Asian Journal of Chemistry Vol. 21, No. 8 (2009), 5847-5850

Formulation and Evaluation of Piroxicam and Aceclofenac Tablets Employing Prosolve by Direct Compression Method

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Prosolve, a new directly compressible vehicle consists of microcrystalline cellulose (98 %) and colloidal silicon dioxide (2 %). Piroxicam (20 mg) and aceclofenac (100 mg) tablets were formulated employing prosolve and three disintegrants namely potato starch, primogel and croscarmellose sodium by direct compression method with a view to enhance their dissolution rate. In the micromeritic evaluation prosolve and its blends with other tablet ingredients exhibited excellent to good flow needed for direct compression. All the tablets formulated employing prosolve fulfilled the official (IP) and GMP standards with regard to various tablet characters. These tablets also gave 2 to 5 fold increase in the dissolution rate when compared to commercial tablets. Among the three disintegrants primogel gave higher dissolution rates with both piroxicam and aceclofenac.

Key Words: Prosolve, Piroxicam, Aceclofenac, Direct compression method.

INTRODUCTION

Great interest in direct compression as a method of manufacture of tablets has been evident in recent years and this has resulted in a wide range of direct compression tablet formulations being introduced. Several directly compressible vehicles with good free flow and compaction properties have been developed in recent years. Prosolve is one such recently developed directly compressible vehicle. Prosolve, also known as silicified microcrystalline cellulose consists of microcrystalline cellulose (98 %) and colloidal silicon dioxide (2 %). Prosolve has improved compaction properties in both wet granulation and direct compression methods compared to conventional microcrystalline cellulose[1,2]. The objective of the present study is to formulate and evaluate piroxicam and aceclofenac tablets employing prosolve by direct compression method for enhancing their dissolution rates. Piroxicam and aceclofenac are widely prescribed non-steroidal antiinflammatory and analgesic drugs. They are practically insoluble in water and aqueous fluids. The poor aqueous solubility of these drugs give rise to difficulties in the formulation of solid dosage forms such as tablets and leads to low and variable dissolution rate and bioavailability. Direct compression method employing prosolve was tried to enhance the dissolution rate of piroxicam and aceclofenac.

EXPERIMENTAL

Piroxicam and aceclofenac were gift samples from M/S Aristo Pharmaceuticals Ltd., Mumbai. Prosolve was a gift sample from M/s. Orchid Health Care Ltd., Chennai. Potato starch, primogel and croscarmellose sodium were procured from commercial sources. All other materials used were of pharmacopoeial grade.

Preparation of tablets: Piroxicam (20 mg) and aceclofenac (100 mg) tablets were prepared employing prosolve by direct compression method as per the formulae given in Table-1. All the ingredients were blended thoroughly in a closed high density polyethylene bottle and were directly compressed into tablets to a hardness of 6-8 kg/sq.cm on a 16-station Cadmach tablet machine using 9 mm round and flat punches.

All the tablets prepared were evaluated for drug content, hardness, friability, disintegration time and dissolution rate.

TABLE-1
FORMULAE OF TABLETS PREPARED EMPLOYING PROSOLVE

Ingredient (mg/tablet)	Formulation					
	F1	F2	F3	F4	F5	F6
Piroxicam	20	20	20	–	–	–
Aceclofenac	–	–	–	100	100	100
Potato starch	30	–	–	30	–	–
Primogel	–	10	–	–	10	–
Croscaramellose sodium	–	–	10	–	–	10
Lactose	–	20	20	–	–	–
Prosolve	142	142	142	100	120	120
Talc	4	4	4	4	4	4
Magnesium stearate	4	4	4	4	4	4

Hardness of the tablets was tested by using a Monsanto Hardness Tester. Friability of the tablets was determined in a Roche Friabilator. Disintegration time was determined in a Thermonic Tablet Disintegration Test Machine using water as test fluid.

Estimation of drug content: Drug content of the prepared tablets was estimated by UV spectrophotometric method based on the measurement of absorbance at 333 nm in the case of piroxicam tablets and at 275 nm in the case of aceclofenac tablets. The methods were validated for linearity, precision and accuracy. The methods obeyed Beer's law in the concentration range 1-10 mg/mL. The accuracy and precision of the methods were in the range of 0.4-0.8 %. No interference from the excipients used was observed.

Dissolution rate study: Dissolution rate of drug from the prepared and commercial tablets was studied using 8-station Dissolution rate test apparatus (LABINDIA, DISSO 2000) employing a paddle stirrer at 50 rpm and 37 ± 1 ºC. Hydrochloric acid (0.1 N) and phosphate buffer of pH 7.4 were used as dissolution fluid (900 mL), respectively for piroxicam and aceclofenac tablets. Samples of 5 mL each

were withdrawn at 5, 10, 20, 30, 40, 50 and 60 min and assayed at 333 nm in the case of piroxicam and 275 nm in the case of aceclofenac using Shimadzu UV-150 double beam UV-spectrophotometer. Each sample withdrawn was replaced with an equal amount of fresh dissolution medium. For comparison, dissolution rate of commercial tablets in each case was also studied. Dissolution rate experiments were conducted in triplicate.

Dissolution data analysis: Dissolution data were analyzed as per zero and first order kinetic models. Dissolution efficiency (DE30) values were calculated as described by Khan[3]. T50 (time for 50 % dissolution) values were recorded from the percent dissolved *vs.* time plots.

Micromeritic evaluation: The flow characteristics of tablet granulations (*i.e.*, blend of powders before compression) were assessed by measuring the angle of repose by fixed funnel method and Carr's compressibility index by standard tapping method.

RESULTS AND DISCUSSION

Piroxicam (20 mg) and aceclofenac (100 mg) tablets were formulated employing prosolve, a new directly compressible vehicle by direct compression method. Angle of repose and compressibility index of prosolve as such and tablet granulations before compression were measured to assess their suitability for direct compression. The results of micromeritic evaluation are given in Table-2. Angle of repose less than 250 indicates excellent flow. Carr's compressibility index values in the range 5-15 indicates excellent flow and in the range 16-21 indicates fair to good flow. Angle of repose value of all the products tested were < 250 indicating excellent flow of prosolve and all the tablet granulations tested. Whereas compressibility index values of the products tested were in the range 9-21 % indicating fair to good flow. As prosolve and the tablet granulations (the blend of prosolve and other ingredients) exhibited excellent to good flow characteristics, they are considered suitable for direct compression method.

TABLE-2
MICROMERITIC PROPERTIES OF PROSOLVE AND ITS TABLET GRANULATIONS

Formulation	Angle of repose (º)	Compressibility index (%)
Prosolve	18.34	15.8
F1	24.04	9.1
F2	19.98	14.9
F3	23.96	20.0
F4	24.24	20.0
F5	21.24	17.5
F6	20.55	16.7

The hardness of the tablets prepared was in the range of 6-8 kg/sq.cm. Weight loss in the friability test was less than 1.0 % in all the cases. The tablets contained drug within 100 ± 3 % of the labeled claim. All the formulated tablets of piroxicam

and aceclofenac disintegrated within 15 s. As such all the tablets formulated employing prosolve are of good quality fulfilling the official (I.P.) and GMP requirements with regard to drug content, hardness, friability and disintegration time.

Dissolution parameters of the formulated tablets are summarized in Table-3. All the tablets formulated employing prosolve gave rapid and higher dissolution than the commercial products with both piroxicam and aceclofenac. Drug dissolution from the tablets followed first order kinetics. A 2 to 5 fold increase in the dissolution rate (K_1) was observed with formulated tablets when compared to commercial tablets. Three disintegrants namely potato starch, primogel and croscarmellose sodium were used in each case. With both piroxicam and aceclofenac, tablets formulated employing primogel gave higher dissolution rates than those formulated with potato starch and croscarmellose sodium. The order of performance of disintegrants in enhancing the dissolution rate was primogel > croscarmellose sodium > potato starch with both piroxicam and aceclofenac.

TABLE-3
DISSOLUTION PARAMETERS OF TABLETS
FORMULATED EMPLOYING PROSOLVE

Formulation	D.T. (s)	T_{50} (min)	DE_{30} (%)	K_1 (min^{-1})
F1	10	8.5	61.52	0.0506
F2	7	4.5	68.03	0.0640
F3	6	4.0	70.52	0.0518
Piroxicam Commercial	19	12.0	50.30	0.0308
F4	18	4.5	60.90	0.0616
F5	14	4.5	57.62	0.0827
F6	14	4.0	65.23	0.0782
Aceclofenac Commercial	21	8.0	53.38	0.0164

Conclusion

(1) Prosolve, a new directly compressible vehicle and blends of prosolve and other tablet ingredients exhibited excellent to good flow needed for direct compression. (2) Piroxicam and aceclofenac tablets of good quality fulfilling official (I.P.) and GMP specifications could be prepared by direct compression method employing prosolve. (3) Tablets formulated employing prosolve gave 2 to 5 fold increase in the dissolution rate with both piroxicam and aceclofenac. (4) Primogel gave higher dissolution rates than potato starch and croscarmellose sodium.

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(*Received*: 18 March 2008; *Accepted*: 18 May 2009) AJC-7548