Archives of Pharmaceutical Sciences and Research
Vol 13 Issue 1 277 - 282 June 2023
Research Article

Formulation and Evaluation of Fast Disintegrating Pioglitazone Hydrochloride Tablet

Dr. A Geethalakshmi, Ms. Liji Chacko, Mr. Robin Roy, Ms. Rehana Sakkeer, Ms. Risahulin Warjri.
Department of Pharmaceutics, RR College of Pharmacy, Bangalore, India

ABSTRACT

The aim of this study was to prepare fast disintegrating tablet of anti diabetic drug for the treatment of diabetes. The fast disintegrating tablet was prepared by different concentration of super disintegrating agent such as sodium starch glycolate, methyl crystalline cellulose, fenugreek, beta yclo dextrin by direct compression technique. The prepared formulation (F1-F16) were evaluated for pre and post formulation test such as hardness, friability, weight variation, drug content, disintegration time, dissolution time. All formulation was complying with the pharmacopoeial standards. All the formulation passes both pre & post formulation test but failed in disintegration time as it showed more and there was no significant increase in the release of drug as increasing the polymer concentration as expected. But formulation F7 and F16 showed less DT (9sec). When compared to other formulation and there significant increase in the release of drug as increasing the polymer concentration, therefore formulation F7 & F16 were selected as best formulation compared to other formulation. F16 showed the maximum release of drug 97.52% CDR in 10 minute when compared to F7. Therefore F16 was selected as best formulation. This method was preferred due to its low cost, patient compliance, easy method of preparation and industrial benefit.

Key word: Pioglitazone; Super disintegrant; Disintegration time

INTRODUTION

Pioglitazone is a selective agonist as peroxisome proliferators – activated receptor gamma [PPAR] in target tissues for insulin action; adipose tissue, skeletal muscle and liver. Activation of PPAR increases the transcription of insulin responsive genes involved in the control of glucose and lipid production, transport and utilization. Through this mechanism, Pioglitazone both enhances tissue sensitivity to insulin and reduces the hepatic production of glucose that is gluconeogenesis. Insulin resistance associated with type 2 diabetes mellitus is therefore improved without an increase in insulin secretion by pancreatic b-cells. Fast disintegrating tablets are convenient for administration and patient compliant for disabled bedridden patients and for travellers and busy people who do not have access to water. Pioglitazone hydrochloride is an oral hypoglycaemic agent, which is a commonly prescribed drug for the treatment of patients with type II diabetes mellitus. Pioglitazone hydrochloride is a basic (pKa = 12.06) which is partially insoluble in water and alkaline buffer solutions, but as per the Biopharmaceutical classification system (BCS) Pioglitazone categorized as class II drug. The oral absorption is uniform, rapid and complete with a bioavailability of nearly 100% and an elimination half life of 3-7 hrs. Delivery systems aim for the same by formulating a dosage form convenient to be administered so as to achieve better patient compliance.[1-2]

MATERIALS AND METHODS

Materials

Pioglitazone and sodium starch glycolate were purchased from Bangalore fine chemicals, Fenugreek was gifted by Akash Rauniyar M. Pharma, Mannitol and Magnesium state were purchased from Thomas Baker Chemicals Pvt. Ltd, Aspartame was purchased from Loba C, hemi Pvt. Ltd, Talc was purchased from SD Chem., Mumbai.

Methods

Preformulation studies

Preformulation testing is the first step in the rational development of dosage forms of a drug substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. The overall objective of pre-formulation testing is to generate information useful to the formulator in developing stable and bioavailable dosage forms which can be mass produced.

Determination of solubility

The pure drug (Pioglitazone HCL) was dissolved in different solvents to check their solubility until it forms precipitate and was recorded. The solvents and used are water, ethanol, phosphate buffer. [3] It was shown in table: 2.

Determination of melting point

Melting point of Pioglitazone was determined by open capillary method. The capillary tube was closed at one end by fusion and was filled with Pioglitazone by repeated tapping. The capillary tube was placed in a digital melting point apparatus. The melting point apparatus was set with the thermometer. The temperature at which the drug started melting was recorded. This was performed thrice and the average value was calculated.[4]

Method of Formulation

Direct compression method

This model drug is thoroughly mixed with the super disintegrants, and then other excipients are added to the mixer and passed through the sieve (#:40). Collect the powder mixer, blend with Magnesium state, Talc (pre sieved), and subject the blend for tablet compression. The drug and the excipients were passed through sieve no: 40 except lubricant. The blend was further lubricated with Magnesium state, Talc (#:60) and the powder blend is subjected to drying for removal of moisture content and was compressed by direct compression method. Then the blended material was slightly compressed on the 4mm flat- biconvex punch using a Rimek MINI PRESS-1 MTT tablet machine (Karnawati Engg. Ltd., Mehsana, India).Tablet of 200mg was prepared by adjusting hardness and volume screw of compression machine properly. The table 1 shows the composition of all 16 formulations.

Content drug uniformity

Selected 20 tablets randomly and powdered. A quantity of this powder corresponding to 200mg of model drug was dissolved in 100ml of 6.8pH phosphate buffer, stirred for 15min and filtered. The 1ml of filtrate was diluted with 100ml with 6.8pH phosphate buffer. Absorbance of this solution was measured at 24nm using 6.8pH phosphate buffer as blank and content drug was estimated.[5]It was shown in table: 3.

In vitro dissolution studies

In vitro disintegration time

Disintegration times for tablets were determined using USP tablet disintegration apparatus with saline phosphate buffer of pH

Evaluation of Tablets

Hardness test

The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of each batch tablet was checked by using Pfizer hardness tester. The hardness was measured in terms of kg/cm^2. 3 tablets were chosen randomly and tested for hardness. The average hardness of 3 determinations was recorded.[5] It was shown in table: 3.

Weight variation

20 tablets were selected randomly from each formulation, weighed individually and the average weight and % variation of weight was calculated.[5]It was shown in table: 3.

Dissolution of the tablet of each batch was carried out using USP II apparatus paddle apparatus was used and paddle was allowed to rotate at 50 rpm. As per the official recommendation of IP 900ml of 6.8 pH of phosphate buffer used as dissolution medium and the temperature of the medium was set at 37± 0.5^{o}c. 5ml of sample was withdrawn at predetermined time interval of 2, 4, 6, 8 and 10min. And same volume of fresh medium was replaced. The withdrawn samples were analysed by an UV spectrophotometer at 244nm using buffer solution as blank solution.[6]It was shown in table: 3.

6.8 as medium, maintained the medium temperature at 37±2^{o}c. The time required for complete disintegration of the tablets with no palatable mass remaining in the apparatus was recorded.[7]It was shown in table: 3.

RESULTS

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16
Pioglitazone	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30
B-cyclo dextrin	4	5	6	7	-	-	-	-	-	-	-	-	-	-	-	-
Sodium starch glycolate	-	-	-	-	4	5	6	7	-	-	-	-	-	-	-	-
MCC	-	-	-	-	-	-	-	-	4	5	6	7	-	-	-	-
Fenugreek	-	-	-	-	-	-	-	-	-	-	-	-	4	5	6	7
Mannitol	158	157	156	155	158	157	156	155	158	157	156	155	158	157	156	155
Aspartame	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Magnesium sterate	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Talc	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Total weight of Tablet	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200

Table 1: Formulation chart

Solvents	Inference
Water	Partially insoluble
Ethanol	Freely soluble
pH 7	Sparingly soluble

Table 2: Solubility studies

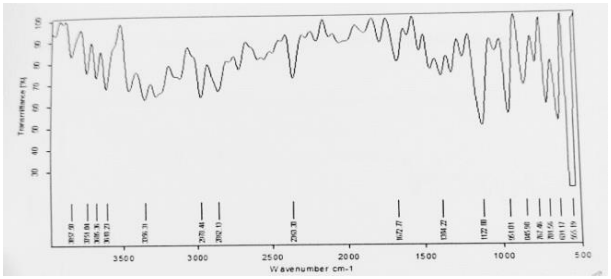

Figure: 1

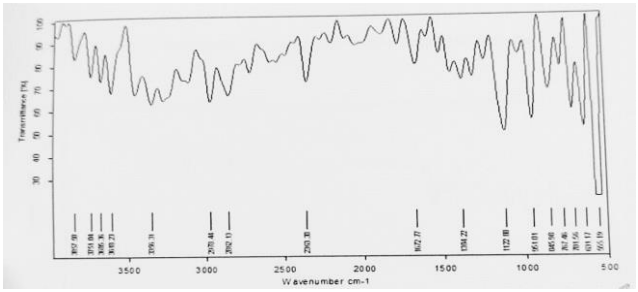

Figure: 2

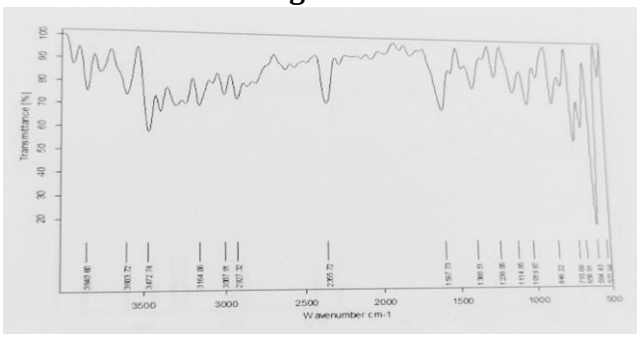

Figure: 3

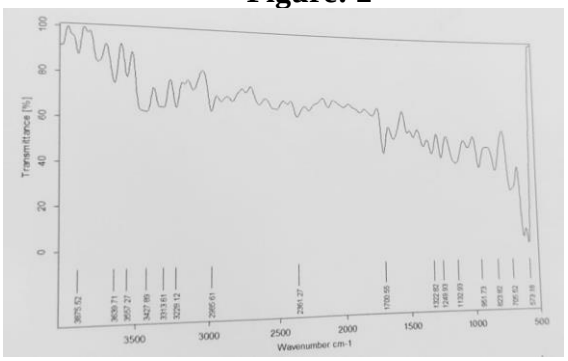

Figure: 4

Figure 1: FT-IR Spectrum of Pioglitazone HCL, Figure 2: FT-IR Spectrum of Pioglitazone HCL+ Beta cyclodextrin, Figure3: FT-IR Spectrum of Pioglitazone HCL+ MCC, Figure 4: FT-IR Spectrum of Pioglitazone HCL+ Sodium starch glycolate

Formulation	Hardness	Friability	Weight variation	Thickness	Drug content	Disintegration Time	In vitro dispersion Time	In vitro drug release	drug content
	kg/cm^2	%	mg	mm	%	sec	sec	%	%
F1	3.8	0.25	202	3.9	86.56	18	16	86.58	80.06
F2	4.1	0.22	200	3.8	87.63	16	13	74.76	73.46
F3	4.1	0.23	200	3.9	87.63	14	12	85.05	78.72
F4	4.2	0.24	200	3.8	87.92	12	11	80.42	82.76
F5	4.1	0.28	201	3.9	76.82	10	12	81.72	78.03
F6	4.1	0.25	203	3.8	76.53	10	10	85.65	80.56
F7	3.8	0.29	201	4.0	94.76	9	9	95.25	82.03
F8	3.8	0.27	200	4.0	79.97	8	16	93.28	75.22
F9	3.9	0.26	201	3.9	94.74	18	14	83.45	78.59
F10	4.0	0.27	202	3.8	93.14	16	13	81.68	80.04
F11	4.1	0.26	201	3.8	94.23	15	11	79.99	82.83
F12	4.2	0.25	200	3.9	88.91	12	12	78.75	78.26
F13	4.0	0.26	200	3.9	88.96	10	10	81.72	79.16
F14	4.0	0.23	201	3.6	92.12	10	10	85.65	80.56
F15	4.0	0.28	200	3.6	96.82	12	12	92.28	74.84
F16	4.1	0.24	200	3.8	96.84	9	9	97.52	78.59

Table: 3 Post Compression Studies and Drug Content Estimation

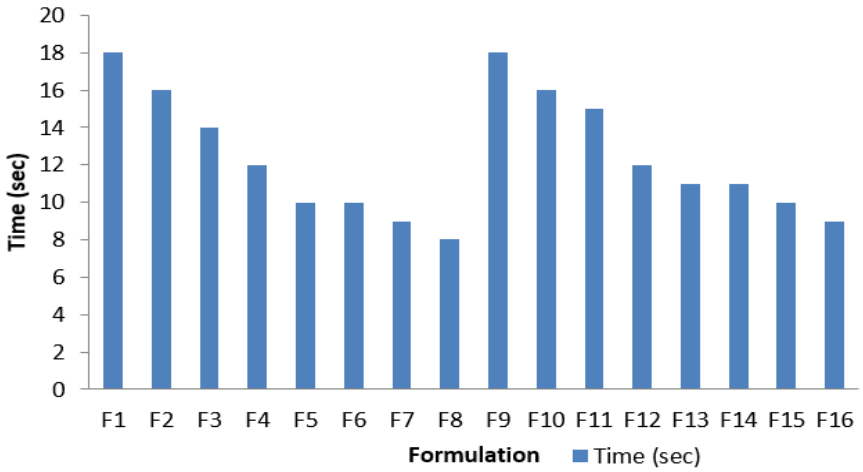

Figure 5: Comparison between disintegration times for formulations (F1-F16)

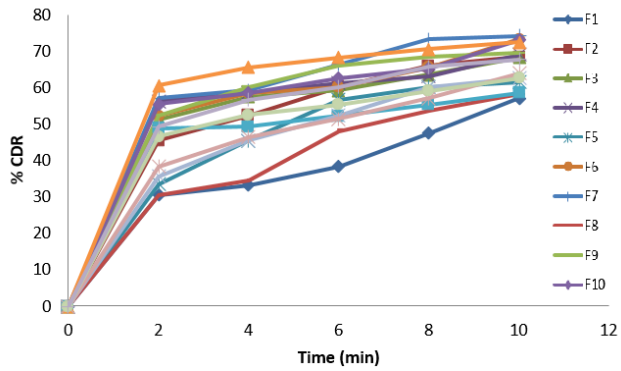

Figure 6: In vitro drug release studies of formulation F1-F16

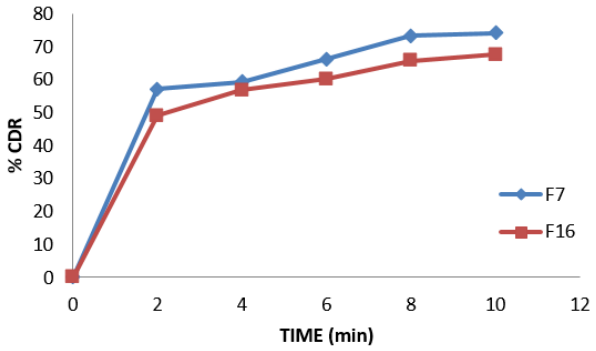

Figure 7: Zero order kinetics of formulation F7, 16

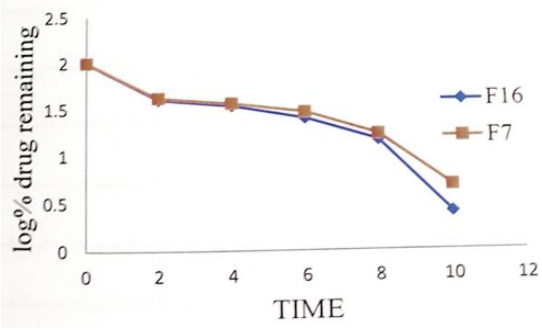

Figure 8: First order kinetics of formulation F7, 16

Formulation	Kinetic drug release	
	Zero order	First order
	Correlation coefficient (r^2)	Correlation coefficient (r^2)
F16	0.8026	0.8749
F7	0.8041	0.9021

Table 4: Kinetic Drug Release

CONCLUSION

In the present study, the main objective was to improve dissolution rate and rapid absorption which provide rapid onset of action of drug Pioglitazone using different super disintegrants by direct compression method. Pure drug was identified by UV spectrum for ʎ max 244nm, FT-IR study and melting point (148ºc) study. Various 16 formulations, each of Pioglitazone of 200mg total weight tablet were formulated using direct compression method by using 4 super disintegrants one of each four formulations with varying concentration. According to that F1, F2, F3, F4 (with β-Cyclodextrin 2%, 2.5%, 3%, 3.5%), F5, F6, F7, F8 (with Microcrystalline 2%, 2.5%, 3%, 3.5%), F9, F10, F11, F12 (with Sodium starch glycolate 2%, 2.5%, 3%, 3.5%), F13, F14, F15, F16 (with Fenugreek 2%, 2.5%, 3%, 3.5%) were prepared. All this formulation (F1-F16) was subjected to pre and post compression tests. From all formulations, F7 & F16 showed less DT compared to other formulation and these was significant increase in the release of drug as increasing the polymer concentration therefore, F7 & F16 were selected as best.

RFERENCES

1) Ved Prakash, Saurabh Maan; Fast disintegrating tablets 2011: 2 (4). K.
2) https://pubchem.ncbi.nlm.nih.gov/compound/pioglitazone. Cited on 12.06.2021

3) Mukesh P. Ratnaparkhi; Dr. G. P Mohanta; Review on fast dissolving tablet 2009 2.
4) Jindal K. Review on solubility: A mandatory tools for pharmaceuticals. Int Res J Pharm.2017;8(11):11-5).
5) Dr. Sujit Pillai, Pinky Yadav; Formulation and evaluation of Pioglitazone HCL fast dissolving tablet. 2018 11 (12).
6) Y Rayate, S Mohite Formulation and fast dissolving tablet of pioglitazone asian journel of 2019.
7) Islam A, Halder S Bachar SC. Formulation and invitro evaluation of fast disintegrating tablet. 2011.
8) Pawan K Rawat, Prakash B Mote; Fast dissolving tablets of Pioglitazone Hcl by using various super disintegrant 2013, 3 (2), 74-79.
9) Mehta SR Kashyap AS, Diabetes mellitus in India; the modern scourage. Med J arm force Ind 2009;65(1);50-4.
10) Nikode S, Upadhya K Aplication and use of polymer 2016;5(7).
11) Gupta A, Mishra AK, Gupta V Recent trends of fast dissolving tablets and overview of formulation technology, Int J pharm and Bio arch 2010.
12) www.medicalnewstoday
13) Dillip Kumar Brahma; Dr. Neeraj Sharma. Design and evaluation of fast dissolving tablet by using novel techniques for effective treatment of diabetes, journel of critical reviews. ISSN 2394-5125 (7)5)2020.