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FORMULATION STUDIES ON CEFACLOR TABLETS : EFFECT OF BINDERS

S. A. SUNIL[*] and V. G. SAHEB

University College of Pharmaceutical Sciences, Andhra University,
VISAKHAPATNAM – 530 003 (A.P.) INDIA

ABSTRACT

Tablets are the most preferable dosage forms for oral use. Cefaclor tablets are not available in the market and no work was reported on cefaclor tablets. The objective of the present study is to develop tablet formulations of cefaclor. Binder is a critical formulation additive in tablets, which has profound influence on tablet qualities and dissolution of the medicament ultimately affecting the bioavailability. The effect of seven commonly used binders on the qualities of cefaclor tablets prepared by wet granulation method was evaluated and results are reported. The efficiency of different binders on the dissolution rate of cefaclor and kinetics of dissolution of cefaclor from formulated tablets was studied.

Key words: Cefaclor tablets, Binder, Wet granulation.

INTRODUCTION

The oral route of drug administration is the most convenient and commonly used method of drug delivery. Even though, there are lots of formulations available and tablets are the most preferable dosage forms for oral use. Binder[1,2] is a critical formulation additive in tablets, which has profound influence on tablet qualities and dissolution of the medicament. Binders play a critical role in manufacturing of tablets by affecting the drug release. The drug release from the tablets also depends on the binder used in the formulation. Cefaclor[3] is an antibacterial drug and is more popular in otitis media, sinusitis and urinary tract infections. Cefaclor tablets are not available and no work was reported on these tablets.

In the present work, studies were conducted on the formulation development of cefaclor tablets. The effect of seven binders on the tablet qualities and dissolution rate of cefaclor from the tablets prepared by wet granulation method were studied. Tablets each

[*]Author for correspondence; E-mail: sunilsonga@gmail.com

containing 250 mg of cefaclor were prepared employing seven different binders namely acacia, sucrose, starch paste, HPMC, PVP, sodium CMC and gelatin. The tablets were evaluated for physicochemical parameters like contents of active ingredient, hardness, friability, disintegration time and dissolution rate.

EXPERIMENTAL

Materials

Cefaclor was a gift sample from M/s Aerobridge. Potato starch from M/s Ozone International, Acacia I.P. from Karnataka Fine Chem., and all other materials were procured from commercial sources and were of pharmacopoeial grade.

Methods

Preparation of tablets

Tablets of cefaclor were prepared by conventional wet granulation method. The required quantities of cefaclor and excipients were mixed thoroughly in a dry mortar by following geometric dilution technique. The binder solution was added and mixed thoroughly to form dough mass. Sodium CMC and HPMC were used as dry binders, which were mixed directly with the drug and other binders were made in solution form with water as granulating agent. The dough mass formed by granulation was passed through mesh No. 14 to obtain the wet granules. These wet granules were dried in an hot air oven at 60°C for 30 minutes to obtain the dried granules, which were later passed through mesh No. 16 so as to obtain free flowing granules. Dried granules were lubricated by using lubricants passed through mesh No. 60 for 2 minutes in a closed polyethylene bag. The tablet granules were compressed into tablets on a single punch tablets compression machine to hardness of 5 – 6 kg/sq.cms.

Evaluation of tablets

Hardness of the tablets was evaluated using a Monsanto hardness tester. Friability of the tablets was determined in a Roche friabilator. Disintegration time of the tablets was determined using a thermonic tablet disintegration test machine using water as medium.

Estimation of cefaclor

An ultraviolet (UV) spectrophotometric method based on the measurement of

absorbance at 264 nm in water was used for the estimation of cefaclor. The method obeyed Beer-Lambert's law in the concentration range of 1-10 µm/mL. When a standard drug solution was assayed repeatedly (n = 6), the relative error (accuracy) and coefficient of variation (precision) were found to be 0.60% and 1.2%, respectively. No interference from the excipients used was observed.

Drug release study

Drug release from the tablets was studied using 8- station dissolution rate test apparatus (Labindia, Disso 2000) employing a paddle stirrer at 50 rpm and at temperature of $37^{o} \pm 0.5^{0}$C. Distilled water (900 mL) was used as dissolution fluid. A 5 mL aliquot of dissolution medium was withdrawn through a filter (0.45 µm) at different time intervals and replaced with fresh dissolution medium so as to maintain sink conditions. Samples were analyzed spectrophotometrically by measuring absorbance at 264 nm. All drug release experiments were conducted in triplicate.

Data analysis

Drug release data were analyzed as per zero order and first order models to assess drug release kinetics and mechanism from the tablets.

RESULTS AND DISCUSSION

Tablets each containing 250 mg of cefaclor were prepared employing seven binders namely acacia, sucrose, starch paste, HPMC, PVP, sodium CMC and gelatin. All the binders were used at a concentration of 3% in the formula.

Hardness of the tablets was found to be in the range of 3-6 kg/ sq.cm. Percent weight loss in the friability test was found to be less than 0.25% in all the cases. All the tablets contained cefaclor within 100 ± 5% of the labeled amount. All the tablets were also disintegrated within 15 min. fulfilling the official (I.P.) requirement for disintegration test. As such, all the batches of the tablets prepared, were of good quality with regard to hardness, friability, drug content and disintegration.

Dissolution rate of cefaclor from the tablets was studied in water. The dissolution profiles were shown in Table 2. Drug release of cefaclor from tablets prepared by employing different binders was nearly completed in 60 min. Dissolution was dependent on the binder

employed. Drug release of cefaclor from all the tablets followed 1st order kinetics[4] (r > 0.957).

Table 1: Formula for the preparation of cefaclor tablets

Ingredient/mg. of tablet	F_1	F_2	F_3	F_4	F_5	F_6	F_7
Cefaclor	250	250	250	250	250	250	250
Lactose	150	150	150	150	150	150	150
Potato starch	60	60	60	60	60	60	60
Acacia	12	-	-	-	-	-	-
Sucrose	-	12	-	-	-	-	-
Starch paste	-	-	12	-	-	-	-
HPMC	-	-	-	12	-	-	-
PVP	-	-	-	-	12	-	-
Sodium CMC	-	-	-	-	-	12	-
Gelatin	-	-	-	-	-	-	12
Talc	8	8	8	8	8	8	8
Magnesium stearate	8	8	8	8	8	8	8

HPMC- hydroxyl propyl methyl cellulose, sodium CMC- sodium corboxy methyl cellulose.

The first order dissolution rate constant (k_1) was calculated from the slope of the linear regression. The dissolution rates (k_1) are given in Table 2. Gelatin, starch paste and sucrose gave relatively rapid dissolution of cefaclor, when compared to other binders. The order of increasing dissolution rate observed with various binders was -

Gelatin > Sucrose > HPMC > PVP > Sodium CMC > Acacia

Thus, the binder used has significant influence on the dissolution rate of cefaclor from the tablets.

Table 2: Dissolution parameters of cefaclor tablets prepared employing various binders

Formulation	Dissolution parameters		
	T_{50} (min)	% Drug released in 30 min	k_1 (hr^{-1})
F_1	33	43.62	0.024
F_2	27	48.06	0.035
F_3	25	52.12	0.037
F_4	30	45.04	0.029
F_5	25	48.11	0.028
F_6	27	45.68	0.028
F_7	26	55.45	0.039

CONCLUSIONS

Cefaclor tablets are not available and no work was reported on these tablets. In the present work, studies were conducted on the formulation development of cefaclor tablets. The effect of seven binders on the tablet qualities and dissolution rate of cefaclor from the tablets made by wet granulation method were studied.

Tablets each containing 250 mg of cefaclor were prepared employing seven binders namely acacia, sucrose, starch paste, HPMC, PVP, sodium CMC and gelatin. The tablets were evaluated for contents of active ingredient, hardness, friability, disintegration time and dissolution rate.

The following are the conclusions drawn from the results –

(i) All the batches of tablets prepared were of good quality and fulfilled the official GMP[5] requirements with regard to drug content, hardness, friability and disintegration time.

(ii) Cefaclor dissolution from the tablets was nearly complete with in 60 min.

(iii) Cefaclor dissolution from the tablets followed first order kinetics.

(iv) Dissolution rate was different with different binders.

(v) The order of increasing dissolution rate observed with various binders was –

Gelatin > Starch paste > Sucrose > HPMC > PVP > Sodium CMC > Acacia

Thus the present study indicates that the binder used has significant influence in the dissolution rate of cefaclor from the tablets. Gelatin, starch paste and sucrose were found to be good binders for cefaclor tablets.

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