Research Article **ISSN:2321-2624**

International Journal of Medicine and Pharmaceutical Research
www.pharmaresearchlibrary.com/ijmpr

Formulation and Evaluation of Glimepiride Fast Dissolving Tablet

Ashwini V*, Poojitha U, Surekha R, Geetha G, Srinath B

Raghavendra Institute of Pharmaceutical Education and Research, Ananthapuramu, AP, India.
Received: 29 September 2014, Accepted: 28 November 2014, Published Online: 10 December 2014

Abstract

The objective of this work was to prepare Glimepiride (1mg) fast dissolving tablets by wet granulation method. Glimepiride was the drug of choice because of its low dose. The prepared Glimepiride FDT were found to have faster onset of action than the conventional Glimepiride tablets. Also, they were effective in lowering fasting blood glucose levels. Glimepiride fast dissolving tablets were prepared using super disintegrants like Croscarmellose sodium, cross povidone, sodium starch glycollate by employing wet granulation technique. Prepared tablets were evaluated for angle of repose, hardness, friability, disintegration, invitro dissolution studies. Dissolution was performed using USP type II apparatus at a temperature of 37±0.5ºc, 50 RPM, 900 ml pH 6.8 phosphate buffer and samples were estimated spectrophotometrically at 228nm.The invitro dissolution studies shown that tablets prepared using cross povidone superdisintegrant showed better drug release when compared to other super disintegrants.

Keywords: Immediate release, wet granulation, Cross povidone

Contents

***Corresponding author**
Ashwini V
Raghavendra Institute of Pharmaceutical Education and Research, Ananthapuramu, AP, India
Manuscript ID: IJMPR2329

PAPER-QR CODE

1. Introduction

Quick dissolving Tablets are crumble or break up quickly in saliva without the requirement for water. A few tablets are intended to disintegrate in saliva surprisingly quick, inside a couple of seconds and are genuine quick dissolving tablets. Others contain operators to upgrade the rate of tablet crumbling in the oral cavity, and are all the more suitably termed quick disintegrating tablets, as they may take up to a moment to totally crumble. Oral conveyance is as of now the highest level in the pharmaceutical business where it is viewed as the most secure, most advantageous and most prudent strategy for medication conveyance having the most noteworthy patient consistence [1-4]. This tablet arrangement is intended to permit organization of an oral robust measurement structure without water or liquid admission. Such tablets promptly break up or crumble in the salivation by and large inside <60 sec. Quick or

mouth dissolving tablets have been defined for pediatric, geriatric and laid up patients and for dynamic patients who are occupied and voyaging and might not have admittance to water. Such details give a chance to product offering augmentation in the a lot of people elderly persons will experience issues in taking traditional oral measurements structures (viz., results, suspensions, tablets and cases) as a result of hand tremors and dysphasia [5-7]. Gulping issues likewise are regular in adolescent people on account of their immature husky and sensory systems. Different gatherings that may encounter issues utilizing traditional oral dose structures incorporate the rationally sick, the formatively impaired and patients who are uncooperative, on decreased fluid admission plans, or are sickened [7].

Criteria for Fast dissolving Drug Delivery System:

The tablets should [8-10]

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasant mouth feel.
- Leave minimum or no residue in the mouth after oral administration.
- Exhibit low sensitive to environmental condition as temperature and humidity.

Glimepiride is an oral hypoglycemic agent, which is a commonly prescribed drug for the treatment of patients with type II diabetes mellitus. It is a weak acid with PKa of 5.3 and it is practically insoluble in water but highly permeable (classII) according to BCS due to its low dose it is selected for formulating in to fast dissolving tablets [11].

2. Materials and Method

Glimepiride was a gift sample from Dr. Reddy's laboratories, Hyderabad, India. Lactose monohydrate, Croscarmellose sodium, Crospovidone, Sodium starch glycollate, Avicel, magnesium stearate and Starch were procured from SD Fine chemicals, Mumbai, India. Distilled water was used in entire experiment.

Methods

Preformulation Studies:

Preformulation testing is the first step in the rationale development of dosage form of a drug substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined excipients. It gives extensive information to bring out good quality at high standard at which optimal dosage desired. Preformulation studies were performed on the drug (API), which included solubility and compatibility studies [12]. The following Preformulation studies were performed for Glimepiride and excipients.

Determination of solubility:

Solubility of Glimepiride was performed in solvents like dichloromethane, dimethyl formamide.

Calibration curve for Glimepiride:

Accurately weighed 100 mg of Glimepiride and added in 100 ml volumetric flask then it is diluted with 100ml of 0.1 N HCl to prepare stock solution of 1mg/ml and from this solution various concentrations are prepared and measure the absorbance by UV spectrophotometer at 228 nm.

Drug-excipientscompatibility studies by FTIR

Excipients are integral components of almost all pharmaceutical dosage forms. Thesuccessful formulation of a stable and effective solid dosage form depends on the careful selections of the excipients, which are added to facilitate administration, promote the consistent release and bioavailability of the drug and protect it from degradation. FTIR spectroscopy is one of the most powerful analytical techniques to identify functional groups of a drug. In the preparation of the tablet formulation, drug and excipientsmay interactas they are in close contact with each other, which could lead to instability of the drug. Preformulation studies regarding the drug – excipients interaction are therefore very critical in selecting appropriate excipients. FTIR spectroscopy was employed to ascertain the compatibility between the Glimepiride and the selected excipients.

Formulation of Glimepiride fast dissolving tablets using various super disintegrants:

Formulae for various formulations was shown in table 1.

a) Preparation of the tablet formulations by Wet granulation method:

Step-1: Sifting of Raw Materials

Glimepiride, Magnesium Stearate, Starch, Avicel, Croscarmellose sodium, Sodium starch glycollate, Crospovidone, Lactose Monohydrate were accurately weighed and sift through #40 separately.

Step-2: Premixing procedure

Glimepiride, Avicel and half amount of superdisintegrants are mixed for 5 min. To this mixture add Lactose monohydrate and mix for 5 min.The above mixture was passed through 40#.

Step-3: Preparation of Binder Solution

Starch was added into distilled water and stir with the help of stirrer to get clear solution.

Step-4: Wet Granulation

The binder solution was added to dry mixed powder under mixing at high speed,extra quantity of water was added if required. After the addition of binder mix at appropriate speed which will enable to break the lumps into granules. Unload the wet granules into tray drier.

Step-5:Sifting

The granules are sieved using mesh # 44.

Then add magnesium stearate, remaining quantity of superdisintegrant extra granularly.

Step-6: Finally compress the above granules using tablet compression machine.

Table 1: Formulation table

Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Glimepiride	1	1	1	1	1	1	1	1	1
Lactose monohydrate	61.4	59.4	57.9	61.4	59.4	57.9	61.4	59.4	57.9
Croscarmellose sodium	1	3	5	_	_	_	_	_	_
Crospovidone	_	_	_	1	3	5	_	_	_
Sodium starch glycollate	_	_	_	_	_	_	1	3	5
Starch	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8
Avicel	34	34	34	34	34	34	34	34	34
Magnesium stearate	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8

Evaluation of Glimepiride fast dissolving tablets:

A. Pre-compression parameters:

The quality of tablet is generally dictated by the quality of physicochemical properties of blends. There are many formulation and process variables involved in mixing step and all these can affect the characteristics of blends produced. The various characteristics of blends tested are as given below [13-17]:

Angle of Repose:

The angle of repose was determined by the funnel method suggested by Newman. Angle of repose is determined by the following formula

Tan θ = h/r

Therefore θ = Tan -1 h/r

Where

θ = Angle of repose

h = height of the cone

r = Radius of the cone base.

B.Post compression parameters:

The tablets after punching of every batch were evaluated for in-process and finished product quality control tests i.e., hardness, friability and *in vitro* drug release studies.

Measurement of tablet hardness:

The hardness of tablet is an indication of its strength. Measuring the force required to break the tablet across tests it. The force is measured in kg and the hardness of about 3-5 kg/cm2 is considered to be satisfactory for uncoated tablets. Hardness of 3 tablets from each formulation was determined by Monsanto hardness tester.

Friability test:

It is measure of mechanical strength of tablets. Roche friabilator is used to determine the friability by following procedure. Tablets were weighed and placed in Roche Friabilator where the tablets were exposed to rolling and repeated shocks resulting from free falls within the apparatus. After 100 revolutions, tablets are removed, dedusted and weighed again. The friability was determined as the percentage loss in weight of the tablets.

% Friability = (Final weight / Initial weight) X 100

Disintegration Time:

The USP device to test disintegration was six glass tubes that are "3 long, open at the top, and held against 10" screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is positioned in 1 liter beaker of distilled water at 37±2^{o}C, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker.

***Invitro* Dissolution**

Freshly prepared phosphate buffer (pH 6.8) of 900 ml was placed in each dissolution vessels of dissolution test apparatus (USP, II paddle method). The tablets were placed in the dissolution medium. The temperature of the dissolution medium was maintained at 37±0.5^{0}C and the paddle was rotated at 50 rpm. 5 ml samples were

withdrawn. The sample volume was immediately replaced with the same volume of fresh media as when a sample was taken. The samples with drawn were filtered, diluted and estimated spectrophotometrically at 228 nm. Cumulative amount of the drug released at each interval was calculated by using standard graph of Glimepiride.

3. Results and Discussion

Preformulation Studies

Determination of solubility

Glimepiride was found to be freely soluble in dimethyl formamide, dilute acids.

Calibration curve for Glimepiride

Calibration curve for Glimepiride was shown in fig 1.

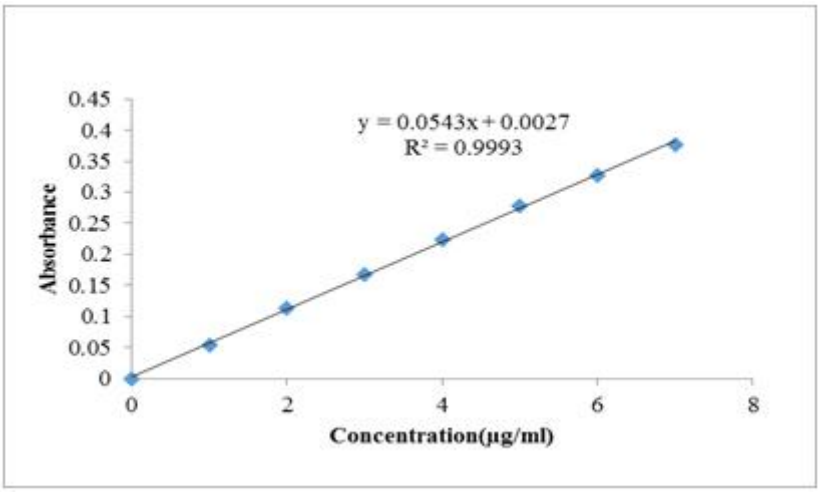

Figure 1: Standard graph of Glimepiride

Evaluation of Glimepiride tablets:

Pre compression parameters

Angle of repose, Hardness, Friability and Disintegration values were shown in table2.

Table 2: Angle of repose, Hardness, Friability and Disintegration

Formulation	Angle of repose (^{o})	Hardness (kg/cm^2)	Friability (%)	Disintegration (sec)
F1	25.67	3.53±0.03	0.64±0.02	64.33
F2	28.60	3.46±0.02	1.00±0.01	64.00
F3	26.40	2.90±0.06	0.83±0.03	56.00
F4	27.30	2.70±0.01	1.16±0.05	55.60
F5	30.60	2.53±0.09	1.00±0.04	54.33
F6	31.60	2.26±0.05	0.50±0.06	52.60
F7	32.50	3.80±0.1	0.66±0.04	78.66
F8	26.40	3.70±0.06	0.33±0.05	75.33
F9	34.20	3.56±0.07	0.66±0.07	71.00

***In Vitro* Dissolution studies:**

The *in vitro* dissolution data of formulations was sown in table 3.

Table 3: Percent drug release for F1 to F9 formulations

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
10	7.39±0.01	11.0±0.03	8.64±0.01	14.4±0.01	7.0±0.1	7.9±0.02	8.7±0.1	3.4±0.1	14.40±0.1
20	24.9±0.02	23.2±0.01	19.4±0.02	25.5±0.06	23.8±0.3	19.9±0.1	19.7±0.2	17.1±0.2	20.47±0.2
30	39.4±0.04	39.5±0.04	26.1±0.06	38.4±0.03	45.6±0.2	46.1±0.1	29.4±0.1	35.5±0.2	31.63±0.1
40	47.2±0.03	58.8±0.05	41.1±0.05	57.1±0.02	51.0±0.2	59.4±0.2	36.0±0.2	49.3±0.1	39.4±0.1
50	58.3±0.06	67.9±0.01	59.9±0.09	67.1±0.01	61.6±0.2	69.9±0.3	44.4±0.1	53.8±0.2	54.96±0.2
60	68.8±0.09	72.1±0.02	72.7±0.02	73.2±0.05	73.2±0.1	77.3±0.1	58.8±0.1	64.9±0.1	64.96±0.1

Comparison of dissolution profiles for F1, F4 and F7 which were prepared using various super disintegrants of 1% concentration was shown in fig.2.

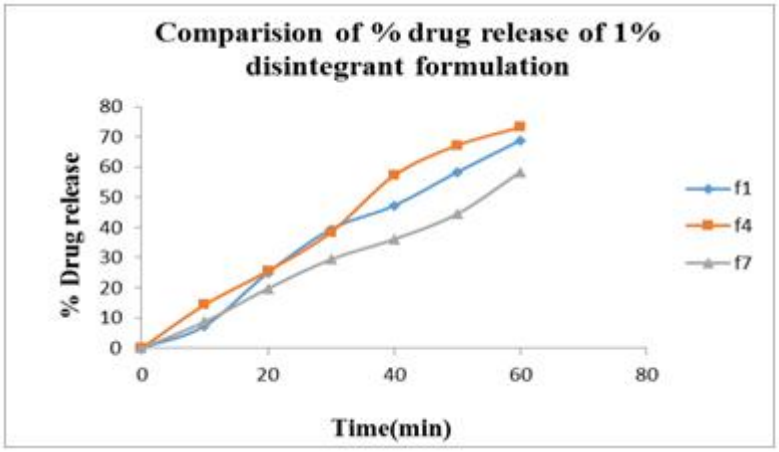

Figure 2: 1% Disintegrantdissolution profile

Comparison of dissolution profiles for F2,F5, F8 which were prepared using various super disintegrants of 3% concentration was shown in fig 3.

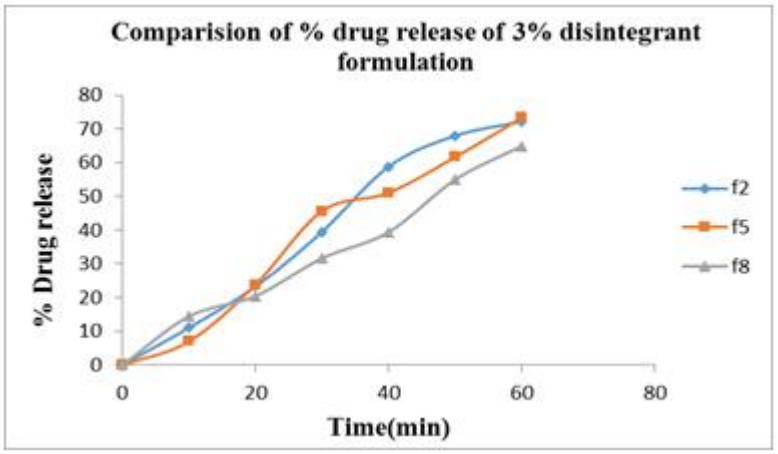

Figure 3: 3% Disintegrantdissolution profile

Comparison of dissolution profiles for F3,F6, F9 which were prepared using various super disintegrants of 5% concentration was shown in fig 4.

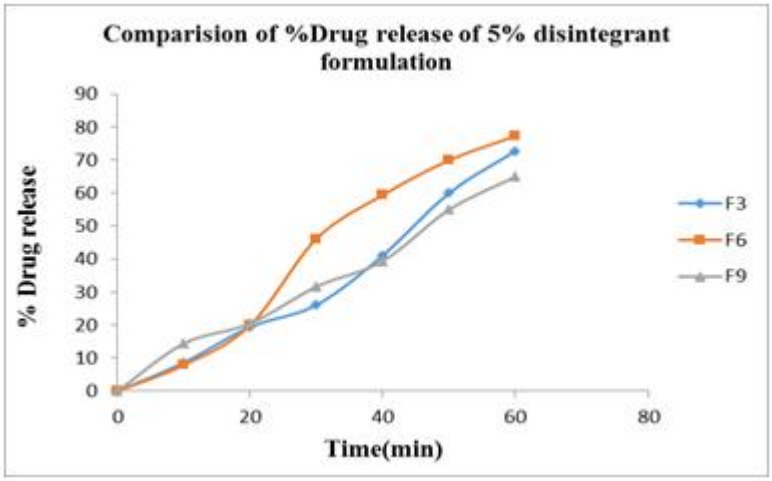

Figure 4: 5% Disintegrantdissolution profile

4. Conclusion

Glimepiride 1mg tablets are prepared as superdisintegrant tablet as Glimepiride is Antidiabetic drug by enhancing its disintegration time we can enhance the onset of action rapidly .To achieve fast disintegration time we have used superdisintegrants like sodium starch glycollate, Crospovidone, Croscarmellose sodium. Super disintegrant tablet provides fast disintegration hence by the study we concluded that formulation which was prepared using Crospovidone as super disintegrating agent is the better trail compare to other trails.

5. References

1. Ms.Parul BP, Amit choudhary GD. Gupta., Fast dissolving drug delivery systems: An update. July **2006.**
2. Virely P, Yarwood R, Zydis. A novel, fast dissolving dosage form. *Manuf. Chem*. **Feb 1990**: 36-37
3. Seager H. *J. Pharm pharmacol*,**1998,** 50(4); 375-382
4. Koizumi KI et al., *Int. J. Pham*, 1997, 152, 127-131.
5. RoweRC, shestey PJ, Weller PJ. Hand book of pharmaceutical excipients, 4th edition. London, Chicago: pharmaceutical press, American pharmaceutical association; **2003.**
6. Mishramoen and keating GM. *Indian drugs*,**2006**, 66(6):883-90.
7. Nissen SE, Nicholls SJ, Wolski K, et al. *JAMA*, **2008,** 299(13): 1561–73.
8. James Klancke., *Dissolution Technologies*, **May 2003,** 6-8
9. Masaki K, Intrabuccally disintegrating preparation and production thereof. US Patent 5,466.464.
10. Bhaskaran S, NarmadaGV. Indian Pharmacist, **2002**, 1(2), 9-12.
11. Davis, Stephen N. 60. Insulin, oral hypoglycemic agents, and the pharmacology of the endocrine pancreas. In Brunton, Laurence L.; Lazo, John S.; Parker, Keith L. (Eds.). Goodman & Gilman's the Pharmacological Basis of Therapeutics. New York: McGraw-Hill. **2005**, p. 1636.
12. Allen LV, Wang B. Process for making a particulate support matrix for making a rapidly dissolving dosage form. **2001**. US Patent 6,207,199.
13. Rajesh Pawan A, Hindustan A Ahad, Venupriya R, Sunitha Rani S, Roopesh GT. *CRBPS*, **2013**, 2 (4): 01-06.
14. Leon Lachmann. Theory and Practice of Industrial Pharmacy, 3rd Edition, Varghese Publishing House, 1991, 430-456.
15. Reddi Prashanth, Hindustan Abdul Ahad, Nareshbabu G, Mohammed Ishaq B, Anil Kumar K. **IJRPLS**, **2013**, 1(2): 68-76.
16. Remingtons, Pharmaceutical Sciences. 16th Edition, Mack Publishing Company: 1980, pp: 1677-1683
17. Aulton ME. Pharmaceutics-The Sciences of Dosages form design, international student Edition, Churchill Livingston, 2001: 129-191.
18. Anuradha CM, Hindustan Abdul Ahad, Abhilash A, Prabhuraj KJ, Swapna K. *IJMPR*, **2013**, 1(1): 164-169.