Acta Chimica & Pharmaceutica Indica

Acta Chim. Pharm. Indica: 3(4), 2013, 250-254
ISSN 2277-288X

EVALUATION OF RELEASE RETARDING EFFICIENCY OF CALCIUM STARCH – A NEW MODIFIED STARCH IN COMPARISON TO KNOWN POLYMERS

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(*Received : 14.09.2013; Accepted : 23.09.2013*)

ABSTRACT

The objective of the present study is to make a comparative evaluation of the drug release retarding efficiency of calcium starch, a new modified starch in comparison to known polymers namely hydroxyl propyl methyl cellulose (HPMC), sodium carboxy methyl cellulose (sodium CMC), ethyl cellulose and olibanum gum. Matrix tablets of gliclazide (30 mg) were prepared employing calcium starch and the other polymers at a polymer concentration of 5% and the tablets were evaluated. Gliclazide release from all the matrix tablets formulated with calcium starch and various other polymers was slow and spread over 12-24 hrs. Non-fickian diffusion was the release mechanism from all the matrix tablets prepared. Gliclazide release from the matrix tablets prepared employing sodium CMC, olibanum gum, ethyl cellulose and HPMC was relatively rapid and the release was complete in 12 hrs. Whereas gliclazide release was slow and spread over 24 hrs with calcium starch. The order of increasing release retarding effect with various polymers was sodium CMC < olibanum gum < Ethyl cellulose < HPMC < Calcium starch. Calcium starch is a better release retarding polymer than sodium CMC, olibanum gum, ethyl cellulose and HPMC for obtaining controlled release over 24 hrs.

Key words: Calcium starch, Controlled release, Gliclazide, Matrix tablets.

INTRODUCTION

In the last two decades, controlled-release dosage forms have made significant progress in terms of clinical efficacy and patient compliance. Drug release from the systems should be at a desired rate, predictable and reproducible. Polymers, which are used as release retarding materials in the design of controlled-release dosage forms play a vital role in controlling the delivery of drug from these dosage forms. Though a wide range of polymers and other release retarding materials are available, there is a continued need to develop new, safe and effective release retarding polymers for controlled release. Starch is a natural, biodegradable polymer and modified starches are reported as fillers, disintegrants and dry binders[1,2]. Calcium starch, a new modified starch developed in our laboratory was found suitable for controlling the release rate of different drugs (diclofenac/gliclazide/diltiazem HCl) from the matrix tablets[3]. In the present study the release retarding and rate controlling efficiency of calcium starch was compared with that of known polymers. Matrix tablets of gliclazide were prepared employing calcium starch and various other polymers and the tablets were evaluated for release characteristics. Gliclazide is an effective oral anti-diabetic agent that belongs to the sulfonylureas drug class. The recommended daily dosage of gliclazide is

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30-120 mg in divided doses 2 to 3 times a day. The drug causes gastro intestinal disturbances such as gastric pain, constipation, nausea and vomiting if present in larger concentration in g.i tract. Controlled release formulation is needed[4] for gliclazide for better control of blood glucose levels to prevent hypoglycemia and enhance clinical efficacy, to reduce g.i disturbances and to enhance patient compliance. A few controlled release formulations of gliclazide are available commercially.

EXPERIMENTAL

Materials and methods

Gliclazide is a gift sample from M/s. Ranbaxy Research Labs., Gurgaon, Haryana. Hydroxy propyl methyl cellulose (K15M, Colorcon), sodium carboxy methyl cellulose (sodium CMC having a viscosity of 1500-3000 cps of a 1% w/v solution at 25^{o}C, Loba Chemie) and olibanum gum (procured from M/s. Girijan Cooperative Corporation Ltd., Govt. of Andhra Pradesh, Visakhapatnam) and ethyl cellulose (viscosity of 5% w/w solution in 80 : 20 toluene: ethanol by weight at 25^{o}C in 18 cps, containing not less than 46.5% ethoxyl groups) were procured from commercial sources. All other materials used were of Pharmacopoeial grade.

Preparation of calcium starch

Potato starch (5 parts) was dispersed in purified water (50 parts) to form starch slurry. Sodium hydroxide (3 parts) was dissolved in water (30 parts) and the solution was added to starch slurry while mixing and mixing was continued for 30 minutes to form a thick gelatinized mass. The mass formed was added to 300 mL of calcium chloride (20% w/v) solution contained in a vessel while stirring at 1000 rpm with a medium duty stirrer. The stirring was continued for 1 hour to precipitate calcium starch formed. The calcium starch formed was collected by vacuum filtration, washed repeatedly with water and dried at 80^{o}C. The dried polymer was powdered and passed through mesh No. 100.

Preparation of tablets

Matrix tablets each containing 30 mg of gliclazide were prepared employing various polymers at 19 : 1 ratio of drug: polymer. The required quantities of medicament and matrix materials were mixed thoroughly in a mortar by following geometric dilution technique. The binder solution (mixture of alcohol and purified water at 1 : 1 ratio) was added and mixed thoroughly to form dough mass. The mass was passed through mesh no. 12 to obtain wet granules. The wet granules were dried at 60^{o} for 4 h. The dried granules were passed through mesh No. 16 to break the aggregates. The lubricants talc (2%) and magnesium stearate (2%) were passed through mesh No. 100 onto dry granules and blended in a closed polyethylene bag. The tablet granules were compressed into tablets on a rotary multi-station tablet punching machine (Cadmach Machinery Co. Pvt. Ltd., Mumbai) to a hardness of 8-10 Kg/sq.cm. using 9 mm round and flat punches.

Hardness of tablets was tested using a Monsanto Hardness Tester. Friability of tablets was determined in a Roche friabilator. Disintegration time was determined in a Thermonic Tablet Disintegration Test Machine using water, 0.1 N HCl and phosphate buffer of pH 7.4 as test fluids.

Estimation of gliclazide

Gliclazide content of the tablets was estimated by UV spectrophotometric method based on the measurement of absorbance at 229 nm in phosphate buffer of pH 7.4. The method was validated for linearity, precision and accuracy. The method obeyed Beer's Law in the concentration range 0-10 μg/mL. When a standard drug solution was assayed repeatedly (n = 6), the mean error (accuracy) and relative standard deviation (precision) were found to be 0.6 and 0.8%, respectively. No interference from the excipients used was observed.

Drug release study

Drug release from the matrix tablets prepared was studied using 8 station dissolution rate test apparatus (Lab India, Disso 2000) employing a paddle stirrer at 50 rpm and at 37 ± 1°C. Phosphate buffer of pH 7.4 (900 mL) was used as dissolution fluid. Samples of 5 mL of each were withdrawn at different time intervals over a period of 24 h. Each sample withdrawn was replaced with an equal amount of fresh dissolution medium. Samples were suitably diluted and assayed at 229 nm for gliclazide using a Shimadzu UV-150 double beam UV-spectrophotometer. The drug release experiments were conducted in triplicate.

Data analysis

Release data were analyzed as per zero order, first order, Higuchi[5] and Peppas[6] models to assess the drug release kinetics and mechanism from tablets.

RESULTS AND DISCUSSION

Calcium starch was synthesized by gelatinizing potato starch in the presence of sodium hydroxide and cross linking by treatment with calcium chloride. The calcium starch polymer formed was found to be fine and free flowing powder upon drying. It was insoluble in water, aqueous fluids of acidic and alkaline pHs. When tested for melting point the polymer charred at 220^{o}C.

Matrix tablets each containing 30 mg of gliclazide were prepared employing calcium starch (a new modified starch), sodium CMC, HPMC, ethyl cellulose and olibanum gum by conventional wet granulation method. A drug: polymer ratio of 19: 1 was used in all the cases. All the tablets prepared contained gliclazide within 100 ± 3% of the labeled claim. Hardness and friability of the tablets were within official (IP) and GMP limits. All the tablets were found to be non-disintegrating in water and aqueous fluids of acidic (1.2) and alkaline (7.4) pHs. As such the prepared tablets were of good quality with regard to drug content, hardness and friability. As the tablets formulated with various polymers were non-disintegrating with acidic and alkaline fluids, they are considered suitable for oral controlled release.

Gliclazide release from all the tablets was slow and spread over longer periods of time (Fig. 1). Analysis of the release data as per zero and first order kinetic models indicated that the drug release from the matrix tablets formulated employing various polymers followed zero order kinetics. The correlation coefficient (r) values were higher in the zero order model than in the first order model. When the release data were analyzed as per peppas equation, the release exponent ‘n’ was found in the range of 0.506-0.902 indicating non-fickian (anomalous) diffusion as the release mechanism from all the tablets prepared. Plots of percent released versus square root of time were found to be linear ($r > 0.867$) with all tablets prepared indicating that the drug release from the tablets was diffusion controlled. Gliclazide release parameters of various tablets prepared are summarized in Table 1.

Table 1: Release characteristics of gliclazide matrix tablets formulated employing various polymers

Formulation	Polymer	Release parameter			
		T_{50} (h)	T_{90} (h)	K_0 (mg/h)	‘n’ in Peppas equation
F1	Calcium starch	7.9	11.2	2.076	0.668
F2	HPMC	5.3	10.3	2.196	0.506
F3	Sodium CMC	3.1	5.3	4.431	0.882
F4	Olibanum gum	4.7	6.9	3.45	0.902
F5	Ethyl cellulose	4.2	7.0	3.099	0.722

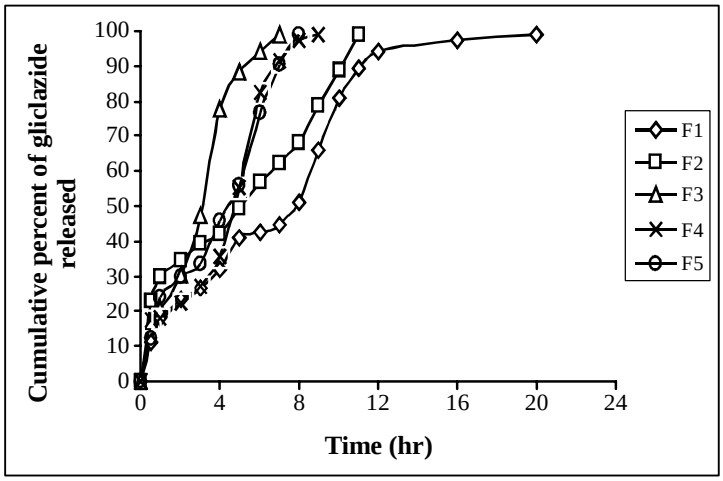

Fig. 1: Release profiles of gliclazide matrix tablets formulated

Employing various polymers

All the release parameters indicated variations or differences in drug release from the tablets formulated with different polymers though all the polymers were used at the same strength i.e. 5% in the formula. The drug release was relatively rapid in the case of sodium CMC, olibanum gum, ethyl cellulose and HPMC and the release was completed within 8-12 hrs with these tablets. Whereas in the case of calcium starch the release was slow, gradual and spread over 24 hrs. The order of increasing release retarding effect with various polymers was sodium CMC < olibanum gum < Ethyl cellulose < HPMC < Calcium starch. Thus calcium starch was found to be a better release-retarding polymer than sodium CMC, olibanum gum, ethyl cellulose and HPMC and could be used in the formulation of controlled release matrix tablets for 24 hrs.

CONCLUSIONS

(i) Gliclazide release from all the matrix tablets formulated with calcium starch and other polymers was slow and spread over 12-24 hrs.

(ii) Non-fickian diffusion was the release mechanism from all the matrix tablets prepared with various polymers.

(iii) Gliclazide release from the matrix tablets prepared employing sodium CMC, olibanum gum, ethyl cellulose and HPMC was relatively rapid and the release was complete in 12 hrs. Whereas gliclazide release was slow and spread over 24 hrs with calcium starch.

(iv) The order of increasing release retarding effect with various polymers was sodium CMC < Olibanum gum < Ethyl cellulose < HPMC < Calcium starch.

(v) Calcium starch is a better release retarding polymer than sodium CMC, olibanum gum, ethyl cellulose and HPMC for obtaining controlled release over 24 hrs.

REFERENCES

1. M. K. Kottke, H. R. Chuech and C. T. Rhodes, Drug Dev. Ind. Pharm., **18**, 2207 (1992).

2. J. Herman and J. P. Remon, Int. J. Pharm., **63**, 201 (1990).

3. K. P. R. Chowdary, P. Tripura Sundari and N. Neelima, Asian J. Chemistry (in press).

4. C. Kilo, J. Dudley and B. Kalb, Diabetes Res. Clin. Pract., **14**, S79 (1991).
5. T. Higuchi, J. Pharm. Sci., **52**, 1145 (1963)
6. P. L. Ritger and N. A. Peppas, J. Control. Release, **5**, 37 (1987).