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Research Article

FORMULATION AND EVALUATION OF CEFIXIME TRIHYDRATE ORAL DISINTEGRATING AGENTS

T.SATYANARAYANA[1*], M.SRAVANTHI[1], P.SURESH KUMAR[1], S.NAVANEETHA KRISHNAN[1], G.SHAJI[1]

[1]Browns College of Pharmacy, Khammam, Andhra Pradesh, India. Email: drtsatya@gmail.com

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ABSTRACT

Oral disintegrating tablets have emerged as an alternative to the conventional oral dosage forms to improve the patient compliance. As the two extreme end age group (paediatric and geriatric) complain about the swallowing of conventional oral solid dosage forms. It became necessary to develop a dosage form which is patient friendly. The ODT's developed here are solid dosage forms that dissolve or disintegrate rapidly in the oral cavity. This results in solution or suspension without the need of water. The main objective of this work is to formulate and evaluate cefixime trihydrate ODT's using different concentration of superdisintegrating agents like croscarmellose sodium (CCS), Sodium Starch Glycolate (SSG). Tablets were prepared by direct compression method and evaluated for hardness, thickness, friability, disintegration time, and percentage of drug release. FT-IR studies revealed that there was no interaction between cefixime trihydrate and the excipients used in the study. The results indicated that formulation prepared with croscarmellose sodium was found to be optimised, which provides maximum drug release (97.3%) and minimum disintegration time (less than 30 second).

Keywords: Cefixime trihydrate, Oral disintegrating tablets, Superdisintegrant, Croscarmellose Sodium, Sodium Starch Glycolate.

INTRODUCTION

In recent years, considerable attention has been focused on the development of novel drug delivery systems (NDDS). The reason for this paradigm shift may be due to relatively low development cost and time required for introducing a NDDS ($ 20-50 million and 3-4 years respectively) as compared to a new chemical entity (approximately $500 million and 10-12 years, respectively). In the form of NDDS, an existing drug molecule can get a 'new life', thereby increasing its market value, competitiveness, and patent life 1.

Tablet is most popular among all dosage forms existing today because of convenience of self-administration, compactness and easy manufacturing. However, patients especially elderly find it difficulty in swallowing tablets, capsules, fluids and thus do not comply with prescription which results in high incidence of noncompliance and ineffective therapy[2] .Patient convenience and compliance oriented research has resulted in bringing out many safer and newer drug delivery systems. Mouth Fast disintegration or dissolving tablets are of such examples, for the reason of rapid disintegration or dissolution in mouth with little amount of water or even with saliva[3]. Significance of this drug delivery system includes administration without water, accuracy of dosage forms, ease of portability, alternative to liquid dosage forms, ideal for pediatric and geriatric patients and rapid onset of action. Usually superdisintegrants are added to a drug formulation to facilitate the break-up or disintegration of tablet into smaller particles that can dissolve more rapidly than in absence of disintegrants[4].

Cefixime is used to treat infections caused by bacteria such as pneumonia, bronchitis, gonorrhoea, and ear, lung, throat, and urinary tract infections [5, 6] .The aim of the study was to formulate an oral disintegrating tablet of cefixime trihydrate using two superdisintegrants separately (croscarmellose sodium and sodium starch glycolate), and to select the best among the two, based on the disintegration time and other tableting properties.

MATERIALS & METHODS

Materials

Cefixime trihydrate was obtained as gift sample from Dr. Reddys laboratory, Hyderabad. Croscarmellose sodium (CCS) and Sodium Starch Glycolate (SSG) was obtained as gift samples from Madras Pharmaceuticals, Chennai. All chemicals used were of analytical grade.

Methods

Preparation of orally disintegrating tablet

Cefixime oral disintegrating tablets were prepared by direct compression method according to the formula. A total number of ten formulations were prepared. All the ingredients were passed through 60-mesh sieve separately and collected. The drug and microcrystalline cellulose were mixed in small portion of both at each time and blended to get a uniform mixture and kept aside. Then the ingredients were weighed and mixed in geometrical order and tablets were compressed to get a tablet of 285 mg weight using a Cadmach 12 station tablet compression machine. Table 1, 2.

Evaluation of blends[7]

Prior to the compression of both granules into tablets, the granules were evaluated for properties like Angle of repose, Bulk density, Tapped density, Compressibility and Hausner's ratio.

Table 1: Formulation of cefixime with sodium starch glycolate

Ingredients	SF1(mg)	SF2(mg)	SF3(mg)	SF4(mg)	SF5(mg)
Cefixime trihydrate	55.90	55.90	55.90	55.90	55.90
Microcrystalline cellulose	216.3	212.3	--	--	219.3
Pregelatinized Starch	--	----	216.3	212.3	-----
Sodium Starch glycolate	8.0	12	8.0	12	5.0
Magnesium Stearate	1.60	1.60	1.60	1.60	1.60
Talc	3.20	3.20	3.20	3.20	3.20
Average weight (mg)	285	285	285	285	285

Table 2: Formulation of cefixime with Croscarmellose sodium

Ingredients	CF6 (mg)	CF7(mg)	CF8(mg)	CF9(mg)	CF10(mg)
Cefixime trihydrate	55.90	55.90	55.90	55.90	55.90
Microcrystalline cellulose	216.3	212.3	--	--	219.3
Pregelatinized Starch	--	----	216.3	212.3	-----
Croscarmellose sodium	8.0	12	8.0	12	5.0
Magnesium Stearate	1.60	1.60	1.60	1.60	1.60
Talc	3.20	3.20	3.20	3.20	3.20
Average weight (mg)	285	285	285	285	285

Evaluation of tablets [8,9,10]

Thickness

Thickness was determined for twenty pre-weighed tablets of each batch using a digital vernier scale (Mitutoyo- Digital) and the average thickness was determined in mm**.** The tablet thickness should be controlled within a ± 5% variation of a standard.

Hardness

Hardness or crushing strength is the force required to break a tablet in diametric compression.

Hardness of the tablets is determined by Monsanto hardness tester which consists of a barrel with a compressible spring. The pointer moving along the gauze in the barrel at which the tablet fractures indicates the hardness of the tablet. Six tablets from each batch were taken randomly and their hardness was determined.

Friability

This test is performed to evaluate the ability of a tablet to withstand abrasion in packing, handling and transporting purpose. Twenty sample tablets were rotated at 25rpm for 4 minutes by a USP-type Roche friabilator, then reweighed after removal of fines and the percentage weight loss was calculated according to the following formula. The tablets were found to pass the friability test, if the percentage weight loss was found to be less than 1%.

$$\% \text{ Friability} = (W_0 - W)/W_0 \times 100$$

Where W_0 =initial weight of twenty tablets

W= weight of 20 tablets after 100 revolutions

Disintegrating Time

The disintegration test is carried out in an apparatus (Electro lab, Mumbai) containing a basket rack assembly with six glass tubes of 7.75 cm in length and 2.15 mm in diameter, the bottom of which consists of a #10 mesh sieve. The basket is raised and lowered 28-32 times per minute in a medium of 900 ml which is maintained at 37±2 °C. Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the mesh (#10) was considered as the disintegration time of the tablet. The disintegration time that patients can experience for oral disintegrating tablets ranges from 5 to 30 sec.

Water absorption ratio

A piece of tissue paper folded twice was placed in a small Petri dish containing 6ml of water.

The weight of the tablet prior to placement in the Petri dish was noted (Wb) utilizing a Shimadzu digital balance. The wetted tablet was removed and reweighed (Wa). Water absorption ratio, R, was then determined according to the following equation.

$$R = 100 \times (Wa - Wb) / Wb$$

Where Wb and Wa are tablet weights before and after water absorption, respectively.

Wetting Time

Five circular tissue papers were placed in a Petri dish of 10 cm diameter. Ten milliliters of water containing 0.5% nigrosine, a water-soluble dye, was added to the Petri dish. The dye solution was used to identify complete wetting of the tablet surface. A tablet was carefully placed on the surface of the tissue paper in the petridish at 250^0C. The time required for water to reach the upper surface of the tablets and to completely wet them was noted as the wetting time. This test was carried out in replicate of three. Wetting time was recorded using a stopwatch.

Dissolution study

Dissolution study was carried out by using USP Type II dissolution apparatus. The dissolution was carried out in pH 7.2 buffer solution as dissolution medium. 5ml sample where collected at 5, 10, 15,20,25,30 and 45 minutes time intervals and after proper dilution they were analysed at 280nm against the blank pH 7.2 buffer solutions using an Elico UV Double beam Spectrophotometer.

FT-IR Spectroscopy Study

The IR spectra of Cefixime trihydrate pure drug and physical mixture of optimised formulation were recorded from 400 to 4000^{-1} on FT-IR spectrophotometer.

RESULT AND DISCUSSION

Oral disintegrating tablets Cefixime trihydrate were prepared by direct compression method using Croscarmellose sodium (CCS) and Sodium Starch Glycolate (SSG) as superdisintegrants in different concentration. A total of ten formulations i.e. (SF_1 to SF_5) Sodium Starch Glycolate and (CF_6 to CF_{10}) Croscarmellose sodium were prepared.

The powder blend of ten formulations (SF_1 to SF_5) & (CF_6 to CF_{10}) was evaluated for Angle of repose, Bulk density, Tapped density, Compressibility and Hausner's ratio, which showed the pre-compressed blend, has good flow property. The results are shown accordingly in Table 3, 4.

Table 3: Physicochemical evaluation of the formulations with sodium starch glycolate

Parameters	SF1	SF2	SF3	SF4	SF5
Angle of repose	28.4	28.3	28.2	28.2	28.1
Bulk density	0.5820	0.5810	0.580	0.5794	0.5786
Tapped density	0.7206	0.720	0.7204	0.7192	0.7208
Carr's Compressibility index	19.8	19.6	19.6	19.6	19.4
Hausner ratio	1.26	1.25	1.26	1.24	1.19

Table 4: Physicochemical evaluation of the formulations with croscarmellose sodium

Parameters	CF6	CF7	CF8	CF9	CF10
Angle of repose	26.1	24.3	25.5	25.1	25
Bulk density	0.5186	0.5178	0.5174	0.5196	0.5166
Tapped density	0.6588	0.6542	0.6556	0.6546	0.6508
Carr's Compressibility index	21.66	21.64	21.62	21.6	21.58
Hausner's ratio	1.30	1.28	1.30	1.26	1.26

The values of different physical tests are given in Table 5, 6. The tablets obtained had drug contents in the range of 98 to 100%. This is within the acceptable limit. Hardness of tablet was found to be in the range of 2.5 to 3.30 kg/cm². Friability was found to be below 1% which indicates good mechanical strength of the tablets. Water absorption ratio and wetting time which are critical parameters for evaluation of performance of ODT's were found to be in the range of 30 to 50 second respectively. All the formulations found to have much faster wetting time when compared to the control with significant increase in the water absorption capacity. The disintegration time (DT) for the formulation prepared with Sodium Starch glycolate (SF_1 to SF_5) was found to be in the range of 40-56 second. In case of formulation prepared with Croscarmellose sodium (CF_6 to CF_{10}) the DT was found to be 30-57 second. Among all the formulations CF_6 were showing promising results as the DT was 30 second. The results are shown in Fig 1, 2.

Table 5: Evaluation of tabletting parameters of sodium starch glycolate

Tablet Parameters	Formula SF1	Formula SF2	Formula SF3	Formula SF4	Formula SF5
Thickness (cm)	0.40	0.37	0.38	0.38	0.39
Hardness (kg/cm2)	3.0	2.90	3.10	3.20	2.80
Friability (%)	0.75	0.78	0.76	0.774	0.764
Disintegration Time	46	40	55	56	52
Wetting Time	40	35	48	47	44
Water absorption Ratio	142	148	151	143	138

Table 6: Evaluation of tabletting parameters of croscarmellose sodium

Tablet Parameters	Formula CF6	Formula CF7	Formula CF8	Formula CF9	Formula CF10
Thickness (cm)	0.39	0.40	0.37	0.39	0.38
Hardness (kg/cm2)	3.30	3.10	3.20	3.20	2.90
Friability (%)	0.73	0.743	0.753	0.742	0.740
Disintegration Time	30	36	48	51	57
Wetting Time	24	22	37	42	46
Water Absorption Ratio	122	113	126	132	130

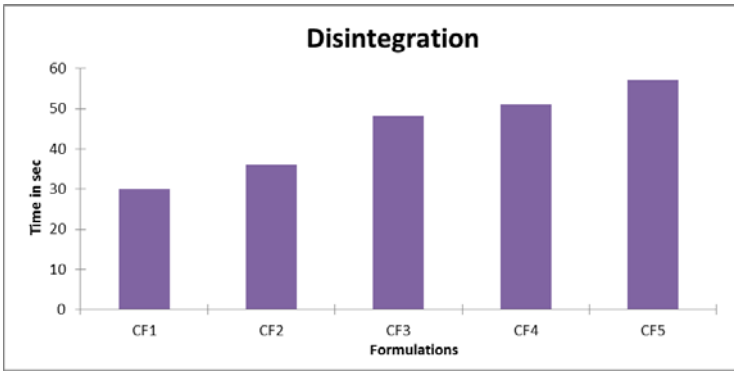

Fig. 1: Disintegration profile of Sodium starch glycolate

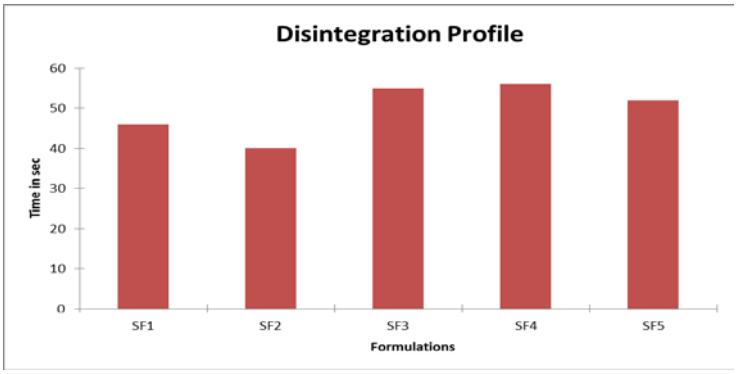

Fig. 2: Disintegration profile of Sodium starch glycolate

In-vitro drug release studies were performed with all formulations. The results are accordingly tabulated in Table 7, 8 and Fig 3, 4. The percentage drug release for the formulation (CF_6) was found 93.7% respectively at the end of 45 minutes. Formulation (CF_6) prepared with Croscarmellose sodium was found to be the optimised formulation.

Table 7: Dissolution profile of the formulations

Formula Dissolution %in 45minutes	SF1	SF2	SF3	SF4	SF5
	84.2	95.3	90.6	86.4	84.3

Table 8: Dissolution profile of the formulations

Formula Dissolution %in 45minutes	CF6	CF7	CF8	CF9	CF10
	97.30	90.5	82.6	84.5	90.6

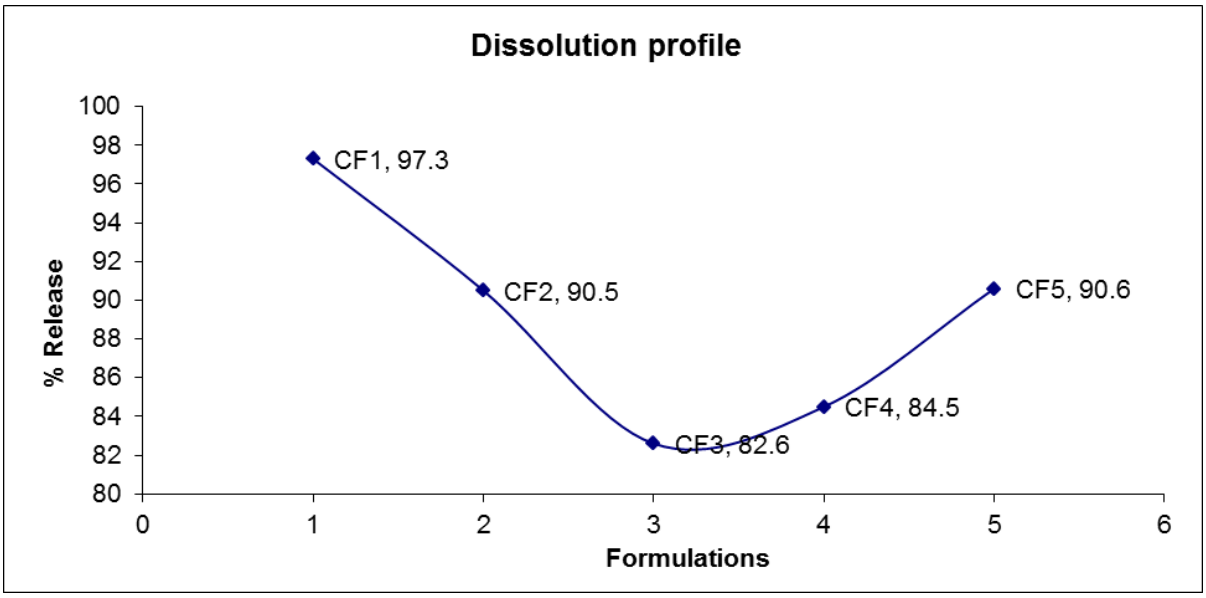

Fig. 3: Dissolution profile of Croscarmellose sodium

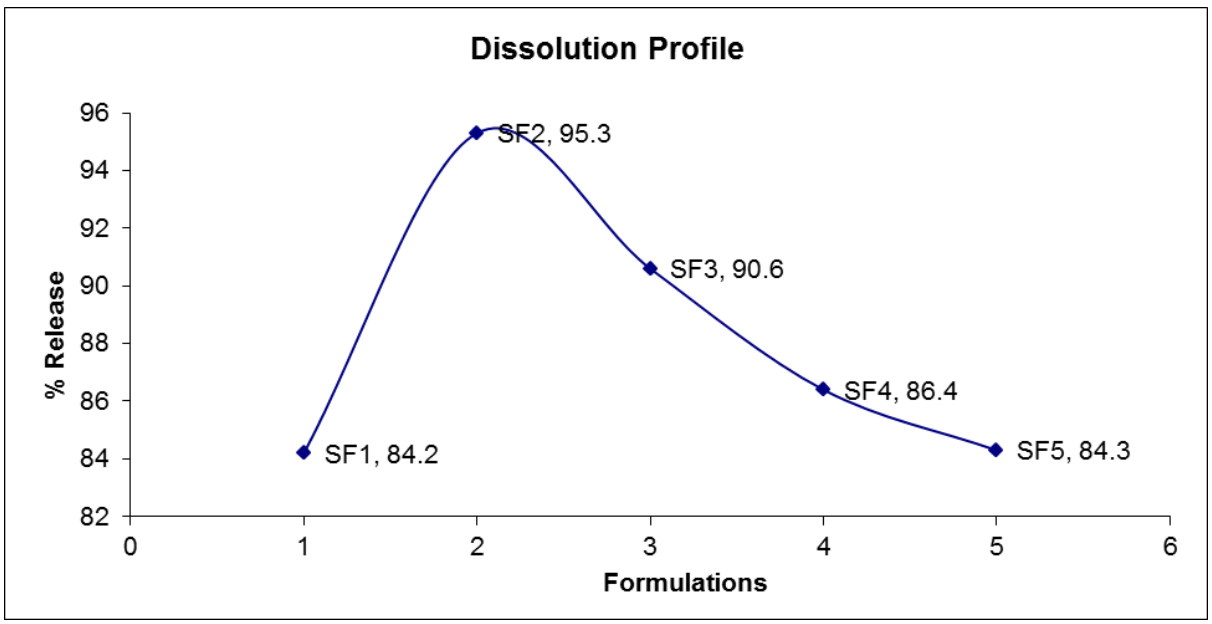

Fig. 4: Dissolution profile of Sodium starch glycolate

The FT-IR spectra are shown as Fig. 5, 6. Based on this study we can state that there is no interaction between Cefixime trihydrate and Croscarmellose sodium used in this study, as there is no change or shift in the characteristic peak of drug.

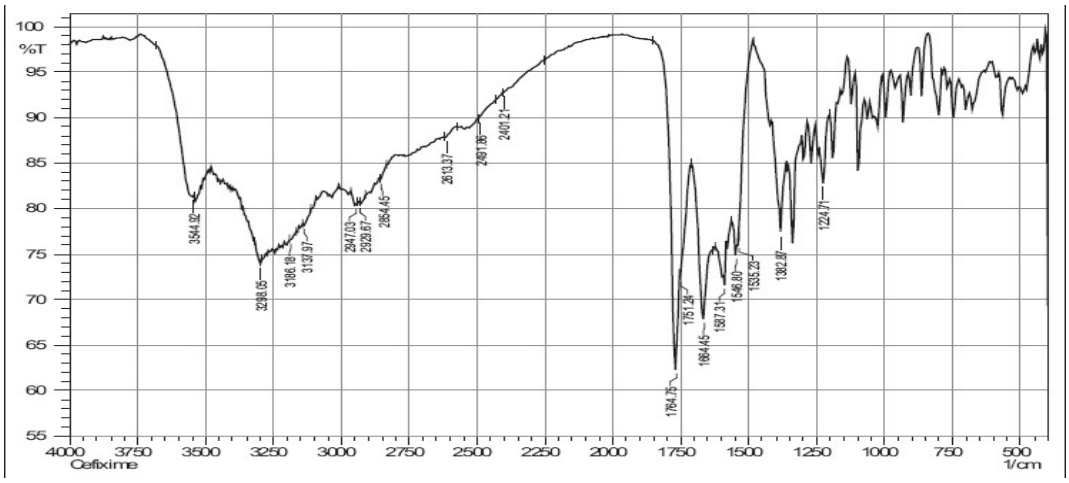

Fig. 5: FTIR spectra of the pure drug

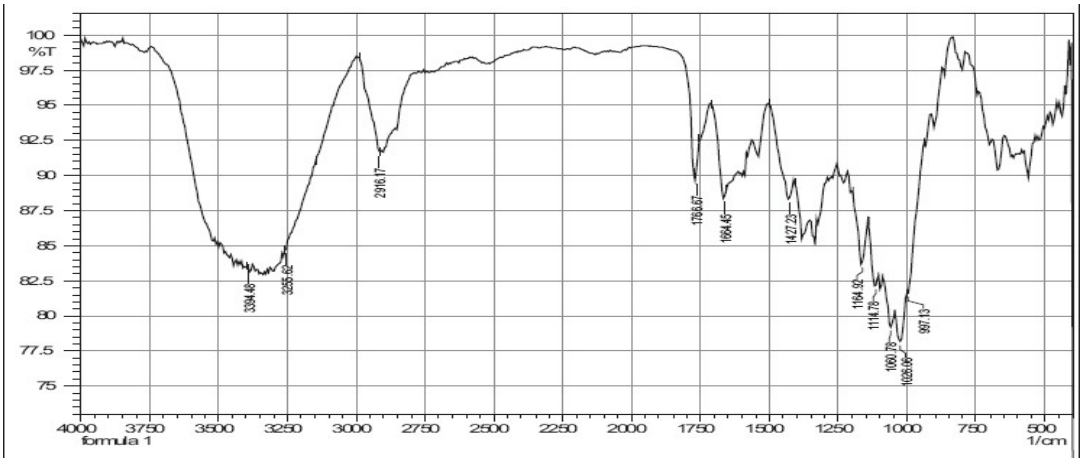

Fig. 6: FTIR spectra of the optimized formula

CONCLUSION

The prime objective of the study was to develop Cefixime trihydrate ODT by using commonly available excipients and conventional technology. From the above study it was concluded that, by employing commonly available excipients such as super disintegrants, hydrophilic excipients and proper filler an oral disintegrating tablet of Cefixime trihydrate can be developed. This can be accordingly commercialized.

ACKNOWLEDGEMENT

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