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Research Article

Effect of Different Binders and Super Disintegrants on Formulation of Glimepiride Immediate Release Tablets by Wet Granulation Method

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ABSTRACT

The present study aims at developing a Glimepiride immediate release tablet formulation for the effective treatment of Type-2 Diabetes mellitus (or) Non-Insulin-Dependent Diabetes Mellitus (or) adult-onset diabetes. Glimepiride is a sulfonylurea antidiabetic drug. Glimepiride acts as an insulin secretagogue. To provide the patients with the most convenient mode of administration, there was a need to develop immediate release dosage form, particularly one that disintegrates rapidly and disperses and helps in enhancing the Bioavailability of the drug. Glimepiride immediate release tablets were formulated by using wet granulation method and povidone k 30, starch as binders, croscarmellose sodium, Sodium Starch Glycolate, Crospovidone as disintegrants, Lactose monohydrate as Diluent and Magnesium stearate as Lubricant. The tablets were evaluated for Pre compression and Post compression Parameters after conducting Preformulation Studies. All the parameters were within the pharmacopoeial limits and the drug disintegration time was less and the Invitro dissolution studies showed that the drug release was fast in Formulation(F2) containing Sodium Starch Glycolate as Super disintegrant and Povidone k 30 as Binder when compared to all other Formulations.

Keywords: Glimepiride, Wet Granulation, Super-disintegrants, Binders, Immediate Release

INTRODUCTION

Drug is an active chemical entity used for diagnosis, prevention and treatment of disease; they also modify physiological state of the body. The oral route of drug administration is the most important method of administrating drugs for systemic effects. Oral route of drug administration has wide acceptance up to 50 to 60% of total dosage forms. Solid dosage forms are popular and most preferred route due to its advantages. Tablets are solid dosage forms containing medicinal substances with or without suitable diluents. They offer safe and convenient ways of active pharmaceutical ingredients (API) administration with excellent physiochemical stability in comparison to some other dosage forms, and provide accurate dosing. Immediate release pharmaceutical formulation includes any formulation in which the rate of release of drug from the formulation is at least 70% (preferably 80%) of active ingredient within 4 hours, such as within 3 hours, preferably 2 hours, more preferably within 1.5 hours, and especially within an hour (such as within 30 minutes) of administration. Various techniques used in the preparation of immediate release tablets are Tablet molding technique, Direct compression technique, Wet granulation technique, Mass extrusion technique. In the present investigation, Wet Granulation Method was taken as it was a robust process which helps in reducing elasticity problems and imparts flowability to a formulation. The Binders used were Povidone k 30 and Starch. The commonly used Superdisintegrants are Croscarmellose sodium, Sodium Starch glycolate and Crospovidone. The use of various Binders and Super disintegrants effects the Disintegration time and Dissolution studies. Glimepiride is a sulfonylurea anti-diabetic drug used to control high blood sugar. It is used in patients with type 2 diabetes (non-insulin-dependent diabetes). It works by stimulating the release of our body's natural insulin. Controlling high blood sugar helps prevent kidney damage, blindness, nerve problems, loss of limbs, and sexual function problems. Proper control of diabetes may also lessen risk of a heart attack or stroke. The objective of the present investigation was to prepare Glimepiride immediate release tablets by Wet Granulation Method using Lactose Monohydrate, Croscarmellose Sodium, Sodium Starch Glycolate, Crospovidone, Starch, Povidone k 30, Avicel PH 102, Magnesium Stearate as excipients in the formulation.

MATERIALS AND METHODS

Materials: Glimepiride was obtained as a gift sample from Dr.Reddy's Laboratories and all other excipients and chemicals used were of analytical grade.

Methods: The method used in the formulation of Glimepiride Immediate Release tablets was wet granulation method. All the batch formulations are formulated by wet granulation method. Accurately weigh specified quantity of raw materials such as Glimepiride, Lactose Monohydrate, Super disintegrants, Avicel PH 102, Magnesium stearate in a weighing balance. Glimepiride and Lactose Monohydrate were sifted through sieve #40. Mix the sifted materials for 5min. Dissolve Binder in Aqueous water under continuous

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Table .No 1: Formulation Batches of Glimepiride Immediate Release Tablets

INGREDIENTS	F1(mg)	F2(mg)	F3(mg)	F4(mg)	F5(mg)	F6(mg)
Glimepiride	1	1	1	1	1	1
Lactose Monohydrate	40	40	40	40	40	40
CCS	2.4	-	-	2.4	-	-
SSG	-	2.4	-	-	2.4	-
CP	-	-	2.4	-	-	2.4
Povidone k 30	1.8	1.8	1.8	-	-	-
Starch	-	-	-	1.8	1.8	1.8
Avicel PH 102	34	34	34	34	34	34
Magnesium Stearate	0.8	0.8	0.8	0.8	0.8	0.8

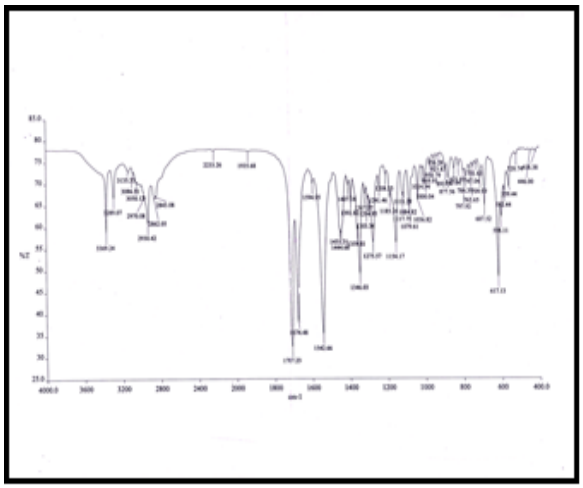

Figure .no 1: FT-IR of the Glimepiride drug

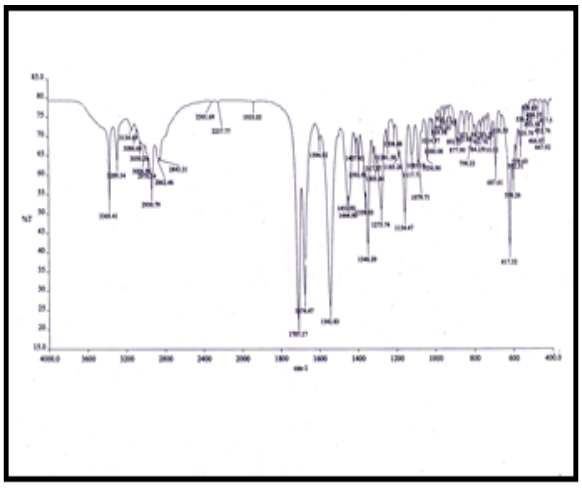

Figure .no 2: FT-IR of Glimepiride and Excipients

Table .No 2: Pre-formulation Studies of Glimepiride

S.No	Parameters	Observations
1	Solubility	Practically insoluble in water, slightly soluble in methanol
2	Particle size determination	Fine powder
3	Hygroscopicity	Non Hygroscopic
4	Melting point	207^0c

Table .No 3: Evaluation of Pre compression Parameters

Formulation Code	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's index (%)	Hausner's ratio
F-1	0.532±0.013	0.595±0.013	10.5±0.02	1.11±0.01
F-2	0.534 ±0.012	0.593 ±0.012	9.94±0.01	1.11±0.02
F-3	0.522±0.025	0.589±0.02	11.37±0.05	1.12±0.03
F-4	0.472±0.0015	0.556±0.012	15.10±0.95	1.17±0.18
F-5	0.486±0.001	0.563±0.013	13.67±0.02	1.15±0.02
F-6	0.484±0.0005	0.574±0.047	15.67±0.61	1.18±0.017

All the values are expressed as mean±SD, n=3

stirring. Granulate with required quantity of binder solution by kneading method. Dry the wet granules in Hot Air Oven at a temperature of 60^0c, until the moisture content of granules is NMT 1-1.5%. Use Sieve # 20 to reduce the size of granules to get the uniform particle size. Avicel PH 102 sifted through Sieve # 40 and mixed along with dried granules for 5 minutes. Finally, the above granules are lubricated using specified quantity of magnesium stearate after sifting it through Sieve # 40 and mix for 3 minutes. Compress the above granules using punches and the tablets were prepared.

Evaluation of Pre compression Parameters**:** It is very important parameter to be measured, since it affects the mass of uniformity of the dose. It is usually predicted in terms of angle of repose, bulk density and tapped density.

Evaluation Post compression Parameters: The formulated

Table .No 4: Evaluation of Post compression Parameters

Formulation Code	Weight Variation	Hardness Kg/cm^2	Friability %	Disintegration Time (sec)
F-1	400.0±0.06	3.3±0.67	0.14±0.01	61.3±0.67
F-2	399.9±0.74	3.5±0.35	0.12±0.00	58.5±0.35
F-3	399.73±0.71	3.0±0.61	0.11±0.00	63.0±0.61
F-4	400.16±1.19	3.0±0.5	0.12±0.00	64.0±0.5
F-5	400.93±1.06	3.5±0.5	0.11±0.00	61.5±0.5
F-6	399.59±1.18	3.0±0.35	0.13±0.00	66.0±0.35

All the values are expressed as mean±SD, n=3.

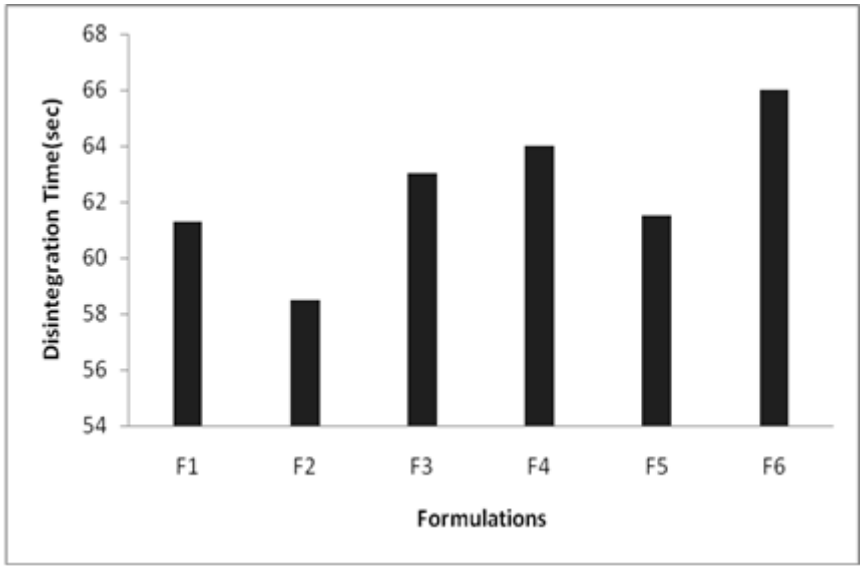

Figure .no 3: In-vitro Disintegration Time of Formulation Batches

Table .No 5: In-vitro Dissolution studies

S.No	Formulation Code	Cumulative % Drug Release(min)					
		5	10	15	30	45	60
1	F1	64.7±0.69	68.5±0.84	74.8±0.54	82.2±0.63	88.9±0.30	91.7±0.81
2	F2	67.7±0.71	71.6±0.84	74.9±0.42	84.8±0.87	91.0±0.87	94.7±0.70
3	F3	63.6±0.51	66.5±1.30	71.0±0.83	78.9±0.58	86.1±0.58	89.1±0.67
4	F4	61.1±0.63	65.8±0.70	68.8±0.77	74.2±0.44	81.2±0.76	85.5±0.97
5	F5	63.0±0.90	67.7±0.67	70.6±0.62	77.7±0.54	83.0±0.38	88.9±1.02
6	F6	59.1±0.65	65.2±0.48	69.6±0.52	73.1±0.90	81.2±0.87	86.8±0.69

All the values are expressed as mean±SD, n=3

Table .No 6: Drug content estimation by UV spectrophotometer

S.No	Formulation Code	% Assay	Assay(mg)
1	F1	93.1	0.93
2	F2	98.3	0.98
3	F3	95.5	0.95
4	F4	96.5	0.96
5	F5	95.1	0.95
6	F6	96.9	0.96

tablets were evaluated for the following parameters such as weight variation, hardness, friability, disintegration and Invitro dissolution studies and the results has been tabulated in table.

RESULTS AND DISCUSSION

Drug Excipients compatibility studies: Physical compatibility studies were assured by FT-IR studies. The crude drug sample and the complete formula of the final formulation were chosen for the study. The FT-IR spectra's of the above samples were studied after a period

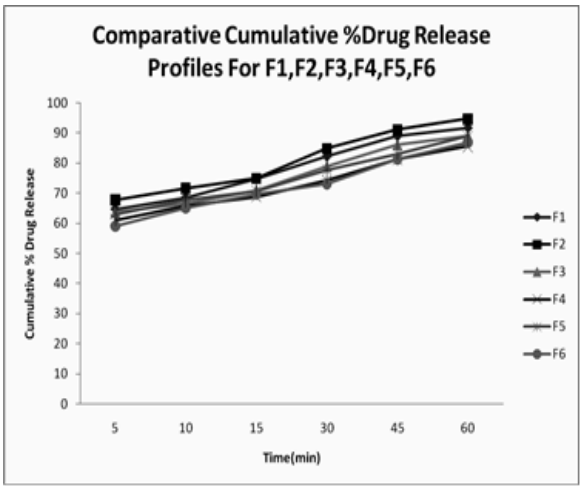

Figure .no 4: In-vitro Dissolution studies of Formulation Batches

of 30 days from preparation of the mixtures, to facilitate prompt detection of incompatibility. Based on the spectral data it has been observed that there are no shift of any major peaks in appearance or disappearance of the peak.

Pre-formulation Studies: Pre-formulation studies of Glimepiride drug were conducted and the results were within the IP limits and were tabulated in Table. No: 2.

Evaluation of Pre compression Parameters: The Pre compression Parameters such as Angle of Repose, Bulk Density, Tapped Density, carr's index, Hausner's ratio were evaluated and the results were tabulated in Table.no:3

Evaluation of post compression Parameters: The Post compressions Parameters such as Weight variation, Hardness, Friability, Disintegration Test, In-vitro Dissolution studies were evaluated and the results were tabulated in Table.

In-vitro Dissolution Studies: The In-vitro dissolution studies were conducted by using USP Type 2 Dissolution Apparatus. 900 ml of pH 6.8 Phosphate buffer was used as Dissolution Medium. Speed was maintained at 75 rpm and temperature maintained at 37˚C ± 0.5^0c. The samples were withdrawn up to 60 min and measured by UV Spectrophotometer at 228 nm and the results were tabulated in Table .No 5.

CONCLUSION

In the present work, Formulations of Glimepiride Immediate Release Tablets were prepared by Wet Granulation Method. Six formulations were formulated and evaluated for both the Pre compression and Post compression Parameters. The Pre compressions Parameters such as Angle of Repose, Bulk Density, Tapped Density, Carr's index, Hausner's ratio were evaluated and the results were tabulated. The Post compressions Parameters such as Weight variation, Hardness, Friability, Disintegration Test, In-vitro Dissolution studies were evaluated and the results were tabulated. Formulation F2 containing Povidone k 30 as Binder and Sodium starch glycolate as super disintegrant had shown the Disintegration time less than 60 sec and better Dissolution than all other Formulations. Hence, Formulation F2 is the best formulation among the six formulations containing different Binders and Super disintegtants.

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