CODEN (USA): IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.546396

Available online at: http://www.iajps.com *Research Article*

ENHANCEMENT OF SOLUBILITY AND DISSOLUTION RATE OF CEFDINIR USING SOLID DISPERSIONS

Lakshmanarao. P *, Prasada Rao. M , Krishnaveni T , Sukanya. B , Lakshmi Priya. P , Sai Krishna. A

Department of Pharmaceutics, M.A.M College of Pharmacy, Narasaraopet, Guntur (Dt), Andhra Pradesh, India.

Received: 20 March 2017 **Accepted:** 26 March 2017 **Published:** 28 March 2017

Absrtact:

The purpose of this study is to enhance solubility and dissolution rate of poorly water soluble drug. Several techniques such as micronisation, cyclodextrin-complexation, use of surfactants, solubilizers and super disintegrants, solid dispersion in water soluble and water dispersible carriers, microemulsions and self emulsifying micro and nano disperse systems have been used to enhance the solubility and dissolution rate of poorly water soluble drugs. Among the various approaches solid dispersion technique is most widely used. Cefdinir is a drug of choice for solubility and dissolution enhancement. Solid dispersions were prepared by solvent evaporation method and melt fusion method using polyethylene glycol 3350 and PVP-K30 as hydrophilic carriers. The prepared solid dispersions were evaluated in terms of drug content, % yield and in-vitro dissolution study. In-vitro release profiles of all dispersions were comparitively evaluated and also studied against pure cefdinir. The results obtained showed that the rate of dissolution of cefdinir was considerably improved when formulated in solid dispersions as compare to pure drug.

Key Words: *Poorly water drug, Solvent evaporation, In-vitro dissolution study, Cefdinir.*

Corresponding author:

Lakshmana Rao. P,
Assistant Professor,
M.A.M College of Pharmacy,
Naarasaraopet,
Mob: 8019809126,
Email-Id: potti.lakshman@gmail.com

QR code

Please cite this article in press as Lakshmana Rao P et al, ***Enhancement of Solubility and Dissolution Rate of Cefdinir using Solid Dispersions****, Indo Am. J. Pharm. Sci, 2017; 4(03).*

INTRODUCTION:

Cefdinir is a third generation oral cephalosporin antibiotic; it is chemically(6R,7R)-7-[(2Z)-2-(2-amino-1,3-thiazol-4-yl)-2-hydroxy imino acetyl)amino]-3-ethyl-8 oxo-5-thio-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. Cefdinir is used for the treatment of the respiratory, skin, soft tissue and ENT infections [1]. Cefdinir is a BCS Class-IV drug with low solubility and low permeability characteristics. Class-IV drugs slowly dissolve in the aqueous environment of the Gastro-intestinal track after oral administration and result in a poor bioavailability, while increasing the dissolution rate will also improve bioavailability [2-4].

Applications of solid dispersions are one of the strategies to increase the dissolution rate of drugs [5, 6]. Solid dispersions consist of two (or more) component systems in which the drug is dispersed monomolecularely (or) as small particles in a hydrophilic matrix. Increased dissolution rate of cefdinir may be due to increase in wetting, hydrophilic nature of the carriers as well reduction in drug particle size. It is possible to improve it's bioavailability by increasing it's aqueous solubility [7, 8]. Solid dispersion techniques have been extensively used to increase the solubility of poorly water-soluble drug. Solid dispersion (SD) is a liable and economic method to enhance the bioavailability of poorly water soluble drug and also it overcomes the limitations of approaches [9, 10].

Standard Calibration Curve of Cefdinir:

Accurately weighed 100mg of cefdinir was dissolved in small amount of 0.1N Hcl and volume make up was done by 0.1N HCl in 100ml calibrated volumetric flask and fill upto the mark to get a concentration of 1 mg/ml (stock-I). The stock-I solution was further diluted to get a solution of concentration 20µg/ml (stock-II). From the stock-II, a series of these dilutions were taken at 286 nm in UV spectrophotometer by using 0.1N HCl as blank. The method obeyed Beer·s law in the concentration range of 0-14 µg/ml shown in table 2 and figure 1..

MATERIALS:

Cefdinir was a gift sample obtained from M/s Hetero Drugs Ltd., Hyderabad. PVP K-30 and PEG 3350 were procured from SD Fine Chemicals Ltd., Mumbai. All other reagents and solvents were of analytical grade.

Solubility Study:

An excess quantity of cefdinir was placed in 20ml capacity volumetric flask containing 20ml of different solutions (Dis.water, 0.1N Hcl and phosphate buffer p^H 6.8). After 15 days sample was sonicated for 10 min at room temperature. The solution was then passed through a Whatman filter paper (Grade-1) and the amount of drug dissolved was analysed spectrophotometrically (UV DOUBLE BEAM SPECTROPHOTOMETER-SYSTRONICS) at 286 nm after suitable dilution. Absorbance was recorded after proper dilution. All solubility measurements were performed three times.

METHOD:

Formulations:

Solid dispersion prepared with Drug with PEG 3350 and Drug with PVP K-30 in different weight ratios 1:1, 1:2, 1:3 & 1:4 shown in table 1.

Table 1: Formulation of Cefdinir Solid Dispertions

Formulation Code	Composition	Ratio (Drug:Carrier)
F_1	Cefdinir + PVP-K30	1:1
F_2	Cefdinir+ PVP-K30	1:2
F_3	Cefdinir+ PVP-K30	1:3
F_4	Cefdinir+PVP-K30	1:4
F_5	Cefdinir+PEG 3350	1:1
F_6	Cefdinir+PEG3350	1:2
F_7	Cefdinir+PEG 3350	1:3
F_8	Cefdinir+PEG 3350	1:4

Table 2: Calibration Curve for the Estimation of Cefdinir in 0.1 N HCl (N=3)

Concentration(µg/ml)	Absorbance ± S.D.*
2	0.129±0.03
4	0.312±0.04
6	0.414±0.05
8	0.513±0.04
10	0.636±0.06
12	0.777±0.05
14	0.907±0.04

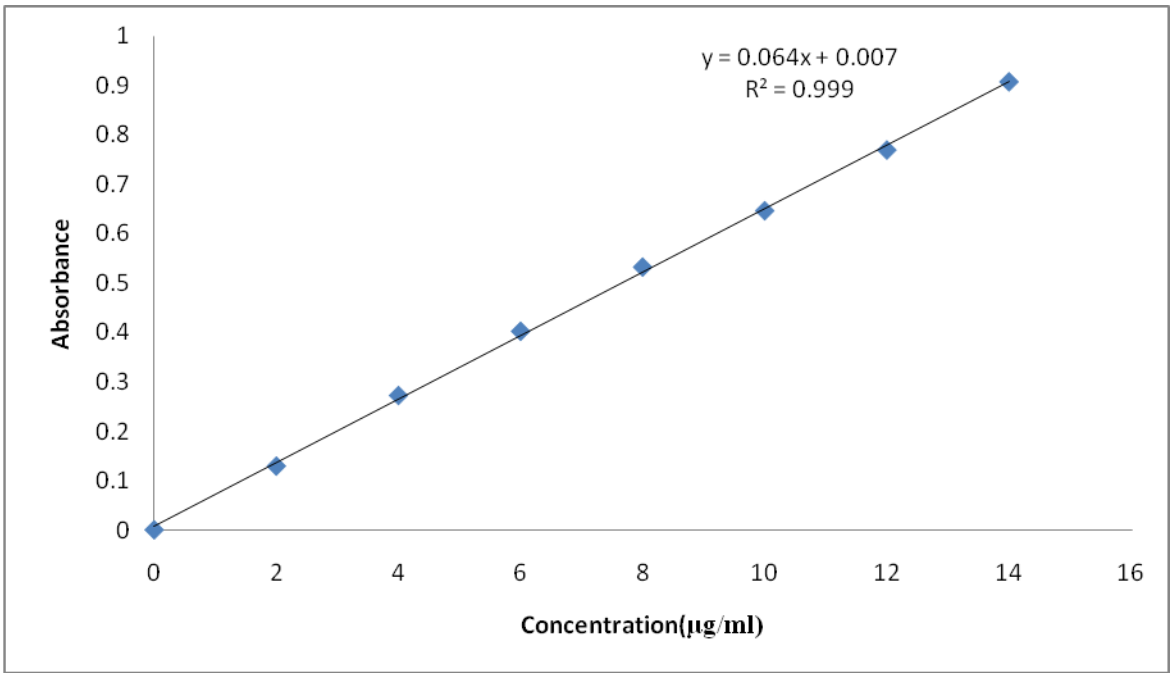

Fig.1: Calibration Curve for the Estimation of Cefdinir in 0.1N HCl

Solvent Evaporation Method:

The SD was prepared by solvent evaporation method. Different SD formulations were prepared with varying ratios of drug to PVP K-30 from 1:1 to 1:4 (F-1 to F-4). Formulations were dissolved in sufficient amount of ethanol and sonicator for 15 min and evaporated ethanol at 40^0c by magnetic stirrer leaving solid residue.

Melt-Fusion Method:

As PEG 3350 has a melting point range of 54-58^0c and therefore SD's were prepared by melt-fusion method with different concentrations of cefdinir (1:1,1:2,1:3,1:4) by melting physical mixture of drug and PEG 3350 on a water bath at 90^0c. The mixture was stirred and the resulting homogenous preparations rapidly cooled over ice bath.

Subsequently, the dispersions were pulverized, poured through a 355µm sieve, and then stored in a desicator at room temperature until use.

Evaluation of Cefdinir solid dispersions

Perecent Practical yield

Perecent Practical yield were calculated to know about percent yield of the method, thus it helps in selection of appropriate method of production. Solid dispersion were collected and weighed to determine from the following equation.

Practical yield(%)=[Practical Mass(Solid dispersion)/ Theoretical Mass(Drug + Carrier)]×100

Drug content

The solid dispersions equivalent to 300 mg of model drug were taken and dissolved separately in 100 ml of methanol. The solutions were filtered and were diluted such that the absorbance falls within the range of standard cure. The absorbances of solutions were determined at 286 nm by UV-Visible spectrophotometer. The actual drug content was calculated using the following equation as follows:

$$\% \text{ Drug content} = \frac{\text{Actual cefdinir content in weight quantity of solid disperson} \times 100}{\text{Theoretical amount of cefdinir solid dispersion}}$$

***Invitro* Dissolution Studies**

Dissolution rate of cefdinir as such and from various solid dispersions was studied using USP Type II rotating paddle apparatus (LABINDIA DISSO 2000). The dissolution rate was studied by placing cefdinir 300 mg (or) solid dispertion equivalent to 300 mg on the surface of dissolution medium [900ml of phosphate buffer, p^H 6.8], maintained at 37± 0.5^0c with a speed of 50rpm. A 5ml aliquot was withdrawn at different time intervals, filtered (through 0.45µ) and replaced with 5ml of fresh dissolution medium. The samples were estimated for dissolved cefdinir by measuring absorbance at 286nm. The dissolution experiments were conducted in triplicate.

RESULTS AND DISCUSSIONS:

Solid dispersion of cefdinir were prepared by solvent evaporation and melt fusion method using carriers like PVP K-30 and PEG 3350. In this present work, total 8 formulations were prepared and their complete detail shown in Table1.

Solubility Study:

The solubility of cefdinir in water at 37± 1^0c was found to be 0.23± 0.061mg/ml, which is in agreement with the previous article. The solubility of values of cefdinir in 0.1N Hcl and phosphate buffer (p^H 6.8) were observed to be approximately 0.11± 0.046mg/ml and 1.651± 0.63 respectively. The p^H of the solution had a significant effect on the solubility of cefdinir. The solubility of cefdinir in water, 0.1N Hcl and phosphate buffer (pH 6.8) are shown in table 3.

Table 3: Solubility Profile of Cefdinir

S.No	Solvents	Solubility ± S.D* (mg/ml)
1.	Dist. Water	0.10±0.01
2.	0.1N Hcl	0.59±0.01
3.	6.8 pH phosphate buffer	0.73±0.02

***N=3**

Perecent Practical yield

The results of perecent yield of cefdinir SDs. The perecent practical yield of the prepared solid dispersion was found in the range of 86.50 - 97.53%.The maximum yield was found 97.53% in F6 formulation.

Drug content

The drug content of the prepared Solid dispersions were in the range of 86.37 – 100.02% indicating the application of the present methods for the preparation of Solid dispersions with high content uniformity. The maximum % drug content was found 100.02% in F6 formulation.

Dissolution Studies

Dissolution of cefdinir from its pure was about 10.45 % in 60 minutes shown in table 4. Solid dispersion brings the drug in close contact with the hydrophilic carrier. The increased dissolution rate can thus be explained as being due to increased wettability and dispersibility of cefdinir. Dissolution profiles of cefdinir SDs are shown in Tables 5&6. The solid dispersions of cefdinir prepared by different methods showed improved dissolution when compared with pure cefdinir (Fig 2 & Fig 3). SDs with Drug: PVP K-30 for ratio 1:1, 1:2, 1:3, 1:4 were showing 47.45%, 57.35%, 88.40%, 93.12% drug dissolved in 60 minutes. In SDs with Drug: PVP K-30 with ratio 1:4 was showing faster dissolution profile.

SDs with Drug: PEG 3350 for ratio 1:1, 1:2, 1:3, 1:4 were showing 46.875, 56.82%, 85.40, 92.50% drug dissolved in 60 minutes. In SDs with Drug: PVP K-30 with ratio 1:4 was showing faster dissolution profile.

The in-vitro dissolution characteristics of different types of preparations were compared with the pure drug. The solid dispersions of cefdinir prepared by different methods showed improved dissolution when compared with pure cefdinir (Figure: 2&3).

Table 4: *In vitro* dissolution profile of pure Cefdinir

Time (min)	Percent Cefdinir Dissolved				
	1	2	3	4	$\bar{x}$ ± S.D
5	3.2	2.7	3	2.8	2.92±0.221
10	4.1	3.9	4.2	4.2	4.1±0.141
15	4.2	4.2	4.5	4.5	4.35±0.173
20	5.9	5.7	5.8	5.2	5.65±0.310
30	7.6	7.5	7.9	7.2	7.55±0.288
40	9.2	8.5	9.0	8.6	8.82±0.330
50	10.5	9.8	9.7	10	10±0.355
60	10.7	10.3	10.3	10.5	10.45±0.191

Table 5*: in vitro dissolution profile of SDS* of Drug: PVP K-30

Time (min)	Percent Drug Dissolved ($\bar{x}$ ± S.D)			
	F1	F2	F3	F4
5	13.62±0.403	16.80±1.07	20.6±0.832	26.65±1.55
10	16.95±0.435	24.60±.496	28.52±0.573	35.05±0.465
15	21.32±1.370	35.0±0.938	38.15±0.90	46.15±0.55
20	26.82±1.230	41.22±0.531	48.45±0.597	56.35±0.613
30	32.97±0.531	44.92±1.268	59.62±1.09	67.60±0.588
40	40.40±0.938	49.02±1.04	74.07±1.25	82.60±1.641
50	43.45±1.340	53.07±0.899	81.23±0.72	86.90±1.248
60	47.45±1.398	57.35±0.826	88.4±0.748	93.12±2.203

Table 6*: In vitro* dissolution profile of SDs of Drug: PEG 3350

Time (min)	Percent Drug Dissolved ($\bar{x}$ ± S.D)			
	F5	F6	F7	F8
5	13.60±0.783	17.85±0.660	22.4±0.783	24.6±0.75
10	16.77±0.303	27.05±0.519	30.6±0.519	34.5±0.44
15	23.32±0.780	35.35±0.785	39.4±1.35	46.8±0.302
20	29.27±0.780	42.25±0.465	51.4±0.607	57.1±1.35
30	35.07±0.607	47.05±0.723	65.1±0.44	67.8±0.464
40	42.92±1.28	51.27±0.788	75.3±0.303	80.4±0.519
50	44.32±0.921	54.50±1.35	81.2±0.752	86.4±0.465
60	46.87±0.75	56.82±0.44	85.4±1.28	92.5±1.23

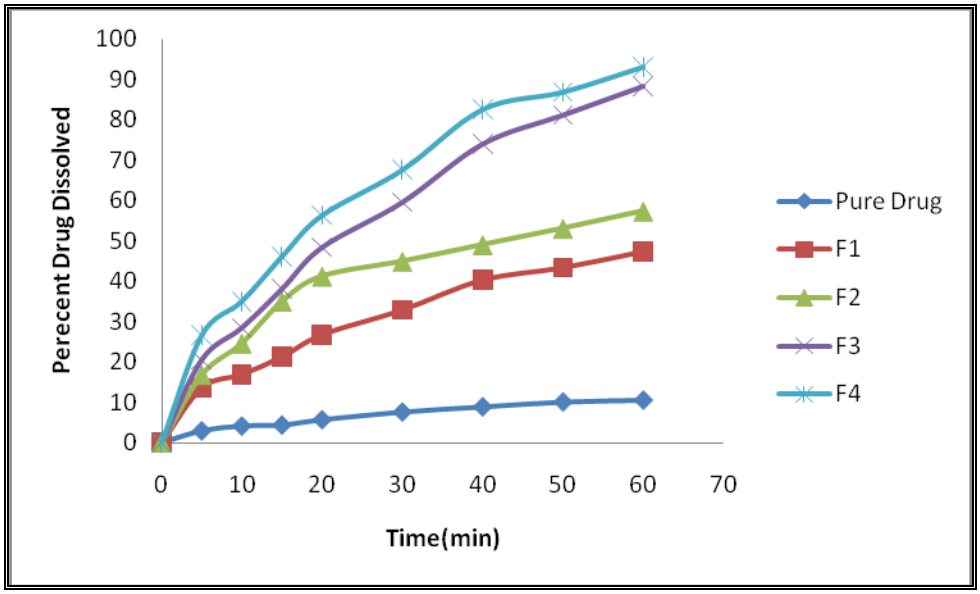

Fig 2: Dissolution studies of Cefdinir and SDs at different Cefdinir/PVP K-30 ratios

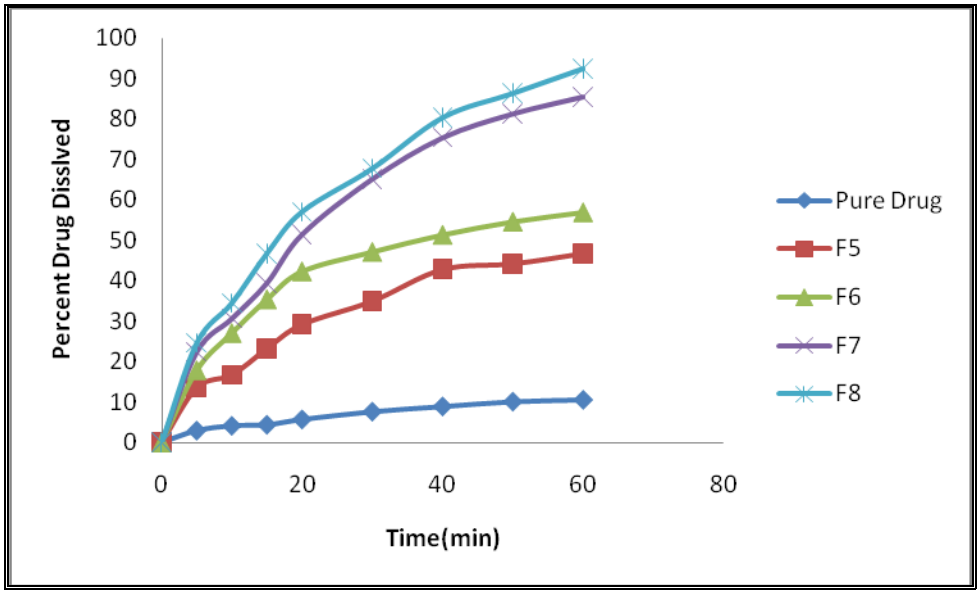

Fig.3: Dissolution studies of Cefdinir and SDs at different Cefdinir/PEG 3350 ratios

CONCLUSION:

The solid dispersions of cefdinir prepared by different methods (solvent evaporation method and melt fusion method) showed improved dissolution when compared with pure cefdinir. Finally it can be concluded that increase in drug solubility and dissolution could be achieved by formulating cefdinir as solid dispersion systems with PVP and PEG 3350.

REFERENCES:

1.https://www.drugs.com/dosage/cefdinir.html

2.K.P.R. Chowdary and K. Surya Prakasa Rao.Individual and Combined Effects of Cyclodextrins, Poloxamer and PVP on the Solubility and Dissolution Rate of BCS Class II Drugs, Asian Journal of Chemistry, 2011;Vol.23, No.10.

3.K.P.R. Chowdary and K. Surya Prakasa Rao. Enhancement of solubility and dissolution rate of BCS class II drugs employing β - cyclodextrin, Poloxamer 407 and PVP, J. Pharmacy Res,2011; Vol. 4 (9).
4.Chowdary K.P.R. and Rao K. Surya Prakasa.Formulation development of etoricoxib tablets employing HP β cyclodextrin- Poloxamer 407- PVP K30: A factorial study, Asian J. Pharm Clin Res,2012; Vol. 5 (1): 161-164.
5.Remington.The Science and Practice of Pharmacy, Lippincott wiliams and Wilkins Publication, 2002;2 (20):1525-2620.
6.Vasconcelos T. and Sarmento B P.Solid dispersions as strategy to improve oral bioavailability of poor water soluble drugs, Drug discovery today,2007; 12:1068–1075.
7.Leuner C. and Dressman J. Improving drug solubility for oral delivery using solid dispersions, Eur. J. Pharm. Biopharm, 2000;50: 47–60.
8.Craig D Q.The mechanisms of drug release from solid dispersions in water soluble polymers, International J. Pharmaceutics, 2002;231:131–144.
9.Abu T M. and Serajuddin.Solid dispersion of poorly water-soluble drugs: early promises, subsequent problems, and recent breakthroughs, Journal of Pharmaceutical Science, 1999;10:1058–1066.
10. Amidon L. Gorden and Raimar Loebenberga. Modern bioavailability,bioequivalence and biopharmaceutics classification system: new scientific approaches to international regulatory standards, Eur. J. Pharm. Biopharmaceutics, 2000;50: 3–12.