbopol 934p. *Asian J Pharm Hea Sci*: Apr-jun 2012-2(2) 316-319.
18) Ravi kumar, Patil SR, Patil MB, Paschalpur MS, Mahalaxmi R. Formulation and evaluation of controlled release diltiazem hydrochloride

matrixs tablets. *Der Pharm Let.* 2010; 2(1): 48-60.

19) Arya RK, Garud G, Jain NK, Garud N. Development and evaluation of mucoadhesive buccal tablets of salbutamol sulphate. Int J Pharm & Pharm Sci. 2010; 2(2): 40-42.

20) Ammar HO, Salama HA, Ghorab M, Mahmoud AA. Formulation and biological evaluation of glimepiride–cyclodextrin–polymer systems. Int J Pharm 2006; 306: 129-38.

Table No.1: Composition of sustained release matrix tablets of Glimepiride.

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Glimepiride	10	10	10	10	10	10	10	10	10	10	10	10
HPMC-K 15M	20	40	60	-	-	-	-	-	-	-	-	-
HPMC- K4M	-	-	-	20	40	60	-	-	-	-	-	-
Sodium acetate	-	-	-	-	-	-	20	40	60	-	-	-
Starch urea	-	-	-	-	-	-	-	-	-	20	40	60
MCC	40	40	40	40	40	40	40	40	40	40	40	40
Mannitol	123	103	83	123	103	83	123	103	83	123	103	83
Mg.stearate	4	4	4	4	4	4	4	4	4	4	4	4
Talc	3	3	3	3	3	3	3	3	3	3	3	3
Total weight	200	200	200	200	200	200	200	200	200	200	200	200

Fig. 1: Cumulative % drug Release Vs Time in hrs from prepared batches F-1, F-2, F3, F-4, F-5 & F-6 of matrix tabletsof Glimepiride prepared by HPMC K-15M and HPMC-K 4M.

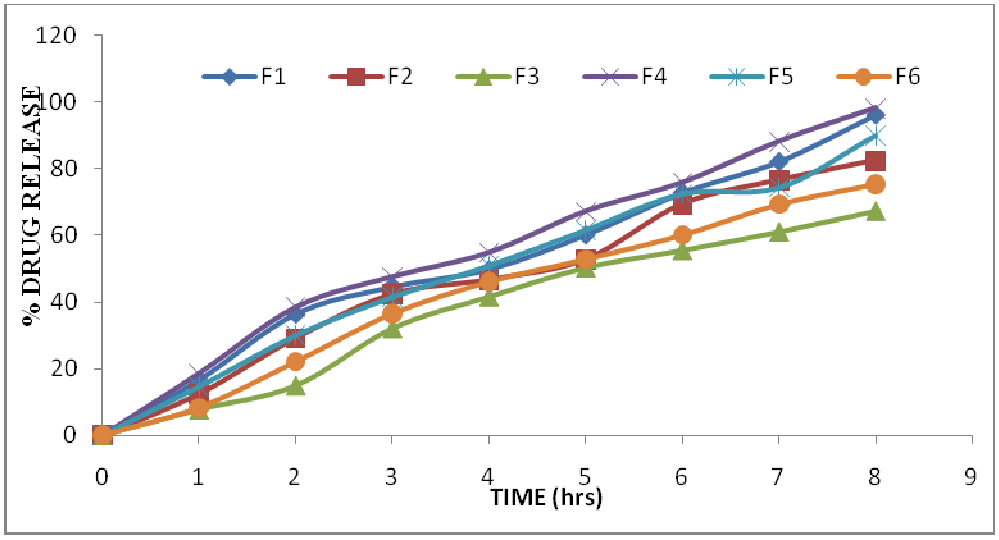

Table No. 2: Pre compression parameters of sustained release matrix tablets of Glimepiride.

Formulation code	Bulk density (g/cc) ±SD, n=3	Tapped density (g/cc) ±SD, n=3	Angle of repose (degree) ±SD, n=3	Carr's index(%) ±SD, n=3	Hausner's Ratio ±SD, n=3
F1	0.3712±0.54	0.4385 ±0.76	26.43± 1.48	15.62±1.05	1.1813± 1.407
F2	0.3846±0.32	0.4255 ±0.46	27.72± 1.22	9.6±1.86	1.1063±1.437
F3	0.4282±0.74	0.4587±0.47	29.87±1.32	12.8±1.27	1.0712±0.635
F4	0.3787±0.37	0.4587±0.28	30.03± 1.56	17.4±1.46	1.2112± 0.736
F5	0.3802±0.92	0.4524±0.59	29.72± 1.41	15.9±1.72	1.1899± 0.641
F6	0.3714±0.43	0.4524±0.63	28.85± 1.33	16.06±2.32	1.2180± 1.465
F7	0.3691±0.58	0.4366±0.68	30.28± 1.26	15.50±1.56	1.1828 ± 0.399
F8	0.3743±0.36	0.4424±0.57	27.52± 1.20	15.47±1.70	1.1819± 1.583
F9	0.3649±0.50	0.4944±0.32	30.19± 1.26	17.8±1.26	1.3548± 0.640
F10	0.3717±0.39	0.4366±0.49	29.03± 1.56	13.46±1.48	1.1746± 1.256
F11	0.3676±0.73	0.4329±0.74	28.72± 1.41	15.08±1.93	1.1776± 1.013
F12	0.3952±0.59	0.4484±0.47	28.85± 1.33	11.8±2.80	1.1346± 0.796

Fig. 2: Cumulative % drug Release Vs Time in min from prepared batches F-7, F-8, F-9, F-10, F-11 & F-12 of matrix tablets of Glimepiride prepared by sodium acetate and starch urea.

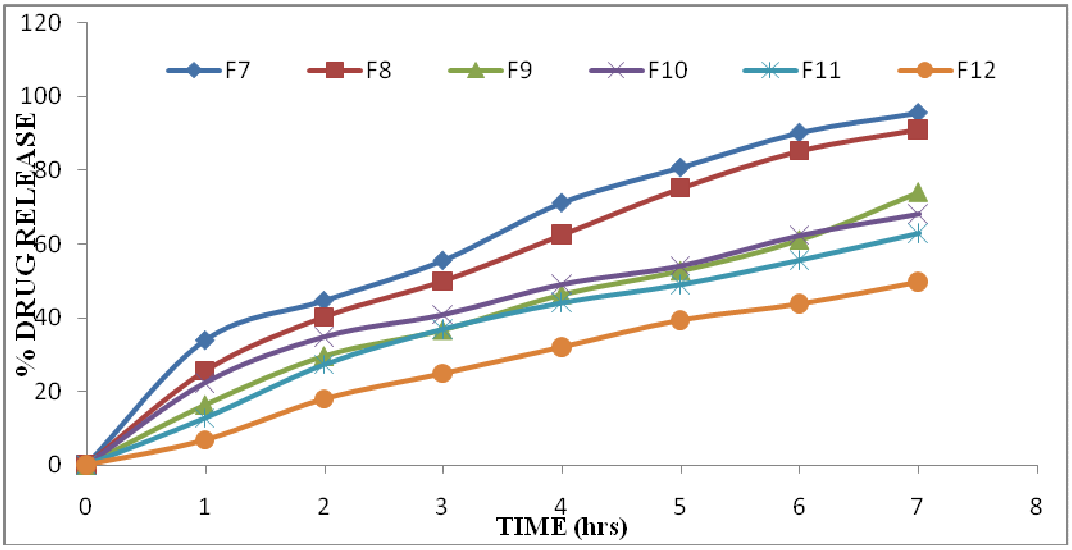

Table No. 3: Post compression parameters of sustained release matrix tablets of Glimepiride.

Formulation code	Hardness* (Kg/cm^2)±SD	Friability (%) ±SD	Thickness* (mm)±SD	Weight variation* (mg) ±SD
F1	7.4±0.19	0.54±0.10	3.90±0.02	199.69±1.8
F2	6.6±0.57	0.54±0.04	4.85±0.01	200.44±0.7
F3	6.9±0.30	0.57±0.05	4.19±0.01	200.69±1.1
F4	7.2±0.28	0.62±0.30	3.40±0.01	199.75±1.5
F5	7.3±0.10	0.64±0.12	3.66±0.01	200.43±1.9
F6	6.4±0.83	0.59±0.02	4.98±0.03	198.33±0.9
F7	6.3±0.52	0.60±0.02	5.12±0.02	200.14±1.2
F8	7.8±0.83	0.64±0.12	3.30±0.03	199.82±1.3
F9	8.2±0.77	0.70±0.15	2.54±0.05	199.86±1.9
F10	6.7±0.35	0.61±0.03	4.61±0.02	200.80±1.7
F11	7.3±0.44	0.59±0.25	3.81±0.05	199.69±0.5
F12	6.8±0.11	0.61±0.14	4.04±0.03	200.42±1.8