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FORMULATION AND EVALUATION OF PIROXICAM AND CELECOXIB TABLETS EMPLOYING PROSOLVE BY DIRECT COMPRESSION METHOD

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ABSTRACT

Prosolve, a new directly compressible vehicle consists of microcrystalline cellulose (98 %) and colloidal silicon dioxide (2 %). Piroxicam (20 mg) and celecoxib (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 (I.P) and GMP standards with regard to various tablet characters. These tablets also gave 2 to 3 fold increase in the dissolution rate, when compared to commercial tablets. Among the three disintegrants, primogel gave higher dissolution rates with both piroxicam and celecoxib.

Key words: Prosolve, Piroxicam, Celecoxib, Direct compression

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

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objective of the present study is to formulate and evaluate piroxicam and celecoxib tablets employing Prosolve by direct compression method for enhancing their dissolution rates. Piroxicam and celecoxib are widely prescribed non-steroidal anti-inflammatory 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 celecoxib.

EXPERIMANTAL

Materials and methods

Materials

Piroxicam and celecoxib 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.

Methods

Preparation of tablets

Piroxicam (20 mg) and celecoxib (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 HDPE 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.

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.

Table 1: Formulae of tablets prepared employing Prosolve

Ingredient (mg/tablet)	Formulation					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
Piroxicam	20	20	20	--	--	--
Celecoxib	--	--	--	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

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 254 nm in the case of celecoxib tablets. The methods were validated for linearity, precision and accuracy. The methods obeyed Beer's law in the concentration range 1 – 10 μg/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^{0}C. Hydrochloric acid (0.1 N) and water containing 1 % SLS were used as dissolution fluid (900 mL), respectively for piroxicam and celecoxib tablets. Samples of 5 mL each were withdrawn at 5, 10, 20, 30, 40, 50 and 60 minutes and assayed at 333 nm in the case of piroxicam and 254 nm in the case of celecoxib 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 analysed as per zero and first order kinetic models. Dissolution efficiency (DE_{30}) values were calculated as described Khan[3]. T_{50} (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 celecoxib (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.

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
F4	17.74	18
F5	21.8	20.3
F6	22.92	22.3

Angle of repose less than 25^0 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 values of all the products tested were < 25^0 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.

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 celecoxib disintegrated within 15 seconds. 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 celecoxib. Drug dissolution from the tablets followed first order kinetics.

Table 3: Dissolution parameters of tablets formulated employing Prosolve

Formulation	D.T. (sec)	T_{50} (min)	DE_{30} (%)	K_1 (min^{-1})
F1	10	8.5	61.52	0.0506
F2	7	4.5	68.03	0.064
F3	6	4	70.52	0.0518
Piroxicam commercial	19	12	50.3	0.0308
F4	14	21	41.15	0.0139
F5	11	20	43.34	0.0145
F6	10	36.5	37.77	0.0103
Celecoxib commercial	72	>60	11.53	0.0051

A 2 to 3 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

celecoxib, tablets formulated employing primogel gave higher dissolution rates than those formulated with potato starch and croscarmellose sodium.

CONCLUSIONS

(i) Prosolve, a new directly compressible vehicle and blends of Prosolve and other tablet ingredients exhibited excellent to good flow needed for direct compression.

(ii) Piroxicam and celecoxib tablets of good quality fulfilling official (I.P) and GMP specifications could be prepared by direct compression method employing Prosolve.

(iii) Tablets formulated employing Prosolve gave 2 to 3 fold increase in the dissolution rate with both piroxicam and celecoxib.

(iv) Primogel gave higher dissolution rates than potato starch and croscarmellose sodium.

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