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Formulation and evaluation of extended release Metformin tablet

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ABSTRACT

In the present work, extended release metformin tablet were designed for non-insulin dependent diabetes for better patient compliance by wet granulation method, HPMC K100M was used as polymer, Stearic acid and IPA as binder agent. Estimation of extended release metformin tablet in the prepared tablet formulations was carried out at 233 nm in phosphate buffer pH 6.8. The prepared formulations were further evaluated for hardness, friability, drug content uniformity, in vitro dissolution time and for in vitro drug release pattern in pH 6.8 phosphate buffer and short-term stability (at 40ºC/ 75% RH for 3 months) and drug-excipient interaction (IR spectroscopy) were studied. Short-term stability studies on the promising formulations indicated that there are no significant changes in drug content and invitro dissolution time.

Keywords: ER Metformin, Acrypol, IPA, HPMC K100M.

INTRODUCTION

Extended release is term used to identify drug delivery systems that are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. The blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced, because a more even blood level is maintained.

A less obvious advantage, implicit in the design of extended release forms, is that the total amount of drug administered can be reduced, thus maximizing availability with a minimum dose. In addition, better control of drug absorption can be attained, since the high blood level peaks that may be observed after administration of a dose of a high availability drug can be reduced by

formulation in an extended action form. The safety margin of high-potency drugs can be increased, and the incidence of both local and systemic adverse side effects can be reduced in sensitive patient.

Glucose is used by the body as fuel, and all people have glucose circulating in their blood. Diabetes, levels of blood glucose are higher than is needed, which is also known as hyperglycemia. If your blood glucose is not properly controlled, you may experience hypoglycemia (low blood glucose) or hyperglycemia (high blood glucose). High blood glucose can lead to serious problems with our heart, circulation and/or kidneys. It is very important to control high blood glucose whether or not you feel unwell. This really helps to avoid serious long-term health problems, which can involve the heart, eyes, circulation, and/or kidneys.

Advantages
The frequency of drug administration is reduced. Patient compliance can be improved, and drug administration can be made more convenient as well.

EXPERIMENTAL SECTION

Metformin was gifted sample from Dr Morepen Laboratories Parwanoo, and Acrypol, HPMC K100M, were gifted sample from Torrent Pharmaceutical Limited Ahmedabad.

Preparation of ER release Metformin tablet

Weigh Metformin HCl and Acrypol 974p and pass it from 60 # mesh sieve. Prepare paste of stearic acid by dissolving stearic acid into isopropyl alcohol. Granulate above blend by using rapid mixer granulator.

Table 1: Composition of Different Batches of ER release Metformin tablet

Sr.No.	Ingredients	FI	F2	F3	F4	F5	F6	F7
1	Metformin HCL	850	850	850	850	850	850	850
2	Acrypol	60	70	80	90	95	100	102
3	Stearic acid	72	75	78	81	83	84	85
4	IPA	q.s	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
5	HPMC K100M	162	150	145	140	135	132	129
6	Talc	5	6	7	7	6	6.5	6.8
7	Mg.stearte	27.2	27.2	27.2	27.2	27.2	27.2	27.2

Dry mixing : 5 Min, Binder addition: 1-2 min, Kneading : 30 sec .Dry the granules in fluid bed drayer using 40-45 C. till 1.62% LOD. Pass the granules through 40 # sieve. Weigh HPMC K 100 and talc. And pass through 40 # mesh. Mix it with Step-5 granules in cage blender for 10 min at 18 rpm.

Weigh Magnesium stearate and pass through 40 # mesh sieve and mix it with step-7 blend in cage blender for 3 min at 18 rpm. Compress the above blend using 14.5 punch at 16 station D-tooling compression machine

Evaluation of ER Metformin tablet

Physical Parameters (Shape, Size, Hardness & Friability)

The punches used to compress the 14.5 punch at 16 station D-tooling compression machine standard oval shaped. The shape and size of the tablets were found to be within the limit. The hardness of the tablets was found to be in the range of 6.9 $\pm$ 0.09 to 7.52 $\pm$ 0.29 Kg/ cm^2. It was within the range of monograph specification.

Thicknesses of the tablets were found to be in the range of 3.37 $\pm$ 0.02 to 3.41 $\pm$ 0.01 mm. The friability of the tablets was found to be less than 1% and it was within the range of standard specification.

Weight Variation and Drug Content

Weight variation test helps to check whether the tablet contain proper quantity of the drug. From each of the formulations ten tablets were randomly selected and weighed. The average weights of the tablets were found to be within the prescribed official limit. Drug content for each of the formulations were estimated. The drug content for all the batches were found to be in the range of 98.12 $\pm$ 0.21 to 100.89 $\pm$ 0.51%

Table 2: Invitro dissolution study

Apparatus	USP XXII Dissolution apparatus
Dissolution medium	Phosphate buffer pH- 6.8
Temperature	37 ± 0.5 ^{0} C
RPM	100
Vol. withdrawn and replaced	5 ml
λ max	233 nm
Blank solution	Phosphate buffer pH- 6.8
Duration of study	12 hrs
Volume of dissolution media	900 ml

In-vitro drug release studies were carried out using USP XXII dissolution apparatus type II (Electro lab, Mumbai, India) at 100 rpm. The dissolution medium consisted of 900 ml of pH 6.8 phosphate buffer, maintained at 37 $\pm$ 0.5^{0}C. The drug release at different time intervals was measured using an ultraviolet visible spectrophotometer (Labindia, Mumbai, India) at 233 nm. The study was performed in triplicate.

FTIR study

FTIR spectra of the selected formulation were taken and compared with the spectrum of pure drug. The characteristic peaks of drug were checked in the formulation spectra.

Stability study

Stability studies of pharmaceutical products were done as per ICH guide lines. These studies are designed to increase the rate of chemical or physical degradation of the drug substance or product by using exaggerated storage conditions.

Method: Selected formulations were stored at different storage conditions at elevated temperatures such as 25^{o}C± 2^{0}C / 60% ± 5% RH, 30^{0}C ± 2^{0}C / 65% ±5% RH and 40^{0}C ± 2^0 / 75% ± 5% RH for 90 days. The samples were withdrawn at intervals of fifteen days and checked for physical changes, hardness, friability, drug content and percentage drug release

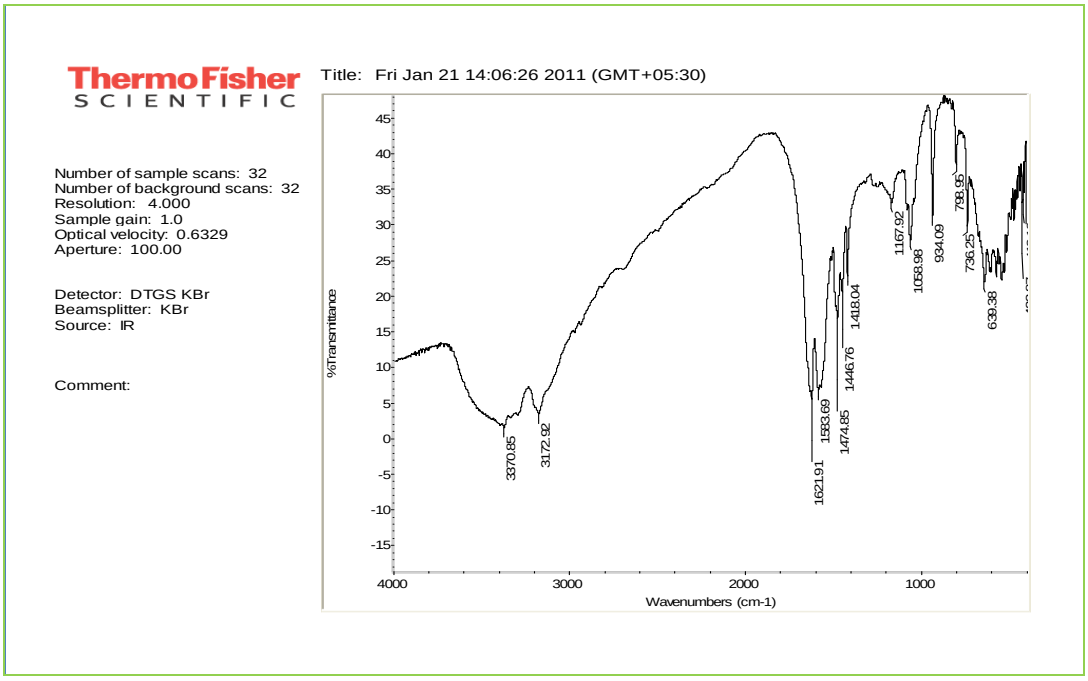

Fig. 1: FTIR spectra of Metformin

RESULTS AND DISCUSSION

Oral route of administration is the most widely accepted route of delivery due to the ease of administration, avoidance of pain and other risks of parenteral administration and has good patient compliance. The main advantage of the oral sustained release dosage form is that it maintains the therapeutic concentration over an extended period of time. Several new technologies have been developed to overcome the physicochemical and pharmacokinetic characteristic of drugs, while improving the patient compliance. One of these technologies is the matrix type of dosage forms.

Evaluation parameters for ER Metformin tablet:

Table 3: Physical appearance of optimized formulations after stability studies

Temp. and relative humidity	F-5 and F-10							Parameters
	Days							
	0	15	30	45	60	75	90	
25°C± 2°C / 60% ± 5% RH	No change							Physical appearance
35°C± 2°C / 65% ± 5% RH								
40°C± 2°C / 60% ± 5% RH								

Table 4: Results for the optimized formulation

Parameter	Formulation code		
	F1	F4	F7
Hardness	7.23 ± 0.72	7.46 ± 0.76	7.5 ± 0.10
Thickness	3.2	3.1	3.2
Friability	0.174	0.169	0.185
Percent drug content	93.55	96.75	97.75

CONCLUSION

The present study conclusively indicates that formulation F7 is very much promising very much drug release than formulation F2 and F4 in invitro dissolution study.

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