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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF CEFUROXIME AXETIL

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ABSTRACT

In this investigation, fast dissolving tablets of Cefuroxime Axetil were prepared using different super disintegrants. A wet granulation method was used as direct compression method unable to formulate dispersible tablet of Cefuroxime axetil. Different super disintegrant were used such as croscarmellose sodium (CCS), sodium starch glycolate (SSG) and crospovidone (CPVP). In all the formulations, water was used as a binding agent to attain hardness. The prepared fast disintegrating tablets were evaluated for weight variation, content uniformity, hardness, disintegration time, wetting time and friability of tablets. Wetting time of formulations containing sodium starch glycolate was least and tablets showed fastest disintegration. All the tablets had hardness 2.0-4.0 kg/cm2 and friability of all formulations was less than 1%, weight variation and drug content were within official limit. Amongst all formulations, formulation F5 prepared showed least disintegrating time of 21.40 secs and faster dissolution.

KEYWORDS: Cefuroxime axetil, Disintegration time, wetting time; FDT, Croscarmellose sodium, sodium starch glycolate and Crospovidone.

INTRODUCTION:

The oral route of administration is the most preferred route due to its many advantages like ease of administration, accurate dosage, self-medication, pain avoidance, versatility and patient compliance[1]. Tablets and capsules are the most popular dosage forms. But one important drawback of such dosage forms is Dysphagia or difficulty in swallowing. This is seen to afflict nearly 35% of the general population. This disorder is also associated with a number of pathological conditions including stroke, Parkinson's disease, neurological disorders, AIDS etc. Parkinsonism, Motion sickness, Unconsciousness, Elderly patients, Children, Mentally disabled persons, Unavailability of water[2] .

To solve the above mentioned problems, pharmaceutical technologists have put in their best efforts to develop a fast dissolving drug delivery, i.e. Mouth Dissolving Tablet that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within 15 secs to 3 min. Most of the MDTs include certain super disintigrants and taste masking agents[3].

The concept of fast dissolving drug delivery system emerged from the desire to provide patient with conventional mean of taking their medication. Fast dissolving dosage forms can be disintegrated, dissolved or suspended by saliva in the mouth. This fast dissolving tablet disintegrates instantaneously when placed on tongue and releases the drug dissolves or disperses in the saliva.[4] Fast dissolving tablets are useful in patients [5, 6] like pediatric, geriatric, bedridden, or mentally disabled, who may face difficulty in swallowing conventional tablets or capsule[7] leading to ineffective therapy[8], with persistent nausea, sudden episodes of allergic attacks, or coughing for those who have an active life style. Fast dissolving tablets are also applicable when local action in the mouth is desirable such as local anaesthetic for toothaches, oral ulcers, cold sores, or teething[9] and to those who cannot swallow intact sustained action tablets/capsules[10].

MATERIALS AND METHODS:

MATERIALS:

The drug Cefuroxime axetil was supplied as a gift sample by Cosmos Pvt. Ltd., Ludhiana (PUNJAB). All other reagents and chemicals were of analytical grade.

PREPARATION OF FAST DISSOLVING TABLETS OF CEFUROXIME AXETIL:

The critical parameters to formulate a fast dissolving tablet are choice of super disintegrant and optimization of concentration of super disintegrant. The main criteria for fast dissolving tablets is to disintegrate or dissolve rapidly in oral cavity in 15-60 seconds, without need of water and should have pleasant mouth feel. The super disintegrant (Ac-Di-Sol, Crospovidone, Sodium starch glycolate) were used to formulate the tablets. Dispersible tablet of Cefuroxime axetil were prepared by granulation according to the formula given in Table **1**.

All the ingredients were passed through #60 mesh separately. Then the granules were prepared with

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intragranular ingredients using water as a binder passing lumps through #8 mesh. Then extragranular ingredients were weighed and mixed in geometrical order with prepared granules and compressed into tablet of 360 mg using 11mm flatpunches on single punch tablet compression machine (Cadmach, Ahemdabad). A batch of 30 tablets were prepared for each of the designed formulations[13].

Table 1: Formulation Codes of cefuroxime axetil fast dissolving tablets

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7
Cefuroxime Axetil	250	250	250	250	250	250	250
CCS	10	20	30	5	-	5	-
Crospovidone	10	5	-	20	30	5	-
SSG	10	5	-	5	-	20	30
SLS	2	2	2	2	2	2	2
MCC	43	43	43	43	43	43	43
Magnessium Sterate	5	5	5	5	5	5	5
Aspartame	5	5	5	5	5	5	5
Mannitol	20	20	20	20	20	20	20
Talc	5	5	5	5	5	5	5

EVALUATION PARAMETERS:

B) Evaluation of Granules: The following evaluation parameters of granules were determined such as Angle of repose, Apparent bulk density, Tapped density, Compressibility index, Hausner's ratio. The results are shown below in Table - 2.

C) Evaluation Of Cefuroxime Axetil Fast dissolving Tablet: These following evaluation parameters of Cefuroxime Axetil tablet was determined i.e General appearance, Thickness, Hardness, Weight variation, Friability, Drug Content, Swelling studies, Buoyancy lag time determination and Total Fast dissolving time. The results of these various parameters are listed below in Table 3 and Table 4.

IN-VITRO DISSOLUTION STUDY:

Dissolution studies of all tablets were performed using dissolution test apparatus (Paddle type, TDT-08L, Electro lab, India). Tablets were added to the 900 ml of 0.1 N Phosphate Buffer at 37°C ± 0.5°C, which was stirred with a rotating paddle at 50 rpm. At time intervals of 5 minutes, 5ml samples were withdrawn and equal volume of fresh medium pre-warmed at the same temperature was replaced in to the dissolution medium after each sampling to maintain its constant volume throughout the test. Assay carried out using UV spectrophotometer (Shimdzu 1700 UV/Visible double beam Spectrophotometer, Japan) at 281nm.

RESULT AND DISCUSSION:

B) Evaluation of Granules: Evaluation parameters of granules are listed below in Table -2:

Formulation Code	Bulk density (g/cc) ± sd, n=3	Tapped density (g/cc) ±sd, n=3	Angle of repose (degree) ±sd, n=3	Carr's Index (%) ± sd, n=3	Hausner's Ratio ± sd, n=3
F1	0.48± 0.20	0.53 ± 0.85	27.47±0.4761	15.29± 0.549	1.18 ± 0.169
F2	0.46±0.0017	0.55± 0.02	29.12 ± 0.631	14.80± 0.207	1.16 ± 0.372
F3	0.48 ±0.015	0.58 ± 0.016	27.62±0.507	16.64± 0.677	1.21 ± 0.008
F4	0.47 ±0.0020	0.51±0.0020	29.15±0.843	6.66±0.282	1.07 ± 0.0163
F5	0.51 ± 2.05	0.62±0.00163	27.13 ± 1.077	17.29 ± 0.658	1.20 ± 0.016
F6	0.50 ± 0.016	0.58 ± 1.632	27.09 ± 0.656	13.10±0.449	1.15 ± 0.016
F7	0.48 ± 0.81	0.55 ± 0.0016	28.07 ± 0.471	11.44±0.711	1.13 ± 0.002

Table 2: Shows various Evaluation parameters of granules

C) Evaluation of tablet: Evaluation parameters of tablet are listed below in Table -3 & Table – 4

Formulation	Hardness (Kg/Cm^2)	Friability	Drug Content	Disintegration Time(Sec.)
F1	2.73±0.129	0.8±0.010	94.67	60
F2	3.53±0.127	0.81±0.014	101.33	56
F3	3.33±0.123	0.85±0.018	102.66	68
F4	3.51±0.173	0.81±0.001	99.99	40
F5	3.46±0.105	0.81±0.019	95.99	45
F6	3.23±0.153	0.81±0.012	97.33	50
F7	3.32±0.143	0.80±0.015	98.66	60

Table 3: Shows various evaluation parameters of tablet

Formulation	Wetting Time	Thickness	Weight Variation	Diameter
F1	47±2.51	6.05±0.064	360.9±4.4	7.90±0.017
F2	49±2.50	6.22±0.085	362.6±5.0	7.98±0.006
F3	48±2.40	5.17±0.110	358.7±2.9	7.96±0.001
F4	40±1.89	6.95±0.056	361.9±3.0	7.98±0.019
F5	50±2.20	5.13±0.067	359.23±3.0	7.98±0.016
F6	48±1.0	6.02±0.124	362.7±3.9	7.97±0.039
F7	43±2.25	5.02±0.124	355.42±3.2	7.96±0.017

Table 4: Shows various evaluation parameters of tablet

In-vitro Dissolution Profile of Formulation F1 TO F7 Phosphate buffer p.H 6.8

Time(Min)	F1	F2	F3	F4	F5	F6	F7
0	0	0	0	0	0	0	0
5	40	38.6	29.33	22.66	23.33	18.67	18.67
10	56	65.13	58.46	52	45.33	33.33	38.67
15	78.67	80	86.67	82.67	76	74	77.33
20	87.33	89.33	89.33	91.3	92.67	91.33	87.33
25	93.33	96	94	96	95.33	93.33	94.67
30	99.33	98.66	97.33	98	98.67	97.3	98.67

Table 5: PERCENTAGE DRUG RELEASE VALUES FOR FORMULATION F1 to F7

Figure 3: In-vitro drug release profile of Cefuroxime Axetil formulations (F1 to F4)

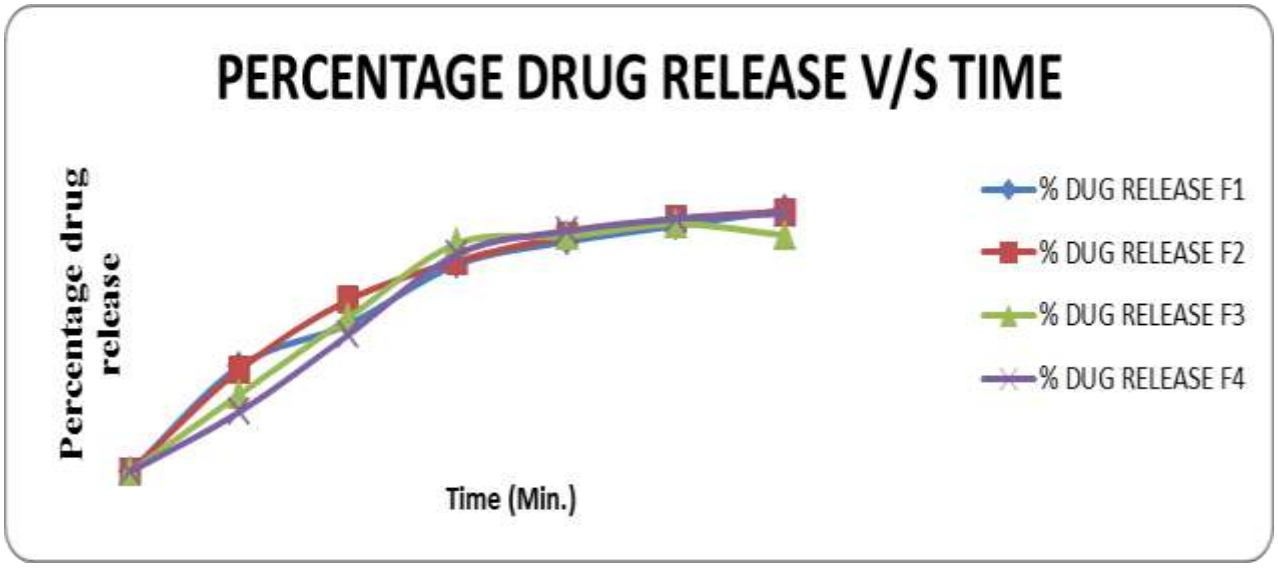

Figure 3: Plot of Percentage drug release vs time for formulation F1 to F4

Figure 4: In-vitro drug release profile of Cefuroxime Axetil formulations (F5 to F7)

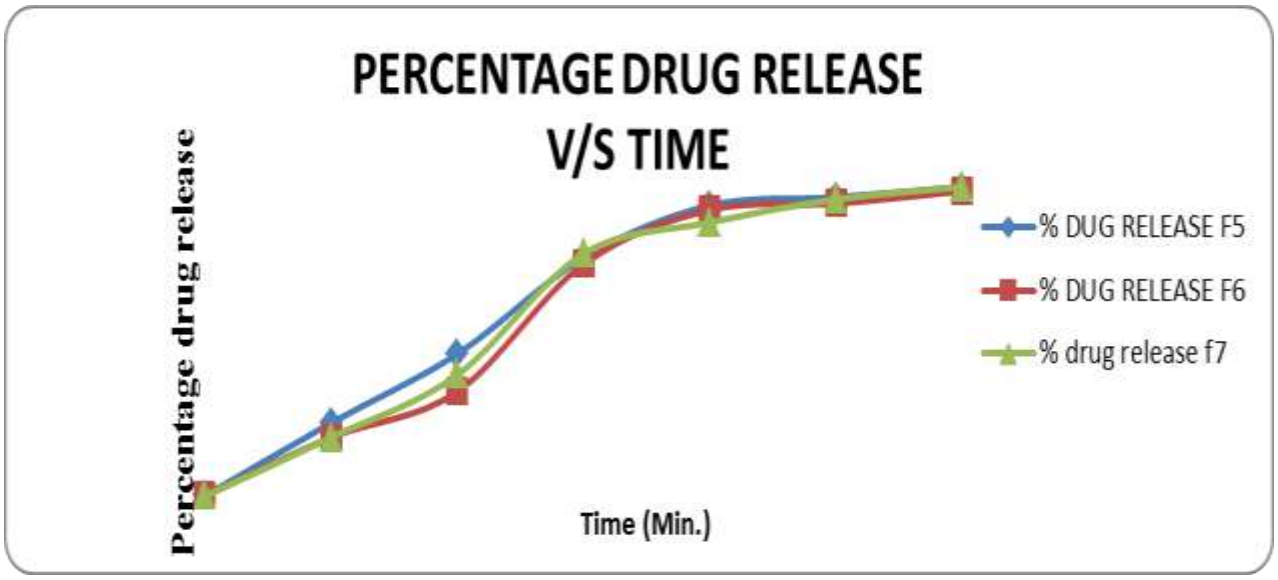

Figure 4: Plot of Percentage drug release vs time for formulation F5 To F7

In-vitro Dissolution Profile of Formulation F1 TO F7 in Phosphate buffer pH 6.8

Time(Min.)	Log % drug remaining f1	Log % drug remaining f2	Log % drug remaining f3	Log % drug remaining f4	Log % drug remaining f5	Log % drug remaining f6	Log % drug remaining f7
0	2	2	2	2	2	2	2
5	1.78	1.79	1.85	1.89	1.88	1.91	1.91
10	1.64	1.54	1.61	1.68	1.74	1.82	1.79
15	1.32	1.30	1.12	1.23	1.38	1.41	1.36
20	1.10	1.02	1.02	0.93	0.87	0.94	1.10
25	0.82	0.60	0.79	0.60	0.67	0.82	0.73
30	0.12	.125	0.10	0.30	0.12	0.43	0.124

Table 6: log percent drug remaining vs time of formulation F1 to F7

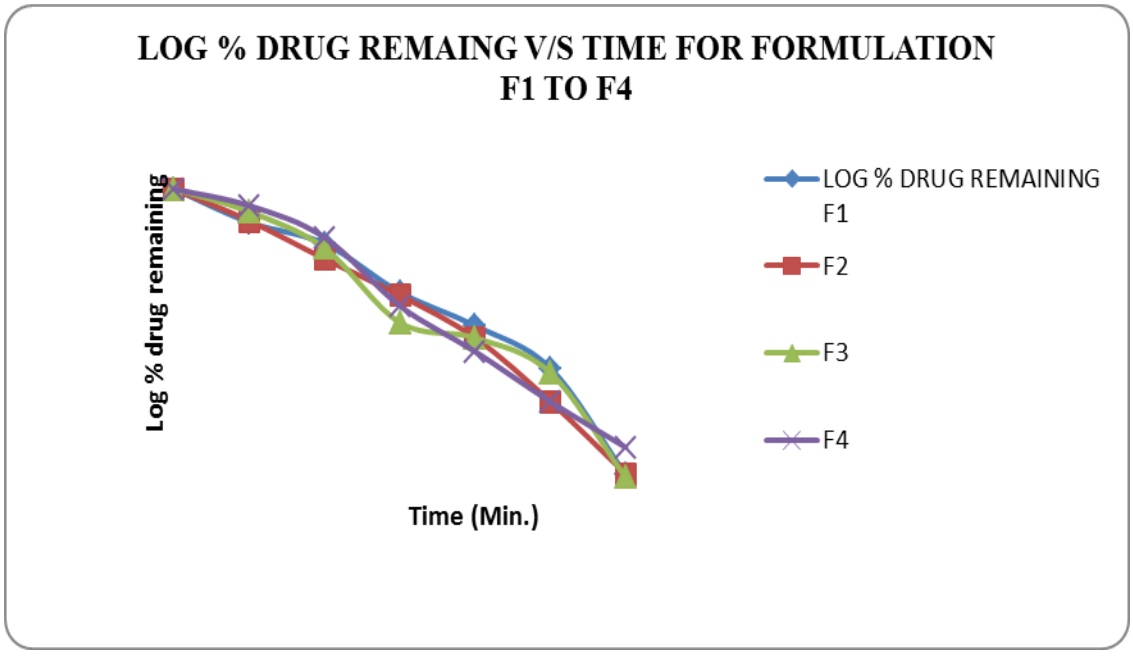

Figure 5: Plot of Log Percentage Drug Remaing Vs Time (First Order) For Formulation F1 to F4

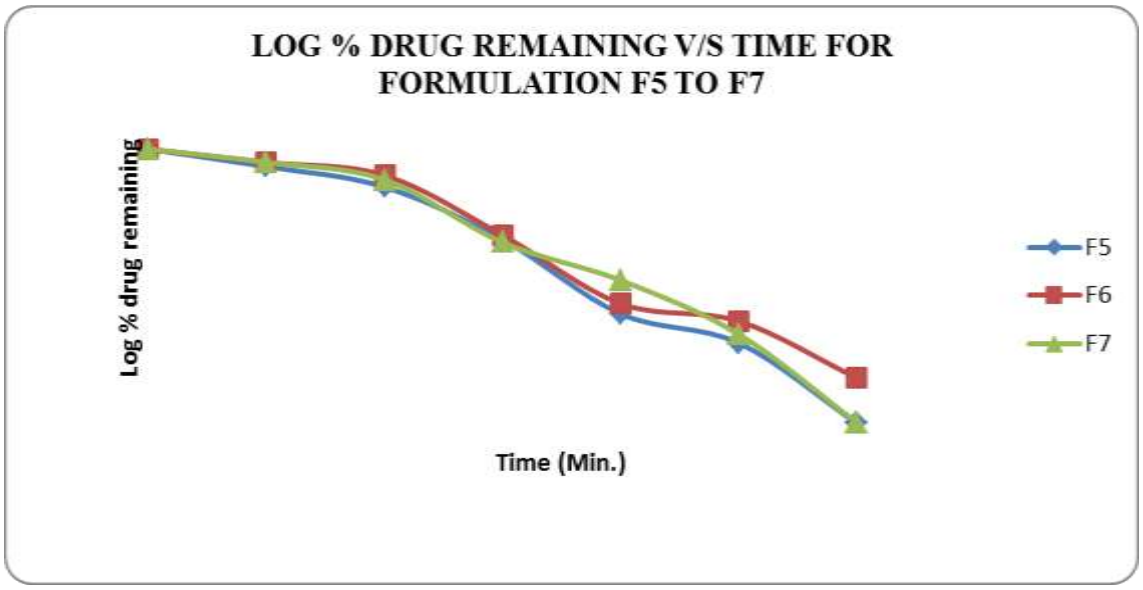

Figure 6: Plot of Log Percentage Drug Remaining Vs Time (First Order) For Formulation F5 to F7

RESULT AND DISCUSSION:

Seven formulations of Cefuroxime Axetil were prepared with different concentration of three superdisintegrants: Sodium Starch glycolate, Croscarmellose sodium, Crospovidone and microcrystalline cellulose were used as a direct compressible vehicle. For each formulation, blend of drug and excipients were prepared and evaluated for various parameters. The powder blend was compressed using wet granulation technique. Bulk density was found in the range of 0.47-0.51 g/cm3 and the tapped density between 0.51-0.63 g/cm3 (Table 2). Using these two density, Hausner's ratio and compressibility index were determined. The powder blend of all the formulations had Hausner's ratio of 1.2 or less indicating good flowability. The compressibility index was found between 6.66 and 17.29 %. The good flowability of blend was also evidenced with angle of repose (range of 23 – 27^{o}) which is below 40^{0} indicating good flowability. Tablets were prepared using wet granulation technique. Thickness of the tablets was measured by vernier caliper by picking tablets randomly from all the batches. The mean thickness was (n=3) almost uniform in all the formulations and values ranged from 5.02 ± 0.124 mm to 6.22 ± 0.085 mm. The standard deviation values indicated that all the formulations were within the range. Since the powder material was free flowing, tablets were obtained of uniform weight due to uniform die fill, with acceptable weight variations as per pharmaceutical specifications. The drug content was found in the range of 94.67 – 102.66 % (acceptable limit) and the hardness of the tablets between 2.0 – 4.0 kg/cm2 (Table 3). Friability of the tablets was found below 1 % indicating a good mechanical resistance of tablets. Wetting time is closely related to the inner structure of the tablet. This showed that wetting process was very rapid in almost all formulations. This may be due to ability of swelling and also capacity of water absorption and causes swelling. The *invitro* dispersion time is measured by the time taken to undergo uniform dispersion. Rapid dispersion within few minutes was observed in all the formulations. The results showed that tablet containing Crospovidone having low dispersion time as compare to other superdisintegrants. The dispersion time increases as the concentration of superdisintegrants increases. The in vitro disintegration time of the tablets was found to be less than 60 sec. All the formulations showed enhanced dissolution rate as compared to Cefuroxime Axetil with out superdisintegrants. The maximum increase in the dissolution rate was observed with crospovidone amongst the three superdisintegrants. The order of enhancement of the dissolution rate with various superdisintegrants found to be

Crospovidone >Crosscarmellose>Sodium starch glycolate.

CONCLUSION:

It was concluded that mouth-dissolving tablets of Cefuroxime Axetilcan will be successfully prepared by wet granulation technique using selected superdisintegrants for the better patient compliance and effective therapy.

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