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Formulation and evaluation of Cefadroxil dispersible tablets

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Abstract

Cefadroxil dispersible tablets were fabricated with crospovidone, sodium starch glycolate and croscarmellose sodium as superdisintegrants with cefadroxil as model drug. Various pre-compressional parameters like angle of repose, compressibility index and hausner's ratio and post compressional parameters like weight variation, thickness, hardness, friability, disintegration time, dispersion time, wetting time, assay and drug release were studied. Formulations containing croscarmellose sodium and sodium starch glycolate showed decrease in angle of repose with increase in concentration. Angle of repose increased with increase in concentration of crospovidone. Formulations prepared with direct compression method showed good release properties when compared with wet granulation method. The wetting time decreased with increase in the concentration of crospovidone, while the wetting time of the tablets containing croscarmellose sodium and sodium starch glycolate did not change with increase in concentration. In dispersion study, the formulations consists of crospovodone have showed better results compared to other formulations. In disintegration study, formulations consists of crospovidone have showed better results compared to other formulations.

Key-Words: Cefadroxil, wet granulation, direct compression, dispersible tablets

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Introduction

Now a day, dispersible tablets are gaining more importance in the market for taste masking property. More is concentrated on dysphegia, migraine, nausea, and vomiting, parkinson's disease, schizophrenia, pediatric emergency[1]. Some patients prefer fast disintegrating tablets to conventional tablets because of ease of administration, swallowing, pleasant taste and the ability in several flavors. For poorly soluble orally administered drugs, the rate of absorption is often controlled by rate of dissolution. The rate of dissolution can be increased by increasing the surface area of available drug by various techniques (micronization, complexation solid

dispersion etc)[3],[4]. Another pre-requesite for the fast dissolution may be disintegration time of the tablets. Because dispersible tablets delivers a fine suspension of drug particles and thus favors the greater dissolution of the drug[5]. Dispersible tablets will dissolve in mouth within 10 seconds[6]. Tablets of this type were designed for pediatric and geriatric patients or any other patients who have difficulty in swallowing the tablets. Dispersible tablets can be prepared by various methods such as lyophilization, sublimation, crystalline transition, molding, mass extrusion and spray drying methods[7-13].

Cefadroxil is a first generation cephalosporin anti-bacterial drug that is the para hydroxyl derivative of cefalexin, and is used similarly in the treatment of mild to moderate susceptible infections and bitter taste. Upon prolonged use of this drug will cause darkened tongue, difficulty in breathin, fever, itching, severe diarrhea etc[18].

In the present study, the tablets can be prepared by direct compression and wet granulation methods. Though, fast disintegrating tablets are prepared by many processes such as lyophilization, sublimation, crystalline transition, molding, mass extrusion and spray drying methods, direct compression and wet granulation methods using different super disintegrants. Among all the methods, direct compression and wet granulation are most preferred since, these methods are economical and includes less procedure steps. Croscarmellose sodium, sodium starch glycolate and crospovidone are used as super-disintegrants[2],[14],[15]. Each disintegrant has optimum concentration at which it is more effective. Therefore, the super-disintegrants are studied at various concentrations to study the effect on disintegration time, wetting time and dissolution.

Materials and Methods

Cefadroxil was a product of Aurobindo pharma, Hyderabad. Crospovidone was a product of ISP Agencies, Chennai. Croscarmellose sodium and sodium starch glycolate were products from FMC PharmaAgencies, Bangalore. Other ingredients used were all of analytical grade.

Preparation of Cefadroxil dispersible tablets by wet granulation method:
Cefadroxil, crospovidone or croscarmellose sodium or sodium starch glycolate and aspartame were accurately weighed, passed through sieve number 60 and mixed geometrically. PVP with required quantity of water were accurately weighed, binder solution was prepared, they were added to the mixture and passed through sieve number 12 and dried in the hot air oven at 60˚C for 30 minutes. The dried granules were passed through sieve number 18. Microcrystalline cellulose was accurately weighed and passed through sieve number 60 and added to the granules. Aerosol and magnesium sterate were accurately weighed and passed through sieve number 60, added to the above mixture and mixed for 2 minures. Finally, the blend was compressed with 12.5mm punches.

Preparation of cefadroxil dispersible tablets by direct compression method:
Cefadroxil, MCC, crospovidone or croscarmellose sodium or sodium starch glycolate and aspartame are accurately weighed and passed through sieve number 60 and mixed geometrically and blended for 10 minutes. Aerosol, talc and magnesium state were passed through sieve number 60, added to the above blend and mixed for 2 minutes. The above blend was compressed

with 12.5mm punches. In the present study, the formulations F_1 to F_6 were fabricated by using wet granulation technique [Table 1] and F_7 to F_{14} were fabricated by using direct compression method [Table-2].

Table 1: Formulation of cefadroxil dispersible tablets by wet granulation method

S.NO	INGREDIENTS (mg)	F_1	F_2	F_3	F_4	F_5	F_6
1	Cefadraxil	250	250	250	250	250	250
2	Crospovidone	52.5	42	31.5	-	-	-
3	Sodium starch glycolate	-	-	-	52.5	42	-
4	Cros-carmellosse sodium	-	-	-	-	-	31.5
5	Aspartame	5.25	5.25	5.25	5.25	5.25	5.25
6	Poly vinyl pyrrolidone	5.25	5.25	5.25	5.25	5.25	5.25
7	Water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
8	Micro crystalline cellulose	216	226.5	237	216	226.5	237
9	Aerosil	10.5	10.5	10.5	10.5	10.5	10.5
10	Magnesium stearate	10.5	10.5	10.5	10.5	10.5	10.5

Table 2: Formulation of cefadroxil dispersible tablets by direct compression method

S.NO	INGREDIENTS (mg)	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}	F_{13}	F_{14}
1	Cefadroxil	250	250	250	250	250	250	250	250
2	Cros povidone	-	-	26.25	21	-	-	52.5	42
3	Sodium starch glycolate	-	-	-	-	26.25	21	-	-
4	Croscarmelose sodium	26.25	21	-	-	-	-	-	-
5	Aspartame	5.25	5.25	5.25	5.25	5.25	5.25	5.25	5.25
6	Micro crystalline cellulose	246.46	241.46	246.46	241.46	246.46	241.46	225.21	236
7	Aerosil	6.3	6.3	6.3	6.3	6.3	6.3	6.3	6.3
8	Magnesium stearate	7.87	7.87	7.87	7.87	7.87	7.87	7.87	7.87
9	Talc	7.87	7.87	7.87	7.87	7.87	7.87	7.87.	7.87

Evaluation of Cefadroxil dispersible tablets:

Various pre-formulation studies such as angle of repose, bulk density, tapped density compressibility index and Hausner's ratio were carried out and the results were tabulated in [Table-3].

Table 3: Pre-compressional parameters of various formulations of cefadroxil

FORMULATION	WEIGHT (gm)	THICKNESS (mm)	HARDNESS (kg/cm^2)	FRIABILITY (%)
F_1	0.548	3.94	4.9	0.654
F_2	0.549	3.99	4.7	0.524
F_3	0.549	3.95	4.7	0.429
F_4	0.549	3.98	4.8	0.761
F_5	0.550	3.95	4.8	0.325
F_6	0.549	3.94	4.3	0.458
F_7	0.549	3.91	4.3	0.456
F_8	0.549	3.91	4.2	0.139
F_9	0.548	3.93	4.2	0.525
F_{10}	0.550	3.89	4.3	0.435
F_{11}	0.548	3.81	4.6	0.412
F_{12}	0.551	3.95	4.5	0.470
F_{13}	0.549	3.99	4.1	0.466
F_{14}	0.547	3.92	4.1	0.621

Pfizer hardness tester was used for the determination of the hardness of the tablets[16]. The tablet was placed in contact between the plungers and the handle was pressed. Then the force of the fracture was recorded. The thickness and diameter of 4 tablets were recorded during the process of compression using the vernier caliperse[17]. The friability was calculated by accurately weighing the two tablets and placing them in the friabilator and operated for 100 revolutions. The tablets were de-dusted and re-weighed. For weight variation test, 10 tablets were selected randomly from the lot and individually weighed to check for weight variation. To carry out the uniformity of dispersion, 2 tablets were placed in 100ml of water and stirred gently until completely dispersed. A smooth dispersion is obtained which was passed through sieve number 22 [Table-4].

To carry out the disintegration test, the tablets were taken and introduced in to the tube of the apparatus, and the tablet rack of the disintegration apparatus was positioned into a 1 liter beaker and the time of disintegration was recorded. To discriminate between the formulations, disintegration was done at room temperature and disc was not used for the study. To calculate the wetting time, a piece of tissue paper folded twice was placed in a small petri dish containing 5ml of distilled water. A tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds.

Table 4: Evaluation of post-compressional parameters of various formulations of cefadroxil

FORMULATION	ANGLE OF REPOSE (θ)	COMPRESSIBILITY (%)	HAUSNER'S RATIO
F_1	25.36	21.76	1.36
F_2	25.17	26.76	1.36
F_3	24.92	19.35	1.24
F_4	24.50	26.80	1.36
F_5	23.20	19.40	1.25
F_6	25.21	19.40	1.25
F_7	25.12	31.74	1.46
F_8	26.59	35.82	1.55
F_9	29.85	36.75	1.58
F_{10}	30.34	37.75	1.60
F_{11}	26.56	36.66	1.59
F_{12}	28.28	36.72	1.57
F_{13}	32.53	38.57	1.62
F_{14}	30.53	34.81	1.53

For calculating the drug content, 10 tablets were weighed and powdered. Powder equivalent to 100mg of cefadroxil was weighed and dissolved in 7.4 pH phosphate buffer and filtered the solution through a whatman filter paper. The filtrate was collected and diluted to a sufficient amount with 7.4 pH phosphate buffer till the concentration of the drug lies within the standard plot range. The diluted solution was analysed for content by UV-Spectrophotometer using 7.4 pH phosphate buffer as blank[Table 5].

Table 5: Evaluation of post compressional parameters of various formulations of cefadroxil

FORMULATION	DISINTEGRATION TIME (sec)	DISPERTION TIME (sec)	WETTING TIME (sec)	ASSAAY (%)	% DRUG RELEASE (%) (15 min)
F_1	25	52	70	93.8	96.60
F_2	27	57	75	90.5	91.82
F_3	30	57	82	91.2	89.76
F_4	32	56	95	94.1	94.90
F_5	33	62	92	90.4	91.27
F_6	33	64	90	92.7	90.12
F_7	27	53	90	96.5	96.87

F_8	28	55	92	95.7	95.07
F_9	24	50	83	97.1	98.44
F_{10}	26	52	84	96.4	95.12
F_{11}	31	60	95	97.1	95.07
F_{12}	33	60	96	98.2	93.38
F_{13}	20	47	65	101.1	102.51
F_{14}	21	45	68	100.4	100.38

To carry out the in vitro dissolution study, USP dissolution apparatus type II was used with 900ml of water as dissolution medium. The paddle was rotated at a speed of 50rpm. For every 3 minutes, 5ml of the medium was withdrawn and the same is replaced again. The sample was filtered with whatman filter paper and diluted with water prior to analyze. The absorbance was noted at 263nm and the cumulative percentage release was calculated.

Results and Discussion

The hardness was found to be within the range of 4 to5 Kg/cm^2 in all the formulations indicating good mechanical strength with an ability indicating physical and mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. In all the formulations, the friability value is less than 1% giving an indication that tablets formulated are mechanically stable. All the tablet formulations passed the weight variation test. The weight of all the formulations was found to be within the limits. The assay of all the formulations was found between 90% to 110% which were within acceptable limits. The assay results are particularly good for F_{13} and F_{14} where crospovidone concentration is increased.

The results of disintegration time of all the tablets prepared by wet granulation and direct compression were found to be in the range of 21 to 33 sec. formulations F_{13} and F_{14} which consists of crospovidone have showed better results compared to other formulations. The disintegration time of the tablets using different disintegrants decreases in the following order sodium starch glycolate > croscarmellose sodium > crospovidone. It is observed that, when crospovidone is used as disintegrant, tablets disintegrate rapidly with in less time compared to other tablets prepared using croscarmellose sodium and sodium starch glycolate disintegrants. Though tablets prepared by croscarmellose sodium and sodium starch glucolate disintegrants in the mean time, but in comparison with crospovidone they are delay. When concentration of crospovidone is increased, the disintegration time was reduced significantly. The tablets prepared with direct compression and wet granulation methods did not showed much variation.

The results of dispersion time of all tablets were found to be in the range of 45 to 65 sec. formulations F_{13} and F_{14} which consists of crospovidone have showed better results compared to other formulations. The dispersion time of the tablets using different disintegrants decrease in the following order sodium starch glycolate > croscarmellose sodium > crospovodone. It is observed that, when crospovidone is used as disintegrant, tablets dispersion time is less compared to other tablets prepared using croscarmellose sodium and sodium starch glycolate. The reason may be due to penetration of water in presence of various disintegrants. Crospovidone when comes in

contact with water gets inflated and immediately bursts out here by releasing the drug in short duration of time. The tablets prepared with direct compression method and wet granulation method showed less deviation.

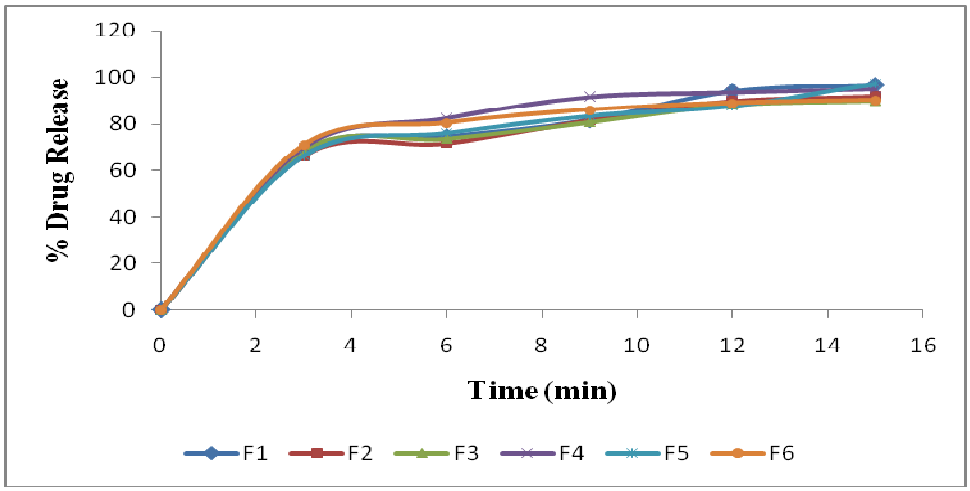

Figure 1: comparative dissolution data from formulations F_1 to F_6 by wet granulation

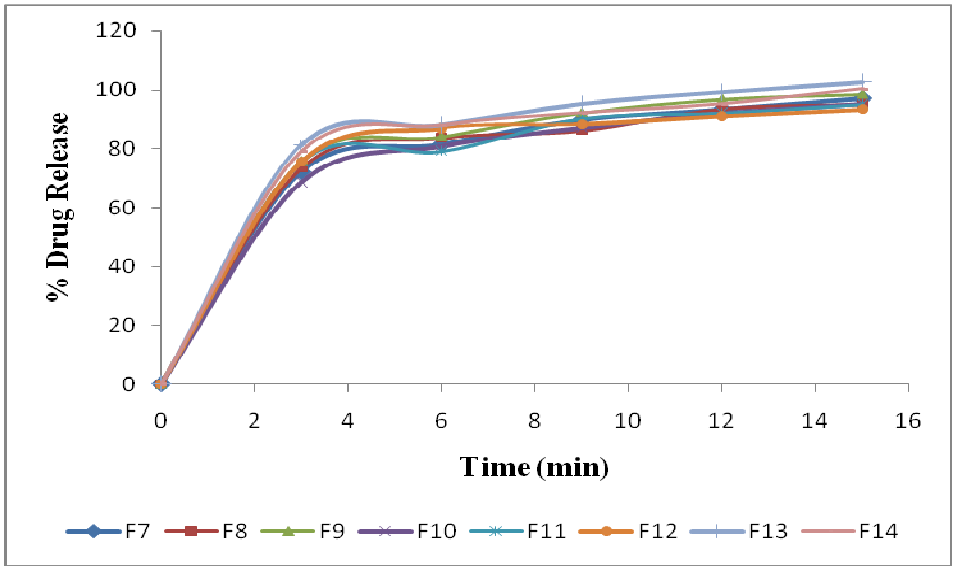

Figure 2: comparative dissolution data from formulations F_7 to F_{14} by direct compression

The wetting time decreased with increase in concentration of crospovidone, while the wetting time of tablets containing croscarmellose sodium and sodium starch glycolate did not change with increase in concentration. Formulations F_{13} and F_{14} which consists of crospovidone have showed the better results compared to other formulations. The wetting time of tablets decrease in the following order: sodium starch glycolate > croscarmellose sodium > crospovidone. Tablets prepared with direct compression method and wet granulation method showed much variation.

The tablets prepared with crospovidone (F_{13} and F_{14}) showed a drug release of 102.51%, 100.38% respectively which are proved to be optimized. Tablets prepared with sodium starch glycolate and sodium starch glycolate and croscarmellose sodium also showed good release properties [Figure-1] and [Figure-2]. Formulations prepared with direct compression method showed good release properties compared to wet granulation method, and they are within acceptable limits.

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