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FORMULATION AND EVALUATION OF PIOGLITAZONE SUSTAINED RELEASE TABLET

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Abstract:

A sustained-release tablet formulation should ideally have a proper release profile insensitive to moderate changes in tablet hardness that is usually encountered in manufacturing. The matrix tablets were prepared by wet granulation method which is now days considered a cost effective and simple method of manufacturing. It is considered as an appropriate method for hygroscopic and thermolabile substances. Four formulations of different polymer percentages were formulated, (F1-F4).The formulated tablets were characterized by hardness, friability, thickness, weight variation and in vitro drug release. The formulated tablets had acceptable physicochemical characters. The quantity of pioglitazone present in the tablets and the release medium were estimated by a simple, rapid and validated UV method. The dissolution results show that increased amount of polymer resulted in reduced and extended drug release. This formulation may provide an alternative for oral controlled delivery of pioglitazone and be helpful in the future treatment of primary normoreactive types of inflammation.

Keywords: *Ibuprofen, HPMC, Wet granulation method, Dissolution*

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INTRODUCTION:

Oral administration of drugs is generally preferred, especially over parenteral administration. Oral products are produced in a more cost-effective manner in comparison with parenteral products and account for approximately 60% of all prescription products worldwide [1]. Sustained-release oral drug products are designed to slowly release the active ingredient over an extended time following administration and offer significant advantages over conventional orally administered products, including reduce side effects, increase safety and patient compliance by reducing the frequency of dosing and decreased drug plasma-concentration fluctuations [2, 3]. Matrix formulations of hydrophilicand/or hydrophobic polymers have been used to control the release of drugs [4, 5] and can be produced using conventional processing equipment. Formulation based on a hydrophilic matrix was chosen, since it is known to give robust formulae that can be manufactured by standard tabletting technology. In addition, it is possible to manufacture such formulations without using organic solvents; environmental risks associated with such solvents cause great concern and they often yield trace residues in finished products. To control and modulate drug release properties of tablets, retardant polymers including hydrophilic polymers such as HPMC and chitosan have been utilized in solid dosage forms. For these reterdants, hydrophilic polymers control drug release from tablets by hydrogelation [6, 7]. HPMC has been employed extensively as hydrophilic matrix former in oral controlled-release dosage forms for different drugs. Its popularity can be attributed to the polymer's non-toxic nature, small influence of processing variables on drug release, ease of compression, and its capability to accommodate high levels of drug loading, its ability to swell upon jellification once in contact with water [8-10]. The present work was envisaged to formulate and systematically evaluate In vitro performances of Pioglitazone for treatment of diabetes type-2, which have the ability to reside in the gastrointestinal tract for an extended period and can be utilized for controlled release of Pioglitazone maleate in oral administration. Also reduce the frequency of administration and to improve patient compliance by once daily sustained release formulation.

MATERIAL AND METHODS:

Material

Pioglitazone was procured from pharmaceutical company, India. HPMC K 15M was obtained from Central Drug House (CDR), Delhi. Lactose, Dicalcium phosphate, Talc was purchased from Loba chem Pvt. Ltd., Mumbai (India) and magnesium stearate was purchased from Moly chem. Mumbai (India). All other solvents and reagents were purchased from Merck (Germany) and were of analytical grade.

Methods

Preparation and evaluation of Pioglitazone Matrix Tablets

Pioglitazone matrix tablets each containing 30 mg of API were prepared by wet granulation employing 50% w/w HPMC K 15M as release controlling polymer. The composition of four formulations F1-F4 is shown in Table 1. The required quantities of drug, HPMC K 15M, PVP, PEG 6000 and diluents were weighed and mixed well. Then it was made into damp mass using a mixture of isopropyl alcohol and distilled water (1:1) as granulating fluid. The resulting damp masse was screened by passing them manually through sieve No. 12 and dried for 45 minutes at 60ºC in the oven and then screened through sieve No. 16. The granules were mixed with the required quantities of lubricants and then compressed into tablets on a multi station rotary tablet compression machine using 9 mm round flat punches [11].

Table 1: Formulation of Pioglitazone matrix tablets

Ingredients	Formulation composition (mg/tablet)			
	F1	F2	F3	F4
Pioglitazone HCL	30	30	30	30
Lactose	66	-	58	-
DCP	-	66	-	58
HPMC K 15 M(50%)	100	100	100	100
PVP (2% w/w)	-	-	4	4
PEG 6000(2%w/w)	-	-	4	4
Talc	2	2	2	2
Magnesium stearate	2	2	2	2
Total Weight	**200**	**200**	**200**	**200**

Characterization of tablets

Tablet thickness

The thickness of ten (10) tablets was determined using a vernier calliper and the mean of these readings was taken as the mean tablet thickness [12].

Tablet weight uniformity

Ten (10) tablets were weighed individually on electric balance from which the mean was calculated and the percentage deviations were determined [13].

Crushing strength

The crushing strength of the three (3) tablets was determined individually with the Monsanto hardness tester and the mean crushing strength was calculated [14].

Friability

The friability of the tablets was determined using the Roche friabilator. Five (5) tablets were weighed and put into the friabilator and set to rotate at 25 rounds per minute for about four (4) minutes [15]. The tablets were then removed and weighed again. The friability (F) is given by the formula; F= (1-W/Wo) ×100

Disintegration test

The prepared matrix tablets were subjected to disintegration test in distilled water, 0.1 N Hydrochloric acid and phosphate buffer of pH7.4 [16].

Drug content

Ten (10) tablets were accurately weighed and powdered. From that powder, equivalent to 50 mg of pioglitazone was weighed and taken into boiling test tube and extracted with 40ml of methanol. The methanolic extract was collected into 50 ml of volumetric flask and the volume was made up to 50 ml with methanol. The solution was subsequently diluted with 0.1N hydrochloric acid and assayed for drug content by UV spectrophotometer at a wavelength of 269 nm [17].

Dissolution rate studies

Drug release studies from different formulated tablets were performed by using USP Type II apparatus in 900 ml of 0.1 N HCl as the dissolution medium, with a rpm of 50 and the bath was maintained at a temperature of 37 ± 0.5° C. Samples were withdrawn at regular intervals of time and these were replaced with equivalent volume of the fresh dissolution media. The withdrawn samples were analyzed after suitable dilutions at a wavelength of 269 nm using UV spectrophotometer. The percentage drug release from the tablets was calculated from the absorbance values [17].

RESULTS AND DISCUSSION:

The major objective of the study was to design and evaluate pioglitazone matrix tablets for controlled release over a period of 24 hours. Four formulations of pioglitazone with selected combinations of diluents and solubilizers as per design were studied. Pioglitazone drug content of the tablets was within 100 ± 1% of the labeled content. Hardness was in the range 9- 10.4 kg/sq.cm. Friability was less than 0.8% in all the cases. The prepared matrix tablets were found to be non-disintegrating in water, 0.1 N Hydrochloric acid and phosphate buffer of pH7.4. Hence all the pioglitazone matrix tablets formulated by employing HPMC K 15M and selected combinations of the three factors were of good quality and fulfilled the official specifications with regard to drug content, hardness and friability. Thus all the prepared matrix tablets were suitable for oral controlled release. All the formulations of pioglitazone were subjected to in-vitro dissolution studies and corresponding results were shown in Figure 3. Drug release from the formulated matrix tablets was slow and spread over more than 24 hours. Drug release parameters of the matrix tablets were summarized in Table. Much variations were observed in the drug release characteristics of the matrix tablets. The release was dependent on the composition or factors involved in the formulation of matrix tablets. Drug release was only 68 – 71.23 % in 24 h in the case of formulations F1, F2 which were formulated employing lactose and DCP alone as diluents respectively. When the solubilizers, PVP and PEG 6000 were included in the matrix tablet formulations, the percent release was improved and the formulation F4 gave 99.04 % release in 24 hours. The results of drug release study indicated that lactose as diluent gave relatively higher release than DCP. This is due to the hydrophilic and water-soluble nature of lactose. PEG 6000 gave relatively higher release than PVP.

Table 2: Results of Evaluation of pioglitazone matrix tablets

Parameters	Formulation Parameters			
	F1	F2	F3	F4
Thickness (mm)	0.291	0.300	0.303	0.307
% Weight variation	0.220	0.223	0.230	0.222
Drug content (%)	95.00	99.92	97.80	101.33
Friability (%)	0.8	0.7	0.7	0.9
Hardness(kg/Sq.cm)	10.4	10	10	9
% Drug released at 24 hr	71.23	68.32	80.95	99.04

CONCLUSION:

The study was undertaken with the aim to evaluate the individual and combined effects of type of diluents (lactose / DCP) and solubilizers (PVP, PEG 6000) on drug release from pioglitazone matrix tablets formulated by employing HPMC K 15M as retarding agent. From the above results and discussion, it is concluded that pioglitazone-controlled release matrix tablets formulated by employing HPMC K 15M as rate controlling polymer at 50% w/w strength with DCP as diluent and solubilizers, PVP and PEG 6000 each at 2% strength, is considered as the best controlled release formulation of pioglitazone over a period of 24 hours i.e. for once a day administration.

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