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Formulation and Evaluation of Cefixime Trihydrate Dispersible Tablets

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ABSTRACT

Therapeutically active ingredients like tablet and capsule are conventional pharmaceutical dosage forms for manufacture, storage and ensure dosage uniformity. However, this dosage forms like capsules and tablets, often present ingestion problems such as difficulty in swallowing for the debilitated patients, particularly for paediatric and geriatric populations. This may result in a high incidence of non-compliance and ineffective therapy, which may prove to be fatal in case of serious conditions. Suspension dosage forms could solve this problem, but they have other associated drawbacks like lower physical and chemical stability and high cost of manufacturing. Suspensions are also inconvenient to carry while travelling and also involve the risk of inaccurate measurement and dosing. Thus, there is a need for oral pharmaceutical composition, which can be taken orally without the need of swallowing it and act as a viable substitute for suspensions. Accordingly, provided are water dispersible tablet compositions, which can either be chewed or can be readily dispersed in water before oral administration. One of the key requirements of water dispersible tablet is they could dissolve in an aqueous medium within a short time period for example, less than three minutes, to form a smooth suspension without any coarse lumps. Dispersible tablets provide advantages of both tablets and liquid formulations. These are convenient to carry, easy to manufacture and more stable dosage forms.

KEYWORDS: *Dispersible tablets, Pharmaceutical dosage forms, coarse lumps, Direct compression, Evaluation parameters*

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INTRODUCTION

Oral drug delivery system has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drug via various pharmaceutical products of different dosage form. The reason that the oral route achieved such popularity may be attributed to its ease of administration as well as the traditional belief that by oral administration the drug is well absorbed as the food stuff ingested daily[1]. The reasons for this preference are obvious because of the ease of administration and widespread acceptance by patients. The most common oral dosage forms include: liquid mixtures like solutions, suspensions, solid dosage forms like tablets and capsules and liquid filled capsules etc. Compared to other oral dosage forms, tablets are the manufacturer's dosage form of choice because of their relatively low cost of manufacture, package and shipment; increased stability and virtual tamper resistance.[2] Tablets represent unit dosage forms in which one usual dose of the drug has been accurately placed. By comparison, liquid oral dosage forms are usually designed to contain me than 50% multiple dose of medication in same container. Such liquid dosage measurements are typically in error by a factor ranging from 20 to 50% when the drug is self administered by the patient.[3] Because of that reason more than 50% of pharmaceutical products are administered by oral route with most effitionly.

DISPERSIBLE TABLETS

Dispersible tablets are defined as uncoated or film coated tablets intended to be dispersed in water before administration giving a homogenous dispersion. Typically a tablet is dispersed in about 5-15 ml of water and the resulting dispersion is administered to the patients. Dispersible tablets are required to disintegrate within 3 minutes in water at 15-25°C.[4]

MATERIALS USED

TABLE.NO.1-LIST OF MATERIALS USED

S. NO	CHEMICALS
1.	Cefixime
2.	Microcrystalline cellulose PH 102.
3.	Croscarmellose sodium
4.	Pregelatinized starch
5.	Sucralose
6.	Aspartame
7.	Pineapple premium flavour
8.	Colloidal silicon dioxide
9.	Tartrazine lake colour
10.	Sodium starch glycolate
11.	Magnesium stearate

METHODOLOGY

FORMULATION OF CEFIXIME DISPERSIBLE TABLETS

In this work cefixime dispersible tablets were prepared by direct compression method.

TABLE: NO.2

S. No	Ingredients (mg)	F1	F2	F3	F4	F5	F6
1.	Cefixime	226.80	226.80	226.80	226.80	226.80	226.80
2.	Microcrystalline cellulose	136.10	122.60	109.10	136.10	122.60	109.10
3.	Pregelatinized starch	22.50	22.50	22.50	22.50	22.50	22.50
4.	Crosscarmellose sodium	14.00	27.50	41.00	-	-	-
5.	Sodium starch glycolate	-	-	-	14.00	27.50	41.00
6.	Sucralose	25.00	25.00	25.00	25.00	25.00	25.00
7.	Colloidal silicon dioxide	2.25	2.25	2.25	2.25	2.25	2.25
8.	Magnesium stearate	4.00	4.00	4.00	4.00	4.00	4.00
9.	Tartrazine lake colour	1.35	1.35	1.35	1.35	1.35	1.35
10.	Pineapple flavour	18.00	18.00	18.00	18.00	18.00	18.00
	Weight of each Tablet	450.00	450.00	450.00	450.00	450.00	450.00

DIRECT COMPRESSION METHOD

MANUFACTURING PROCEDURE

1. API was weighed accurately and passed through sieve #20.
2. All the ingredients were passed through sieve #40 except die.
3. The drug and sifted excipients were mixed thoroughly in a polythene bag.
4. Tartrazine lake colour was passed through sieve #100 and mixed with above blend.
5. Finally accurately weighed magnesium stearate was added with above blend.
6. The powder was blend thoroughly.
7. Compressed the tablet using 10.5mm round shaped deep concave punches.

EVALUATION OF POST COMPRESSION PARAMETERS

GENERAL APPEARANCE:

Tablets from all batches were randomly selected and evaluated the general appearances involves the measurements of attributes such as tablet size, shape, color, odour, taste, surface textures, physical flows and consistency[5].

HARDNESS

Hardness or tablet crushing strength is the force required to break a tablet in a diametric compression. A tablet is placed between two anvils, force is applied to the anvils and the crushing strength that just causes the tablet to break is recorded. Hardness is referred as the tablet crushing strength. Hardness of the tablet was measured by using Monsanto tablet hardness tester. The values were expressed in Kg/cm^2.

THICKNESS

The thickness of five tablets was measured using digital verniercaliper. The extent at which the thickness of each tablet deviated from ± 5% of standard value was determined. The diameter was also determined by vernier callipers. Six tablets were evaluated to determine the average thickness. The thickness was denoted in millimetre[6].

WEIGHT VARIATION TEST:

To study weight variation 20 tablets of each formulation were selected at a random and average weight was calculated. Then percentage deviation from the average was calculated.

TABLE: NO. 3. IP STANDARDS OF PERCENTAGE OF WEIGHT VARIATION

AVERAGE WEIGHT OF TABLETS (mg)	PERCENTAGE DEVIATION ALLOWED
80 mg or less	10%
More than 60 mg but less than 250mg	7.5%
250 mg or more	5%

$$\text{Percentage deviation} = \frac{\text{Individual weight} - \text{Average weight} \times 100}{\text{Average weight}}$$

FRIABILITY TEST

The friability of tablets was determined by using Roche Friabilator. Twenty tablets were weighed and placed in friabilator and rotated at 25 rpm for 4 minutes. Then the tablets were taken out, dedusted and reweighed. A maximum loss of weight (from a single test or from the mean of the three tests) not greater than 1.0 per cent is acceptable for most tablets[7].

The percentage friability of the tablets were calculated by the formula,

$$\text{Percentage friability} = \frac{\text{Initial weight } (W_o) - \text{Final weight } (W) \times 100}{\text{Initial weight } (W_o)}$$

UNIFORMITY OF DISPERSION

Tablet is placed in a 200 ml beaker with about 100ml of water in it. The system is stirred gently to obtain a smooth dispersion and allow to passes through a sieve screen with a nominal mesh aperture of 710 mm *(*sieve number 22*).* No particles or lumps should remain on mesh[8].

WETTING TIME AND WATER ABSORPTION RATIO

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipients. It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity[9]. A piece of tissue paper was placed in a Petri dish containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds.

Water absorption ratio (R) was then determined according to the following equation:

Water absorption ratio (R) = $\frac{Wa - Wb}{wb} \times 100$.

IN-VITRO DISPERSION TIME:

In-vitro dispersion time was measured by dropping a tablet in a 10 ml measuring cylinder containing 6 ml of buffer solution (pH 7.2).

DISINTEGRATION TEST:

The *in-vitro* disintegration time was carried out by using disintegration test apparatus. Tablet was placed in each of the 6 tubes of the apparatus and one disc was added to each tube and run the apparatus using distilled water maintained at 37 ± 20°C as the immersion liquid. The assembly should be raised and lowered between 28-32 cycles per minute in the distilled water maintained at 37 ± 20°C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

DRUG CONTENT ESTIMATION

20 tablets were weighed and powdered. An amount of the powder equivalent to 20 mg of Cefixime was dissolved in 100 ml of pH 7.2 phosphate buffer, filtered and diluted suitably and analyzed for drug content at 288 nm using UV-Visible spectrophotometer.

INVITRO DRUG RELEASE STUDIES:

Dissolution parameters:

Medium	: 0.05 M Potassium phosphate buffer
Type	: Apparatus type 1(basket)
Rpm	: 100
Quantity	: 900 ml
Temperature	: 37°C±0.50°C
Sampling time	: 15 min, 30 min, 45 min

PREPARATION OF MEDIUM

0.05 M Potassium phosphate buffer (pH 7.2) solution was prepared by dissolving 6.8 gm of monobasic potassium phosphate in 1000ml of water, adjusted to pH 7.2 with 1 M sodium hydroxide.

PROCEDURE[10]

The *in vitro* dissolution studies of Cefixime dispersible tablets was carried out using USP type 1(Basket) dissolution apparatus using 900 ml of pH 7.2 phosphate buffer maintained at 37±0.5°C at a speed of 100 rpm. At known regular intervals 5 ml of sample of dissolution medium were withdrawn by means of syringe fitted with pre-filter and analyzed for drug release by measuring the absorbance at 288 nm after suitable dilution with pH 7.2 phosphate buffer. The volume of dissolution fluid was adjusted to 900 ml by replacing each 5 ml aliquot withdrawn with 5 ml of pH 7.2 phosphate buffer. The *in vitro* release of marketed product was carried out in the similar manner and the results were compared with the best formulation.

IR SPECTRAL ANALYSIS

FTIR studies were done to detect the possible interactions between the drug and excipients. All the prepared samples were subjected to FTIR spectroscopic studies to determine drug-carrier interaction. FTIR spectra were recorded on samples prepared in potassium bromide (KBr) disks using Fourier Transform IR spectrophotometer (Perkin Elmer, RXi FTIR system).[11] Samples were prepared in KBr disks by means of a hydrostatic press. The scanning range was 400 to 470cm^{-1} and the resolution was 2cm^{-1}.

ACCELERATED STABILITY STUDIES

Stability studies:

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light, and to establish a re-test period for the drug substance or a shelf life for the drug product and recommended storage conditions. The choice of test conditions defined in this guideline is based on an analysis of the effects of climatic conditions in the three regions of the EC, Japan and the United States.[12] The mean kinetic temperature in any part of the world can be derived from climatic data, and the world can be divided into four climatic zones, I, II, III & IV.

This guideline addresses climatic zones I and II. The principle has been established that stability information generated in any one of the three regions of the EC, Japan and the United States would be mutually acceptable to the other two regions, provided the information is consistent with this guideline and the labelling is in according with national/regional requirements.

TABLE: NO. 4. CONDITION FOR STABILITY STUDIES

Study	Storage condition	Minimum time period covered by data at submission
Long term	25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH	12 months
Intermediate	30°C ± 2°C/65% RH ± 5% RH	6 months
Accelerated	40°C ± 2°C/75% RH ± 5% RH	6 months

Testing condition:

Accelerated**:** 40^0C ± 2^0C/75% RH ± 5% RH

Sampling period **:** 0, 3 and 6 month(s).

Evaluation studies for stability:

1. Color and appearance
2. Hardness
3. Disintegration time
4. *In-vitro* dissolution time.

MICROBIOLOGICAL ASSAY OF CEFIXIME[13]

It is based on the comparison of the inhibition of growth of bacteria by measured concentration of antibiotic under test with that produced by known concentration of standard preparation of antibiotics having known activity.

The antimicrobial susceptibility of Cefixime Dispersible Tablets was tested by **Kirby –Bauer antibiotic sensitivity test[14].** In this method filter paper discs of uniform size were impregnated with different concentrations of Cefixime and then placed on the surface of an agar plate that has been seeded with the organism to be tested. The efficacy of drug was determined by measuring the diameter of the zone of inhibition that results from diffusion of the drug into the medium surrounding the disc. The susceptibility of the organism to a drug was determined by the size of the zone.

Media: Mueller Hinton Agar No- 2**:** The media consists of Casein acid hydrolysate, Beef heart infusion, Starch soluble and Agar.[15]

Preparation of media: Suspend 38 grams of Muller Hinton Agar media in 1000 ml distilled water, mixed well and heated to boiling to dissolve the medium completely. Then it was sterilized by autoclaving at 15 lbs per square inch pressure at 121^0C for 15 minutes. [16]

Organisms: The test organisms[17] selected were Escherichia *coli, Bacillus subtilis* and *salmonella colony.*

Procedure:

1. Muller Hinton agar plates were prepared and labelled with name of test organism to be inoculated.
2. A sterile cotton swab was dipped into a well mixed saline test culture and excess inoculums were removed by pressing the saturated swab against the inner wall of the Culture tube.
3. Using the swab, the entire agar surface were streaked horizontally, vertically and around the outer edge of the plate to ensure a heavy growth over the entire surface and all culture plates were allowed to dry for about 5 minutes.
4. Using sterile techniques, 3 wells were made in each agar plate for blank (B) , 4 dilutions(10^{-1} to 10^{-4}).
5. Test sample was serially diluted in saline up to 10^{-4} dilutions.
6. 100 ml of blank and diluted sample was poured into respective wells and incubated at 30- 35°C for 24 hours.
7. After incubation the diameter of inhibition zone was measured and noted.[18]

RESULTS AND DISCUSSION

The present study was undertaken to formulate Cefixime dispersible tablets using two superdisintegrants such as Sodium starch glycolate and Croscarmellose sodium prepared by direct compression method with 3 different concentrations (3%, 6%, and 9%) of each superdisintegrant. Before compression the blend was subjected to various evaluation studies such as angle of

repose, bulk density, tapped density, compressibility index and Hausner ratio. After compression the following studies such as hardness, thickness, weight variation, disintegration test, water absorption test, drug content estimation, in-vitro release studies, microbiological studies and accelerated stability studies were carried out. All the results were presented in appropriate tables and figures.

PREFORMULATION STUDIES

The following Preformulation studies were preformed on Cefixime and excipients.

ORGANOLEPTIC PROPERTIES:

The Organoleptic properties like color, odor, and taste of the API were evaluated. The color of Cefixime was found to be white to off white powder, odourless and slight sour taste.

EVALUATION OF CEFIXIME (API)

A. Physical characteristics of API

TABLE: NO.5. PHYSICAL CHARACTERISTICS OF API

S.NO	TESTS	RESULTS
1.	Bulk Density	0.689±0.021g/cm^3
2.	Tapped Density	0.769 ±0.021g/cm^3
3.	Compressibility Index	10.344±0.2 %
4.	Hausner Ratio	1.115
5.	Angle of Repose	28^o.89$'$

The angle of repose was found to be 28^o.89$'$. The bulk density and tapped density was determined as 0.689±0.021g/cm^3 and 0.769 ±0.021g/cm^3. The Hausner ratio and compressibility index was found to be 1.115 and 10.344±0.2 %. The above results revealed that the blend evaluation parameters of API were found to be within the limits indicating good flow properties.

B. Particle Size distribution of API (PSD):

Initial weight of powder = 50gm

Final weight of powder = 49.69gm

$$\text{Percentage of drug passed} = \frac{\text{Amount of drug passed} \times 100}{\text{Initial weight}}$$

$$= \frac{49.69 \times 100}{50}$$

$$= 99.38\%$$

TABLE: NO.6. PARTICLE SIZE DISTRIBUTION

Sieve No.	Sieve Size (µ)	Quantity Retained(g)	% Retained	Cumulative %Retained
#20	850	0.00	0.00	0.00
#40	425	0.00	0.00	0.00
#60	250	3.98	8.01	8.01
#80	180	20.52	41.29	49.30
#100	150	0.980	1.97	51.27
Pan	-----	24.21	48.72	99.99

From the particle size analysis it was concluded that no particle was retained in any sieve. Almost 99.38% of drug passes through all sieves. Thus the particles size of the API was found to be less than 150µm.

SOLUBILITY:

Cefixime was found to be slightly soluble in water, freely soluble in methanol sparingly soluble in ethanol, insoluble in ethyl acetate. Solubility analysis is important because the drug has to dissolve in the solvents and also in the dissolution medium used.

PHYSICAL DRUG: EXCIPIENTS COMPATIBILITY STUDIES REPORT:

The drug excipients compatibility studies were performed by preparing blend of different excipients with drug and stored at 45^{o}C/ 75% RH for one month. The blend was evaluated for every 15 days for changes like caking, liquefaction, discoloration and odor formation.

TABLE: NO. 7. DRUG: EXCIPIENTS COMPATIBILITY STUDIES

S.NO.	COMPOSITION	DESCRIPTION		
		INITIAL PERIOD	2 WEEKS	4 WEEKS
1.	Cefixime	White to off White powder	NCC	NCC
2.	Cefixime+ Microcrystalline cellulose	White to off white powder	NCC	NCC
3.	Cefixime+ Croscarmellose sodium	White to off white powder	NCC	NCC
4.	Cefixime+Sodium Starch Glycolate	White to off white powder	NCC	NCC
5.	Cefixime+Aspartame	White to off white powder	NCC	NCC
6.	Cefixime+Sucralose	White to off white powder	NCC	NCC
7.	Cefixime+Colloidal Silicon dioxide	White to off white powder	NCC	NCC
8.	Cefixime+Magnesium stearate	White to off white powder	NCC	NCC
9.	Cefixime+Pineapple flavour	White to off white powder	NCC	NCC
10.	Cefixime+Tartrazine lake color	Pale yellow coloured powder	NCC	NCC

NCC: No characteristic change

From the drug excipients compatibility study, it was observed that there was no change or interaction between drug and excipients. Thus it was concluded that the excipients selected for the formulation were compatible with Cefixime.

Water content

The water content is determined titrimetrically by Karl Fischer titration.

$$\text{Water content} = \frac{\text{Titre volume} \times \text{Mean KF factor}}{10 \times \text{Weight of the sample}}$$

= 11.78%

DETERMINATION OF AMOUNT OF CEFIXIME TO BE USED IN A TABLET

The actual quantity of Cefixime to be used in preparation of a tablet containing 200 mg of Cefixime DT can be calculated from the assay value of the active ingredient and the water content by Karl-Fischer method.

Assay on anhydrous basis = 100.26%

Water content by KF titration = 11.78 %

Conversion factor = 1.134 %

Required dose = Label claim × Conversion factor
= 200×1.134
= 226.80mg

The required amount of Cefixime was calculated using the formula and was found to be 226.80 mg.

TABLE NO: 8. INNOVATOR PRODUCT EVALUATION REPORT

S.NO	PARAMETER	REPORT
1	Average weight	436 mg
2	Diameter (mm)	1.2 mm
3	Thickness (mm)	4.32 mm
4	Hardness:(Kg/cm^2)	10.4 kg/cm^2
5	Disintegration (Min)	23 seconds
6	Dispersibility	30 seconds
7	Drug content	95.70%
8	% drug release	
	After 15mnts	78.40 ± 0.825
	After 30mnts	84.90 ± 0.788
	After 45mnts	90.23 ± 0.923

TABLE: NO. 9. EVALUATION OF PRECOMPRESSION PARAMETERS

S. No	Formulation code	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Compressibility Index (%)	Hausner ratio	Angle of repose (θ)
1.	F1	0.597 (±0.004)	0.710 (±0.009)	15.910 (±0.005)	1.428 (±0.021)	32.42 (±0.068)
2.	F2	0.601 (±0.006)	0.705 (±0.007)	14.705 (±0.003)	1.172 (±0.017)	25.66 (±0.052)
3.	F3	0.556 (±0.003)	0.667 (±0.005)	16.670 (±0.009)	1.201 (±0.009)	31.56 (±0.061)
4.	F4	0.592 (±0.007)	0.719 (±0.004)	17.647 (±0.008)	1.124 (±0.012)	28.77 (±0.054)
5.	F5	0.588 (±0.009)	0.712 (±0.006)	17.410 (±0.021)	1.071 (±0.025)	27.23 (±0.062)
6.	F6	0.591 (±0.004)	0.718 (±0.002)	17.647 (±0.016)	1.214 (±0.018)	29.25 (±0.066)

***All values are expressed as mean ±SD, n=3**

The angle of repose was found to be between 25.66 (±0.052) and 32.42 (±0.068). The bulk density and tapped density values were found between 0.556 (±0.003) to 0.601(±0.006), and 0.667 (±0.005) to 0.719(±0.004) g/cm^3respectively. The compressibility index was found between 14.705 % (±0.003) and 17.647 %(±0.018) and the Hausner ratio was found to be in range of 1.071 (±0.025) and 1.172 (±0.017). The above results revealed that the blend evaluation parameters were found to be within the limits indicating good flow properties.

TABLE: NO.10. EVALUATION OF POST COMPRESSION PARAMETERS

S. No	PARAMETERS	F1	F2	F3	F4	F5	F6
1.	Average weight (mg)	451 (± 2.081)	449 (±0.572)	444 (±2.003)	445 (±1.004)	453 (±2.545)	454 (±1.56)
2.	Thickness (mm)	5.4 (± 0.012)	5.2 (± 0.034)	5.38 (±0.016)	5.28 (±0.028)	5.26 (±0.051)	5.42 (± 0.063)
3.	Hardness (kg/cm^2)	4.6 (± 0.153)	4.8 (± 0.116)	4.4 (± 0.509)	4.0 (± 0.259)	5.0 (± 0.166)	4.2 (± 0.303)
4.	Friability (%)	0.414 (± 0.041)	0.423 (± 0.032)	0.411 (± 0.013)	0.420 (± 0.044)	0.416 (± 0.015)	0.418 (± 0.066)
5.	Disintegration time (sec)	23 (±0.021)	13 (±0.015)	18 (±0.006)	22 (±0.041)	17 (±0.051)	20 (±0.011)
6.	Drug content (%)	99.82 (±1.051)	100.10 (±0.987)	99.05 (±0.198)	98.75 (±1.045)	99.45 (±0.997)	98.21 (±1.851)
7.	Wetting time (sec)	25 (±0.824)	15 (±0.324)	22 (±0.188)	24 (±0.623)	19 (±0.214)	21 (±0.126)
8.	Water absorption ratio (%)	99.763 (±1.23)	98.75 (±2.06)	107.43 (±1.87)	109.12 (±0.989)	99.45 (±1.02)	101.15 (±2.65)
9.	Fineness of dispersion	Passes	Passes	Passes	Passes	Passes	Passes

***All values are expressed as mean ± SD, n=3.**

The formulated tablets were evaluated for Organoleptic characters. All the tablets showed elegance in appearance. The average weight of all the formulations was found to be between 444 (± 2.003) to 454 (±1.56) mg. The thickness of the tablets was in the range of 5.2 (± 0.034) to 5.42 (± 0.063) mm. The prepared tablets in all the trials possessed good mechanical strength with sufficient hardness in the range of 4 (±0.259) to 5(± 0.166) kg/cm^2. The friability of the tablets were found to be within 1%. The disintegration of tablets containing Sodium starch glycolate as superdisintegrant were comparatively slower than the tablets containing Croscarmellose sodium. This may be due to wicking and swelling ability of Croscarmellose sodium. The percentage of drug content was found among different batches of the tablets and ranged from 98.21 (±1.851) to 100.10 (±0.987)% of which was within the acceptable limits. The wetting time of the tablets were reduced in tablets containing Croscarmellose sodium which may due to wicking effect of croscarmellose sodium. Water absorption ratio was found to be between 95 to 110% ± 2 %. In fineness of dispersion test the tablets from all formulations passed through sieve no.22. The post compression parameters were found to be within the pharmacopoeial limits.

TABLE: NO.12. *IN VITRO* DRUG RELEASE OF CEFIXIME FROM FORMULATIONS F1- F6

Time (mnts)	F1	F2	F3	F4	F5	F6
	3% CCS	6% CCS	9% CCS	3% SSG	6% SSG	9% SSG
15	79.46 (±1.293)	86.36 (±0.935)	83.12 (±1.263)	76.65 (±0.364)	82.16 (±0.102)	78.68 (±0.745)
30	83.88 (±1.872)	90.54 (±0.240)	86.22 (±0.133)	80.34 (±0.267)	85.32 (±0.348)	84.52 (±0.867)
45	89.34 (±0.681)	97.82 (±0.503)	91.44 (±0.610)	82.84 (±0.506)	90.98 (±0.434)	88.35 (±0.187)

***All the values are expressed as mean ±SD, n=6.**

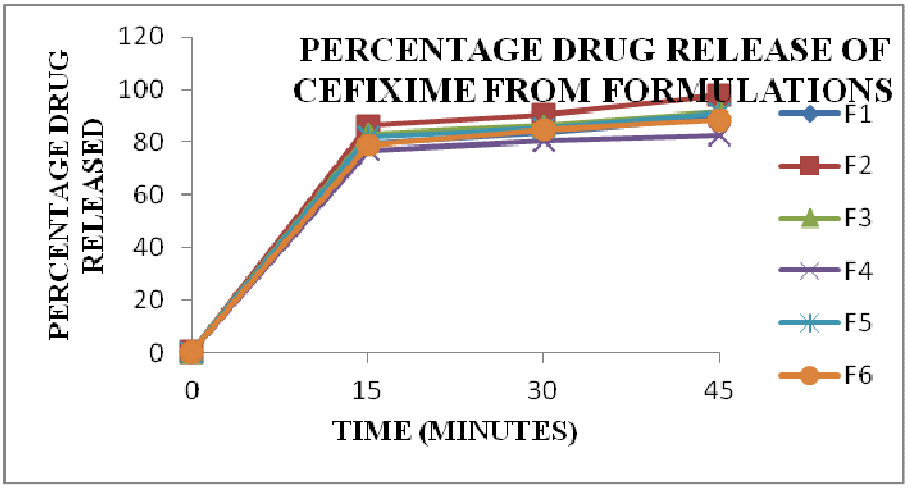


FIGURE: NO.1. PERCENTAGE DRUG RELEASE OF DRUG FROM FORMULATIONS

The dissolution study of Cefixime Dispersible tablets were prepared by direct compression method using superdisintegrants like sodium starch glycolate and Croscarmellose sodium and the results were compared. The drug release of trial F1, F2 and F3 containing 3%, 6% and 9% Crosscarmellose sodium as superdisintegrant was found to be 89.34% (±0.681), 97.82% (±0.503) and 91.44% (±0.610) respectively. The drug release of trial F4, F5 and F6 containing 3%, 6% and 9% sodium starch glycolate as superdisintegrant was found to be 82.84% (±0.506), 90.98% (±0.434) and 88.35% (±0.187) respectively. Among all these six trials , tablets prepared by using 3%, 6% and % Croscarmellose sodium showed a rapid drug release than the tablets prepared with sodium starch glycolate as superdisintegrant. It was observed that when Croscarmellose sodium is used as superdisintegrant, the tablet disintegrates rapidly within less time due to easy swelling ability of Croscarmellose sodium when compared to other tablets prepared by using Sodium starch glycolate. Croscarmellose sodium when comes in contact with water gets inflated and immediately burst out thereby releasing the drug in short duration of time. In all the six formulations, trial F2 containing 6% Croscarmellose sodium as disintegrant shows a rapid drug release. From the above results, 6% Croscarmellose sodium was found an optimum concentration in the formulation of Cefixime dispersible tablets by direct compression method. Based on the results trial F2 was considered as optimized formulation.

IR SPECTRAL ANALYSIS:

The FT-IR studies of pure Cefixime and superdisintegrants were carried out to study the interaction between the drug : superdisintegrants used. It was revealed that there was no difference in the position of absorption bands, hence providing evidence for the absence of interaction of drug with superdisintegrants.

FIGURE: NO. 2. IR SPECTRUM OF CEFIXIME

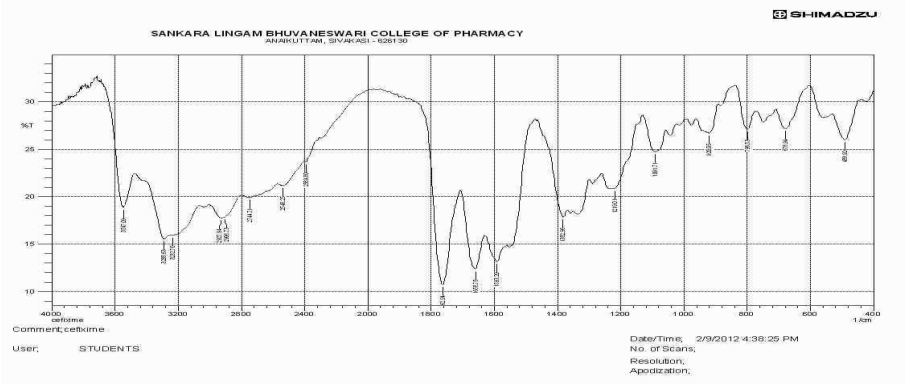


FIGURE: NO.3. IR SPECTRUM OF CEFIXIME-CCS

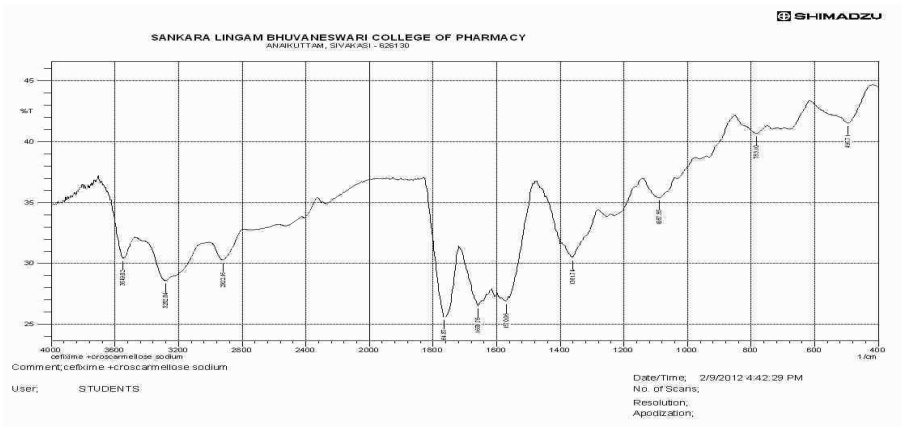
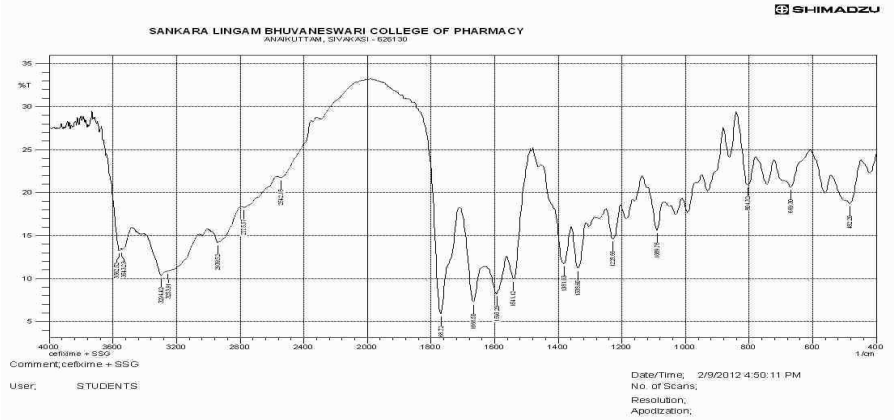


FIGURE: NO.4. IR SPECTRUM OF CEFIXIME- SSG



ACCELERATED STABILITY STUDIES:

The Accelerated Stability study was conducted for optimized formulation according to procedure described in the methodology. There was no significant changes in taste, color and odor at storage condition 40°C/75% RH. There was no significant variation in the *in vitro* dispersion time, disintegration time, drug content and *in vitro* dissolution profiles during the period of 3 months at 40°C/75% RH of the optimized formulation. The results are shown in table:

TABLE: NO.13. STABILITY STUDY RESULTS OF OPTIMIZED FORMULATION

PARAMETERS	STORAGE CONDITION: 40°C/75% RH			
	INITIAL PERIOD	1 MONTH	2 MONTH	3 MONTH
Color	White to off white color	White to off white color	White to off white color	White to off white color
Taste	Sweet	Sweet	Sweet	Sweet
Disintegration Time	14 (±0.015)	14.20 (±0.004)	14.32 (±0.012)	14.40 (±0.009)
Drug Content (%)	100.10 (±0.986)	100.08 (±0.122)	99.98 (±0.212)	99.95 (±0.185)
In vitro drug release after 45minutes (%)	97.82 (±0.504)	97.78 (±0.646)	96.88 (±0.787)	96.74 (±0.623)

The stability study of Cefixime dispersible tablets were carried out at 40°C/75% RH for a period of three months. The result reveals that there was no change in color, disintegration time, drug content and *in vitro* drug release.

TABLE: NO. 15. ANTIMICROBIAL ASSAY OF CEFIXIME OPTIMIZED FORMULATION (F2)

S.NO	ANTIBIOTIC	CONCENTRATION (µ/ml)	ZONE OF INHIBITION DIAMETER (mm)		
			Bacillus subtilis	*Escherichia Coli*	*Salmonella colony*
1.	Blank	-	-	-	-
2.	Cefixime DT	2	30	-	40
3.	Cefixime DT	20	25	-	34
4.	Cefixime DT	200	-	28	-
5.	Cefixime DT	2000	-	23	-

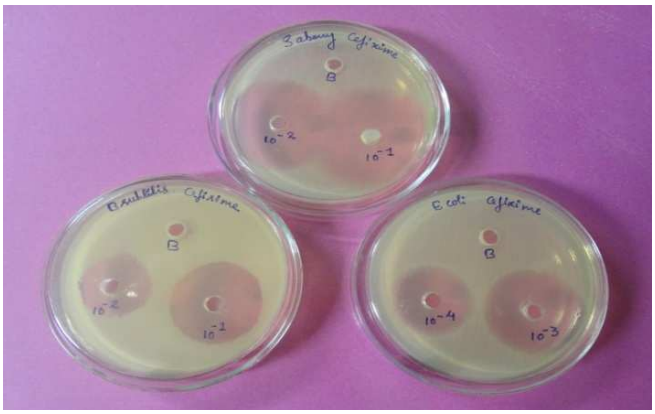


FIGURE: NO. 5. ANTIMICROBIAL ACTIVITY OF DRUG AGAINST *BACILLUS SUBTILIS, E.COLI, SALMONELLA COLONY*

The results show that the zone of inhibition is increases with increase in concentration of Cefixime. The formulation (F2) exhibited good antimicrobial activity against *Bacillus subtilis, Salmonella colony* & *Escherichia coli.*

SUMMARY AND CONCLUSION

Cefixime is a third generation cephalosporin antibiotic. It is widely used in the treatment of typhoid fever, uncomplicated cervical/ urethral gonorrhoea and otitis media. Drug administration for elderly patients and paediatric patients has become more important due to decline in swallowing ability in the form of conventional tablets. The formulation of dispersible tablets was aimed to administer in a more palatable form by dispersed in water to obtain a dosage form especially for paediatric patients, dysphagic patients, mentally ill and nauseated patients, those with motion sickness, sudden episodes of allergic attack or coughing.

- Under the preformulation studies API characterization and drug excipients compatibility studies were carried out.
- Cefixime dispersible tablets were prepared by direct compression method using croscarmellose sodium and sodium starch glycolate as superdisintegrants in different concentrations.
- The prepared powder blend was evaluated for precompression parameters like angle of repose, bulk

density, tapped density, Hausner ratio and compressibility index. The results obtained indicate that it has good flow property for direct compression technology.

- The prepared tablets were evaluated for weight variation, hardness, and thickness, wetting time, water absorption ratio, friability, drug content, disintegration time and *in vitro* drug release. All these parameters were found to be within the pharmacopoeial limits.
- The obtained data suggested that the formulation containing croscarmellose sodium as superdisintegrant shows better wetting time, water absorption ratio, disintegration time and dissolution studies compared to sodium starch glycolate as superdisintegrant. The results show that the dispersible tablets prepared by using croscarmellose sodium were more superior as compared to sodium starch glycolate.
- Out of six formulations, the formulation F2 containing 6% croscarmellose sodium showed 97.82% (±0.503) drug release after 45 minutes. So the trial F2 was considered as the optimized formulation.
- Comparative *in vitro* dissolution study of optimized formulation (F2) and marketed product shows that the percentage drug release of optimized formulation was rapid (97.82 % ± 0.503) compared to the marketed product (90.23 % ± 0.921) after 45 minutes.
- IR spectroscopic analysis of drug with superdisintegrants was shows that the drug was compatible with superdisintegrants which was used in the formulation.
- The accelerated stability studies of optimized formulation (F2) at 40°C/75% RH for a period of 3 months indicated that there were no significant changes in taste, color, *in vitro* dispersion time, disintegration time, drug content and in *vitro* dissolution profiles. The result shows that the formulation (F2) was stable.

The antimicrobial activity of the optimized formulation (F2) shows good antimicrobial activity against Bacillus *subtilis, Salmonella colony* & *Escherichia coli.*

CONCLUSION

From all the above observations it was concluded that the formulation F2 containing 6% Croscarmellose sodium was better one compared to other formulations. Due to the rapid disintegration of tablets they can be ingested as a solution after dispersing in water especially for administration to paediatric patients. Thus the study concluded that dispersible tablets of Cefixime can be successfully prepared by direct compression technique using selected superdisintegrant for better patient compliance and effective therapy.

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