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Research Article

EVALUATION OF RELEASE RETARDING EFFICIENCY OF DIFFERENT POLYMERS ON DILTIAZEM HCL CR TABLETS

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ABSTRACT

Calcium starch a new modified starch was found suitable for controlling the release rate of Diltiazem from the matrix tablets. The release retarding and the rate controlling efficiency of calcium starch was compared with that of known polymers. Matrix tablets of Diltiazem were prepared employing calcium starch and various other polymers and a comparative evaluation of their release characteristics was made. The results are presented in this chapter.

Keywords: calcium starch, diltiazem tablets, polymers, matrix tablets.

INTRODUCTION

Diltiazem is in a group of drugs called calcium channel blockers. It works by relaxing the muscles of your heart and blood vessels. Diltiazem is used to treat hypertension (high blood pressure), angina (chest pain), and certain heart rhythm disorders. Diltiazem may also be used for purposes not listed in this medication guide. Do not use diltiazem if you have certain heart conditions such as "sick sinus syndrome" or "AV block" (unless you have a pacemaker), low blood pressure, or if you have recently had a heart attack. Before taking diltiazem, tell your doctor if you have kidney disease, liver disease, or congestive heart failure. Diltiazem may impair your thinking or reactions. Be careful if you drive or do anything that requires you to be alert. Do not stop taking this medication without first talking to your doctor. If you stop taking diltiazem suddenly, your condition may become worse. Diltiazem may be only part of a complete program of treatment that also includes diet, exercise, and other medications. Follow your diet, medication, and exercise routines very closely. If you are being treated for high blood pressure, keep using diltiazem even if you feel well. High blood pressure often has no symptoms.

EXPERIMENTAL

Materials

Diltiazem HCL is a gift sample from M/s. Micro labs Ltd., Pondicherry. 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 25º C, Loba Chemie), methyle cellulose (Loba Chemie), sodium alginate (Loba Chemie) and gelatin (Loba Chemie) were procured from commercial sources. All other materials used were of pharmacopoeial grade.

Preparation of tablets

Matrix tablets each containing 90mg of Diltiazem were prepared employing various polymers at 17: 3 ratio of drug: polymer (i. e. at 15% polymer concentration in the formula). The required quantities of medicament and matrix materials were mixed thoroughly in a mortar by following geometric dilution technique. The binder solution (mixer 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 60º 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 on to dry granules and

blended in a closed polyethylene bag. The tablet granules were compressed in to tablets on a rotary multi-station tablet punching machine (Cadmach Machinery Co. Pvt. Ltd., Mumbai) to a hardness of 8-10kg/sq. cm using 9mm round and flat punches.

Estimation of Diltiazem in Tablets

Five tablets were accurately weighed and powdered. Tablet powder equivalent to 50mg of medicament was taken into oiling test tube and extracted with 4 x 10 ml quantities of methanol. The methanolic extracts were collected into 50 ml volumetric flask and the volume was made up to 50 ml with methanol. The solution was subsequently diluted and assayed for the drug content by method discussed earlier.

Hardness

Hardness of the tablets was tested using a Monsanto Hardness Tester.

Friability

Friability of the tablets was determined in a Roche Friabilator.

Disintegration time

Disintegration times were determined in thermonic tablets Disintegration test Machine using dissolution Fluids 0.1 N HCL, Dist. Water, pH 7.4 phosphate buffer.

Drug release study

Drug release from the matrix tablets prepared was studied using 6 station dissolution rate test apparatus (Electro lab) employing a paddle stirrer at50 rpm and at37±1º C distilled water (900ml) was used as dissolution fluid samples of 5ml of each were with drawn at different time intervals over a period of 24h each sample withdrawn was replaced with equal amount of fresh dissolution medium. Samples were suitably diluted and assayed at240 nm for diltiazem using an Elico double beam UV-spectrophotometer. For comparison, diltiazem release from dilzem SR and DMT 90 SR tablets (commercial) was also studied the drug release experiments were conducted in triplicate.

RESULTS

Release data were analyzed as per zero order, 1st order, Higuchi [1] and peppas [2] equation models to assess the drug release kinetics and mechanism from tablets.

Table 1: Formulation of Diltiazem CR Tablets Prepared Employing Various Polymers

Ingredients (mg/tablet)	Formulation				
	CR F7	CR F8	CR F9	CR F10	CR F11
Diltiazem	90	90	90	90	90
HPMC	33	-	-	-	-
Methyl Cellulose	-	33	-	-	-
Sodium CMC	-	-	33	-	-
Sodium Alginate	-	-	-	33	-
Gelatin	-	-	-	-	33
Lactose	88.2	88.2	88.2	88.2	88.2
Talc	4.4	4.4	4.4	4.4	4.4
Magnesium Stearate	4.4	4.4	4.4	4.4	4.4
Alcohol-Water(1:1)	q.s	q.s	q.s	q.s	q.s
Weight of the Tablet (mg)	220	220	220	220	220

Table 2: Drug Content, Hardness, Friability and Disintegration Time of the Diltiazem CR Tablets Prepared

Formulation	Diltiazem Content (mg/tab)	Friability	Disintegration Time	Hardness(kg/Sq.cm)
CR F7	90.6	0.2	Non-Disintegrating	9.5
CR F8	90.3	0.2	Non-Disintegrating	10.0
CR F9	89.7	0.1	Non-Disintegrating	8
CR F10	89.5	0.2	Non-Disintegrating	9
CR F11	89.9	0.3	Non-Disintegrating	8.5

Table 3: Drug release profiles of diltiazem CR tablets prepared employing various polymers

Time(hrs)	cumulative percent of diltiazwm released(x±s.d)					
	CR F3	CR F7	CR F8	CR F9	CR F10	CR F11
0	0	0	0	0	0	0
0.5	25.23±0.25	20.51±0.05	47.8±0.02	18.67±0.25	20.53±0.76	92.61±0.05
1	30.91±0.31	29.75±0.74	87.2±0.05	26.51±0.31	26.17±0.21	97.93±0.03
2	43.46±0.34	42.66±0.49	99.1±0.13	37.86±0.34	36.92±0.22	100
3	57.61±0.46	56.24±0.31	100	51.58±0.46	48.02±0.33	
4	64.75±0.56	70.55±0.03		61.51±0.56	57.50±0.04	
5	70.04±0.68	75.14±0.10		72.50±0.68	64.48±0.07	
6	76.54±0.76	82.76±0.74		83.07±0.44	71.26±0.16	
8	80.05±0.89	96.35±0.50		96.15±0.18	86.21±0.02	
10	87±0.11	99.11±0.23		98.81±0.33	94.58±0.57	
12	87.25±1.32	100		100	98.58±0.51	
16	93.68±1.33				100	
20	100					
24						

Table 4: Correlation coefficient(r) values in the analysis of release data as per zero order,first order, higuchi and peppas equation models

Formulation	r values			
	zero order	first order	higuchi	peppas
CR F7	0.9260	0.9660	0.9895	0.9868
CR F8	0.9107	0.9935	0.9811	0.9510
CR F9	0.9425	0.9668	0.9899	0.9899
CR F10	0.9262	0.9678	0.9899	0.9900
CR F11	0.7178	0.9043	0.8970	1

Matrix tablets each containing 90mg of diltiazem ere prepared employing calcium starch (a new modified starch), sodium cmc, HPMC, methyl cellulose, sodium alginate and gelatin by conventional wet granulation method. A drug: polymer ratio of 17:3 was used in all the cases. All the tablets prepared contained diltiazem within 100±3% of the labeled claim. Hardness and friability of the tablets were with in official (IP) and GMP limits. All the tablets were found to be non – disintegrating in water and aqueous fluid 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.

Diltiazem release parameters of various tablets prepared are summarized in table 14.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. 15% in the formula. The drug release was relatively rapid in the case of gelatin, methyl cellulose and sodium alginate and calcium starch. the order of increasing release retarding effect with various polymer was calcium starch>sodium alginate > HPMC> sodium CMC> methyl cellulose >gelatin. Thus calcium starch was found to be a better release retarding polymer than others. Calcium starch could be used in formulation of controlled release tablets of diltiazem for 24 hours i.e. once daily administration

CONCLUSION

Calcium starch, a new modified starch is a better release – retarding polymer than methyl cellulose, sodium cmc, HPMC, sodium alginate, and gelatin. Calcium starch could be used in the formulation of controlled release tablets of diltiazem for 24 hours i.e. .once daily administration.

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