COMPARATIVE STUDY OF DISINTEGRANTS IN FORMULATION OF CEFADROXIL DISPERSIBLE TABLETS

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Summary

Dispersible cefadroxil tablets were prepared employing three disintegrants, croscarmellose sodium, crospovidone and sodium starch glycolate in two separate quantities separately along with microcrystalline cellulose. Direct compression method was followed for all formulations. Thus six formulations (F1-F6) were prepared and compared among themselves and with one marketed product (MP) in evaluations. Evaluations for precompressional parameters like angle of repose, compressibility and hardness ratio were done. Evaluations for post compressional parameters like weight variation, thickness, hardness, friability, disintegration time, dispersion time, wetting time, assay and dissolution study were carried out. Formulation containing 26.25 mg of croscarmellose sodium per tablet was found suitable and better than marketed and formulated tablets in disintegration time, dispersion time and dissolution study.

Key words: Cefadroxil,dispersible tablets,disintegrants

Introduction

The trend towards formulation of dispersible tablets is evident in Europe [1]. Dispersible tablets are uncoated tablets that product a uniform dispersion in water and may contain permitted coloring matter and flavoring agent [2]. Elderly and pediatric patients find difficulty in swallowing drugs as tablet or capsule. A suspension or a liquid dosage form is the premier option to improve compliance. Dispersible table is a good option, as an alternative to oral suspension and offer dosing convenience and accuracy. Cefadroxil is a first generation cephalosporin antibiotic [3]. Direct compression is used to define the process by which tablets are compressed directly from the powder blends of active ingredient(s) and suitable excipients. No pretreatment of the powder blends by wet or dry granulation is involved [4]. In the present work, an attempt has been made to develop dispersible tablets of cefadroxil by direct compression technique using three superdisintegrants, croscarmellose sodium, crospovidone and sodium starch glycolate in two concentrations of 5%w/w and 4%w/w separately along with microcrystalline cellulose.

The aim of the study is to investigate the performance of disintegrants among themselves and their two concentrations and the effect of other variables on the characteristics of dispersible tablets.

Materials

Cefadroxil was procured from Arabindo Pharma, Hyderabad. Crospovidone (ISP agencies), croscarmellose sodium (FMC Pharma agencies), sodium starch glycolate (DMB international), microcrystalline cellulose, (Signet Pharma Agencies), aspartame (Neutrasweet Pharma Agencies), aerosil (Cabot Samnol Pharma Agencies) and talc (Gokul Das Agency) were obtained from commercial sources and used as received.

Methods

S. No	Ingredients in mg/tablet	Formulations					
		F1	F2	F3	F4	F5	F6
1	Cefadroxil	250	250	250	250	250	250
2	Microcrystalline cellulose	221.46	226.71	221.46	226.371	221.46	226.71
3	Croscarmellose sodium	26.25	21.0				
4	Crospovidone			26.25	21.0		
5	Sodium starch glycolate					26.25	21.0
6	Aspartame	5.25	5.25	5.25	5.25	5.25	5.25
7	Aerosil	6.3	6.3	6.3	6.3	6.3	6.3
8	Talc	7.87	7.87	7.87	7.87	7.87	7.87
9	Magnesium stearate	7.87	7.87	7.87	7.87	7.87	7.87

Table 1. Formula of Dispersible Tablets

According to Table 1, cefadroxil, microcrystalline cellulose, crospovidone or croscarmellose sodium or sodium starch glycolate and aspartame were accurately weighted, passed through sieve number 60, mixed geometrically, and blended for 10 minutes. Aerosil, talc and magnesium stearate was passed through sieve number 60 and added to the above blend and mixed for 2 minutes. The above blend was compressed using 12.5 mm punches in a Cadmach machine. Prior to compression, blends were evaluated for their flow and compressibility properties. The flow property of blend was assessed by determining angle of repose by the funnel method [5].

The compressibility index of the blend was determined by Carr's compressibility index [6]. The prepared tablets were tested as per standard procedure for weight variation, thickness, hardness, friability, disintegration time, uniformity of dispersion and drug content. Uniformity of dispersion was carried out by placing 2 tablets in 100 ml water and stirring gently for 2 minutes. The dispersion was passed through sieve number 22 [7]. Wetting time was measured by taking a piece of tissue paper folded twice in a small petridish containing 5 ml of distilled water.

A tablet was placed on the paper, and time for complete wetting of the tablet was measured in seconds. The in vitro dissolution studies were carried out using USP dissolution apparatus [8] type 2 (Paddle) at 50 rpm in 900 ml distilled water at 37 ± 0.5°C. For each sampling 5 ml of dissolution medium was withdrawn and the same volume was replaced at time interval of 3 minutes for 15 minutes. The samples were analyzed at λ_{max} of 263 nm by using UV-1700 Shimadzu spectrophotometer.

Results and Discussion

Parameters	Formulations					
	F1	F2	F3	F4	F5	F6
Angle of repose in degree	25.12	26.59	29.85	30.34	26.56	28.28
Compressibility index in %	31.74	35.82	36.75	37.75	36.66	36.72
Hausners ratio	1.46	1.55	1.58	1.60	1.59	1.57

Table 2. Pre compression data

The results of angle of repose, compressibility index and hausners ratio are in the range of 25.12 - 30.34, 31.74-37.75 and 1.46-1.60 respectively (Table2). F1 is having lowest angle repose of 25.12 and its compressibility index and hausners ratio values are also lowest among all six formulations (Table 2). F4 is having highest value of angle of repose, 30.34. Its compressibility index and hausners ratio values are also highest among all six formulations. If F2 and F5 are compared for these values, such correlation does not exist. The angle of repose less than 30° indicates good flow properly. Almost all formulations (except F4) having less than 30° degree of angle of repose showed good flow properly. F4 having angle of repose of 30.34° passes all test of evaluations for dispersible tablet. Though F1 in precompression studies found more suitable than other formulations, showed excellent performance after compression also. Table 3 depicts physical parameters (hardness, weight variation, thickness, friability, disintegration time, dispersion time and wetting time) and drug content (assay) of all the fabricated tablets. All the tablet formulations showed acceptable pharmaceutical properties and complied with pharmacopoeial and non pharmacopoeial specifications for dispersible tablets.

Parameters	Formulations						
	F1	F2	F3	F4	F5	F6	MP
Weight in gm	0.526	0.526	0.527	0.525	0.526	0.527	0.525
Thickness in mm	3.91	3.91	3.93	3.89	3.81	3.95	3.95
Hardness in kg/cm^2	6.4	6.4	6.8	6.8	6.3	6.3	6.3
Friability in %	0.139	0.525	0.458	0.412	0.325	0.528	0.325
Disintegration time in seconds (Sec)	22	24	30	28	28	31	80
Dispersion time in sec	33	37	43	52	47	56	100
Wetting time in sec	90	95	83	70	88	98	115
Drug content in %	100.96	104.92	98.99	96.02	104.92	104.92	98

Table 3. Evaluation Data of Compressed Dispersible Tablets

The three superdisintegrants croscarmellose, crospovidone and sodium starch glucolate are taken in 26.25 mg per tablet separately in F1, F3 and F5 respectively and 21.0 mg/tablet of them are taken in F2, F4 and F6 respectively (Table1). Other ingredients are common to all six formulations. This reflects two formulations of each superdisintegrants differing in quantity of 5.25 mg/tablet. This difference of 5.25 mg/table is compensated by microcrystalline cellulose in F2, F4 and F6 (Table 1). According to Table 3, the performance of superdisintegrants for hardness is

Crospovidone > croscarmellose sodium > sodium starch glycolate

The performance of superdisintegrants for disintegration time is

Croscarmellose sodium < Crospovidone < sodium starch glycolate

The performance of superdisintegrants for dispersion time is

Croscarmellose sodium < Crospovidone < sodium starch glycolate

The quantity of 5.25 mg/tablet of microcrystalline cellulose replaced in one formulation of each superdisintegrants (F2,F4,F6) resulted in raise of disintegration time and dispersion time for croscarmellose sodium and sodium starch glycolate but decrease in disintegration time and increase in dispersion time for crospovidone (Table1 and Table 3).

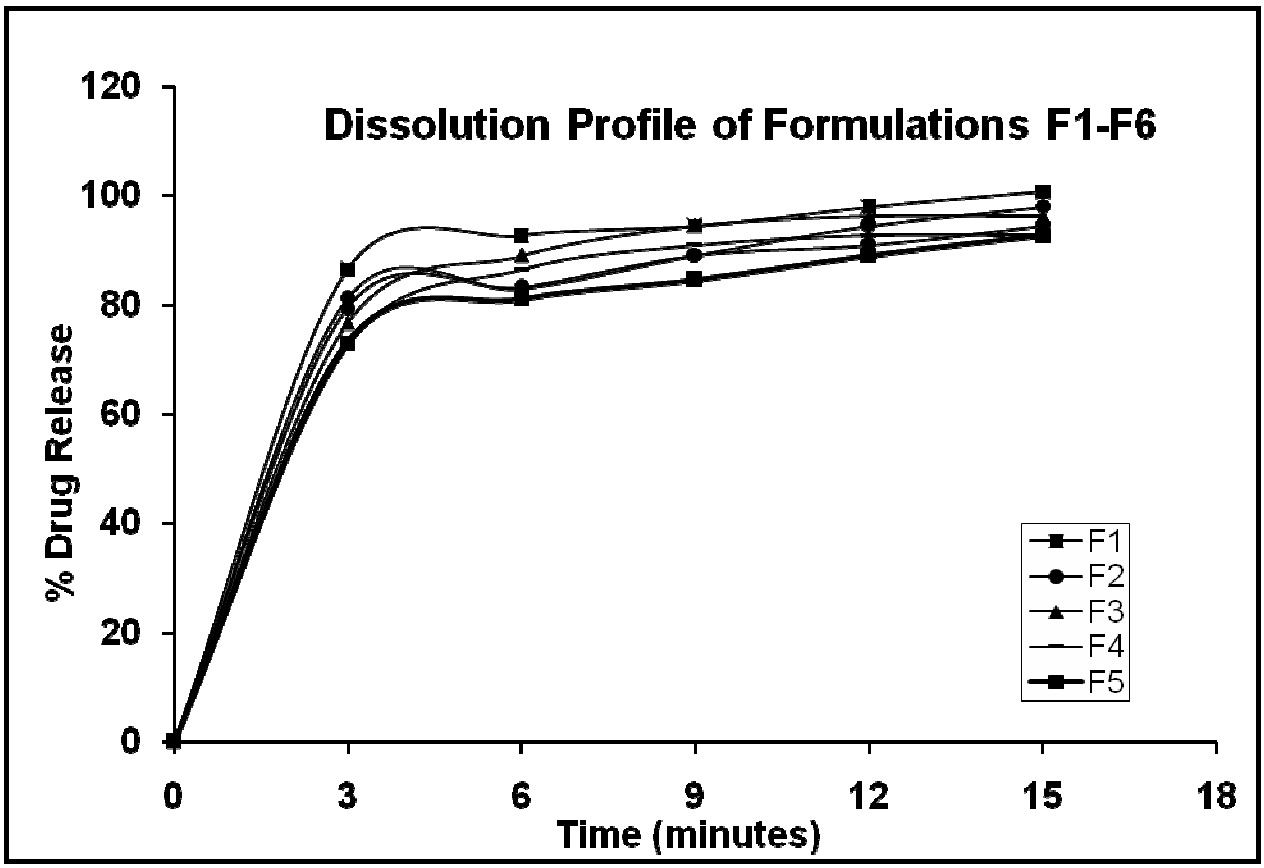

Figure 1. Dissolution Profile of Formulations F1-F6

Thus microcrystalline cellulose played important role in present study also. MP released 86.82% of drug in 15 minutes in dissolution study. Fig.1 showed dissolution release profile of fabricated products. F1 is best formulation among fabricated and marketed dispersible tablets (Table 3, Fig.1).

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