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Research Article

Formulation and In Vitro Evaluation of Liquisolid Compacts of Cefuroxime Axetil for Dissolution Rate Improvement

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ABSTRACT

Cefuroxime axetil is a broad-spectrum, β-lactamase stable, second generation cephalosporin antibiotic. Cefuroxime axetil, an orally absorbed pro-drug of cefuroxime is used to treat elderly group of patient with sympathomimetic urinary tract infections. The drug is practically insoluble in water and exhibits slow intrinsic dissolution rate and poor bioavailability. The objective of this work was to enhance the dissolution rate of cefuroxime axetil by converting it into liquisolid compacts. Liquisolid compacts consisted of microcrystalline cellulose (Avicel pH 102) as carrier material, Aerosil 200 as coating material, and propylene glycol as nonvolatile solvent. Solubility studies of cefuroxime axetil in propylene glycol, Tween 80, polyethylene glycol 400 and glycerin were carried out and propylene glycol (11.12± 1.06 mg/ml) was selected as a non volatile solvent in which drug is having the highest solubility. The drug concentration was kept constant in all formulations. Optimization was carried out using Box-Behnken design by selecting liquid load factor, amount of nonvolatile solvent, and carrier coating ratio as independent variables; cumulative percentage drug release, hardness, and angle of repose were considered as dependent variable. Any interaction between cefuroxime axetil and the other components were evaluated by FTIR. Dissolution test was carried out at pH 1.2. The results showed that liquisolid compacts demonstrated significantly higher drug release rates than those of directly compressed tablet.

INTRODUCTION

A poor dissolution rate of water-insoluble drugs is still a major problem in development of the pharmaceutical dosage forms. A number of new chemical entities do not reach the public merely because of their poor oral bioavailability due to inadequate dissolution [1]. For drugs belonging to Bio-pharmaceutical classification system (BCS) class II (poor water solubility and high permeability) dissolution rate is often the rate determining step in the drug absorption [2]. Over the years, various formulation techniques like the formation of water-soluble molecular complexes, drug micronisation, and use of surfactants as solubilising agent, pro-drug approach, solid dispersion, coprecipitation, microencapsulation, and lyophilisation are some major techniques which have been shown to enhance the dissolution characteristics of water-insoluble drugs [3, 4].

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Among these the most promising method for promoting dissolution rate is, use of liquisolid compacts. "Liquisolid compact technique" is successful tool to improve the solubility and dissolution of poorly water soluble drugs and hence bioavailability [5, 6]. The concept of Liquisolid compact system is a powdered form of drug formulated by converting liquid drug or drug suspension or solution of water-insoluble solid drug in suitable nonvolatile solvent system, into dry looking, nonadherent, free-flowing, and readily compressible powder mixtures by blending with selected carrier and coating materials [7-14].

Various grades of cellulose, lactose, sorbitol, and starch are used as the carrier materials, where as silica of various grades like cab-o-sil M5, Aerosil 200, Syloid 244FP are used as the coating material. The good flow and compression properties of liquisolid system may be attributed to large surface area and fine particle size of these carrier and coating materials. Hence liquisolid compact containing water-insoluble

drugs expected to display enhanced dissolution characteristics and consequently improved oral bioavailability [15]. Rapid releasing liquisolid compacts technique for various drugs such as piroxicam [16]; famotidine [17], ripaglinide [18] etc are reported. More recently, the potential of liquisolid compacts technique in producing sustained release systems using propranolol hydrochloride [19] and theophylline [20] were explored.

Although the enhanced dissolution rate achieved by means of liquisolid compacts technique has been extensively studied, no reports, thus far, explored whether this technique can be beneficial for cefuroxime axetil. Thus, the aim of this work was to examine the hypothesis that liquid solid compacts technique could be exploited to enhance the dissolution rate of cefuroxime axetil. In this study, cefuroxime axetil was selected as a model drug, since it is a sparingly soluble in water; it is an ideal candidate for testing the potential of rapid-release liquisolid compacts. Cefuroxime axetil is a 2nd generation cephalosporin antibiotic used mainly elderly group of patient with sympathomimetic urinary tract infections. It is a hydrophobic drug, which belongs to BCS class II, and its half-life is 80 minutes with bioavailability 37 percent on empty stomach, up to 52 percent if taken after food [21]. Cefuroxime axetil formulated into liquisolid compacts using a liquid vehicle and studied for its pre- and post compression parameters. Optimization of formulation was carried out using Box-Behnken design by selecting amount of non-volatile solvent, liquid load factor, and carrier coating ratio as independent variables and hardness, angle of repose and cumulative percentage drug as dependent variables and the effect of formulation.

EXPERIMENTAL

MATERIALS

Cefuroxime axetil was kindly gifted by Ranbaxy laboratories Pvt. Ltd. (Indore, India) Microcrystalline cellulose (Avicel PH 102) and Aerosil 200, was purchased from Vishal chem. Pvt. Ltd. (Mumbai, India). Propylene glycol was purchased from Loba chemie Pvt. Ltd. (Mumbai, India).

Solubility Studies

For selecting best non-volatile solvent solubility study of cefuroxime axetil were carried out in different non-valatile solvents, i.e. propylene glycol, polyethylene glycol 400, glycerine, and tween 80. Saturated solutions were prepared by adding excess amount of drug in 10.00 ml volumetric flask with liquid vehicle. The containers were sealed and kept in orbital shaker bath for 48 h at ambient temperature under constant shaking. After 48 h, the solutions were filtered through 0.45 µm Millipore filter, diluted suitably and analyzed spectrophotometrically at 281 nm. The results were extrapolated to determine the solubility of cefuroxime axetil as percent mg/ml in its saturated solution by using various solvents [22].

Infrared Spectra Analysis

Drug excipient interaction study was carried out by FTIR analysis. IR spectra of the Liquisolid system were recorded by the KBr pellet method. The spectrum of pure cefuroxime axetil, cefuroxime axetil with Avicel pH 102 and Aerosil 200, and physical mixture of liquisolid compacts was obtained.

Flow Properties of Liquisolid System

The flow properties of Liquisolid system were estimated by determining the angle of repose, Carr's index, and Hausner's ratio. The angle of repose was measured by fixed funnel method. The bulk density and tapped densities were determined for the calculation of Hausner's ratio and Carr's index [23, 24].

X-Ray Powder Diffraction (XRPD)

X-ray diffractograms of pure cefuroxime axetil and Liquisolid formulation were studied using Philips Analytical XRD instrument. The scanning range was from 5 to 80 at 2 theta scale [25].

Differential Scanning Calorimetry (DSC)

DSC was performed in order to assess the thermotropic property by using differential scanning calorimetry (Model: Mettler Toledo, Switzerland). About 2.00 mg of the sample were sealed in the aluminium pans and heated at the scanning rate of 10^0C/min, covering a temperature range of 40^0C- 300^0C under nitrogen atmosphere [26].

Formation of Cefuroxime Axetil Liquisolid System

The flowable liquid retention potential (Φ - values) of powder excipients were used to calculate the required carrier and coating material quantities [27]. Flowable liquid-retention potential for Avicel PH 102 and Aerosil 200 was 0.16 and 3.33 respectively [28]. The liquid load factor was calculated accordance with equation (1) using an R value (excipient ratio).

$$L_f = \Phi + \varphi_{(1/R)} \quad (1)$$

Where, L_f_liquid load factor

Φ - Flowable liquid retention potential of carrier material

$\varphi_{(1/R)}$ - Flowable liquid retention potential of coating material

The most suitable quantities of carrier (Q) were calculated using equation (2).

$$L_f = W/Q \quad (2)$$

W – Weight of liquid medication

Q – Amount of carrier material

The optimum quantities of carrier (Q) and coating material (q) were obtained from eqation (3).

$$R = Q/q \quad (3)$$

q- Amount of coating material

Experimental Design of Cefuroxime Axetil Liquisolid Compacts

The optimization of cefuroxime axetil liquisolid compacts was carried out by taking into consideration the amount of non-volatile liquid, carrier coating ratio, and liquid load factor as independent variables and hardness, angle of repose, and cumulative percentage drug release as dependent variable. The experimental runs or formulation design were based on Box-Behnken designs using response surface methodology and utilized to evaluate the response variables. The responses were subjected to multiple regression analysis to find out the relationship between the factors used and the responses obtained. The effect of formulation variables on the response variables were statistically evaluated by applying analysis of variance (ANOVA) using Design Expert 8.0.4 trial version (Stat Ease, USA). The Box-Behnken design suggested total 17 runs out of which 5 runs were repeated. The design was evaluated by quadratic model, which bears the form of following equation:

$$Y = b_0 + b_1X_1 + b_2X_2 + b3X3 + b_4X_1X_2 + b_5X_1X_2 + b_6X_1X_3 + b_7X_1^2 + b_8X_2^2 + b_9X_3^2$$

Where Y is the measured response; X is the levels of factors; b_0 the constant and b_1, b_2, b_3 …….b_9 is the regression coefficient. X_1 and X_2 stand for the mail effect; X_1X_2 are the interaction terms they show how response changes when two factors are simultaneously charged. X_{12}, X_{22} are quadratic terms of the independent variables.

A description of the dependent and independent variables is given in Table no.1.

Table 1: Independent Variables and Dependent Variables (Factors and Levels for Box-Behnken Design)

	Factors	Low	Middle	High
Independent Variables	Amount of non volatile liquid (%w/w)[X_1]	25	50	75
	Carrier coating ratio (%w/w)[X_2]	10	15	20
	Liquid load factor[X_3]	0.33	0.41	0.49
	Factors	**Min**		**Max**
Dependent Variables	Hardness (Kg/cm^2)[Y_1]	3.0		3.9
	Angle of repose (degree)[Y_2]	19.17		30.46
	% Cumulative drug release [Y_3]	86.05		100.24

Table 2: Experimental Runs suggested by Box-Behnken design

RUN	Amount of non volatile liquid X_1(%w/w)	Carrier coating ratio X_2(%w/w)	Liquid load factor X_3	Drug added (mg)
1	75	10	0.41	25
2	25	15	0.49	25
3	50	10	0.33	25
4	75	15	0.33	25
5	75	20	0.41	25
6	50	15	0.41	25
7	75	15	0.49	25
8	50	20	0.33	25
9	25	10	0.41	25
10	50	15	0.41	25
11	50	15	0.41	25
12	50	15	0.41	25
13	25	20	0.41	25
14	50	10	0.49	25
15	50	20	0.49	25
16	25	15	0.33	25
17	50	15	0.41	25

Preparation of Liquisolid Tablets

Liquisolid formulations containing microcrystalline cellulose (Avicel PH 102) as the carrier material and Aerosil 200 as the coating material at different powder excipient ratio (R) were formulated. The nonvolatile liquid in which cefuroxime axetil is maximum soluble was

selected for liquid medication preparation. The nonvolatile liquid was taken at different quantity from 25.00 to 75.00 mg. Different liquid load factor, L_f, 0.33, 0.41 and 0.49 w/w were employed. Different carrier coating ratio 10, 15 and 20 was used for liquisolid system. Sodium starch glycolate (SSG) 4 % was used as a disintegrant and 1% talc as a lubricant in all systems. Liquisolid tablets were prepared by dispersing cefuroxime axetil in propylene glycol and this dispersion was mixed with Avicel PH 102 and Aerosil 200 with continuous mixing in mortar. Finally SSG was mixed and then talc was added before compression as a lubricant [29] (Table no. 02).

Post Compression Studies of Liquisolid Compacts

Drug Content

The drug content of tablets was measured according to IP 2010. For the purpose of content uniformity determinations average weight of powder of single tablet of cefuroxime axetil Liquisolid tablets containing equivalent of 25.00 mg of the drug were dissolved in 1.2 pH HCl buffer and suitably diluted. The analysis of cefuroxime axetil liquisolid tablets was carried out by using UV spectrophotometer (Schimadzu, 1700, Japan) at 281 nm.

Friability and Hardness

The friability of the prepared formulae was measured using Digital Roche Friabilator (Electrolab, India), and the percentage loss in weights were calculated and taken as a measure of friability. The hardness of the liquisolid tablets prepared was evaluated using Monsanto hardness tester, the mean hardness of each formula was determined [30].

% Friability = (loss of mass / initial mass) × 100

Weight Variation

The weight variation test was performed on 20 tablets of Liquisolid compacts as per Indian Pharmacopoeia 2010 [31].

Disintegration Test

The disintegration test was performed at 37 ± 1^0C in distilled water for six tablets from each formulation using the tablet disintegration unit. The tablets were considered completely disintegrated as no residue remains on the screen. Generally, ideal tablet hardness should be produced without applying excessive compression force where rapid tablet disintegration and drug dissolution are maintained at the same time [32].

In Vitro Dissolution Studies

In vitro dissolution profile from liquisolid compacts tablets were obtained using dissolution test apparatus USP-II. The dissolution studies were carried out in 900 Ml of 1.2 pH buffer as the dissolution medium at 37^0C ± 1^0C and 50 rpm. Then, 5.00 mL samples were collected for up to 60 min at 5 min intervals up to 30 min and then 15 min intervals from 30 to 60 min. After each sample withdrawal the dissolution medium was replaced with 5.00 mL fresh dissolution fluid. The withdrawn samples were filtered and analyzed spectrophotometrically at 281 nm [33].

Comparison of dissolution test of optimized liquisolid tablet and direct compressed tablet (without nonvolatile liquid) was determined by the same method described above.

RESULTS AND DISCUSSION

Saturation Solubility Studies

The drug solubility in non-volatile solvents is an important parameter in formulation of Liquisolid tablets. As greater the solubility, the more would be the drug particles dissolved in the liquid vehicle prior to the adsorption onto the carrier materials. The saturation solubility of cefuroxime axetil increases in the order of water < glycerin < tween 80 < propylene glycol 400 < propylene glycol. Solubility of cefuroxime axetil was significantly increased in presence of propylene glycol i.e. 11.12 mg/ml.

IR Spectrum of Cefuroxime Axetil

IR spectrum of pure cefuroxime axetil (a), mixture of cefuroxime axetil, Avicel pH 102 and Aerosil 200 (b) optimized liquisolid formulation (c) is shown in Figure 1. The IR spectra of cefuroxime axetil exhibited distinctive peaks at 1060 cm^{-1} due to ethereal linkage stretching, 1726 cm^{-1} owing to C=O stretching of the carboxyl ion, at 2939 cm^{-1} peak due to amide streching and at 3308 cm^{-1} because of N-H stretching. The FTIR spectra of mixture and liquisolid compacts displayed same characteristic peaks ruling out the possibility of any chemical interaction between the drug and excipients used in the formulation.

Flow Properties of the Cefuroxime Axetil Liquisolid System

The values of bulk density were found to be an in the range from 0.188 to 0.366 g/cc; tapped density was in the range of 0.213 to 0.443 g/cc, which indicated that the powder blends were

having good flow properties. Angle of repose was found to be in the range of 19 to 31 indicating acceptable flow properties. The Carr's for all formulations lies within range of 6.74 ± 2.14 to 28.27 ± 0.875. Housner's ratio was found to be in a range of 1.06 ±0.03 to 1.39 ± 0.02, Table no. 03.

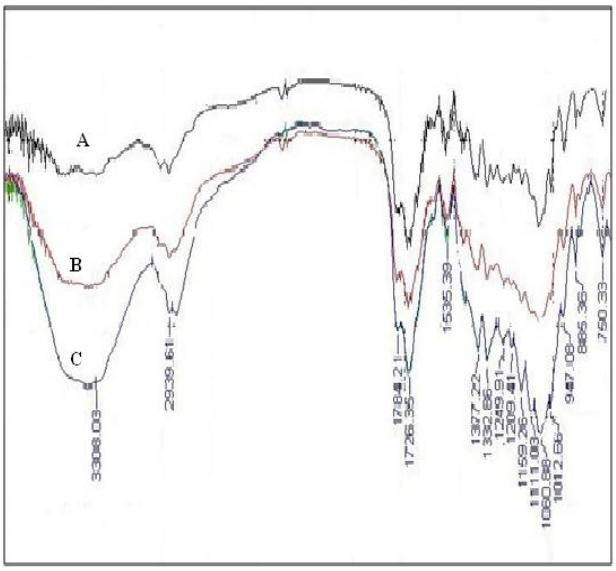

Figure 1: IR spectra of a = cefuroxime axetil, b = cefuroxime axetil + Avicel pH 102 + Aerosil 200, c = physical mixture of liquisolid compact

X-ray powder diffractometry:

X-ray diffractogram of pure cefuroxime axetil show the peaks appearing at 17.4, 20.5, 23.5 2θ values supporting crystalline nature of drug while the liquisolid powder X-ray diffraction pattern Figure 2 showed only one sharp diffraction peak at 2θ angle of 22.5 belonging to Avicel PH 102, indicating that only Avicel PH 102 maintained its crystalline state. Such absence of cefuroxime axetil specific peaks in the liquisolid X-ray diffractogram indicated that drug has almost entirely converted from crystalline to amorphous or solubilized form.

Differential Scanning Calorimetry (DSC)

DSC thermogram of cefuroxime axetil was shown in Figure 3(A). DSC thermogram of cefuroxime axetil exhibited a broad exothermic peak at 233°C, with the onset at 214 °C and latent heat of fusion was found to be 59.27 mJ. The thermogram showed that crystallinity around 253 %. The cefuroxime axetil was in crystalline state.

The DSC thermogram of liquisolid system was showed in Figure 3(B). In which there was no exothermic peak observed. The crystallinity of liquisolid system was observed to be 35 % it was very less as compared to the pure cefuroxime axetil crystallinity. This study indicated that drug has almost entirely converted from crystalline to amorphous or solubilized form. Therefore, there should be increase in solubility of cefuroxime axetil.

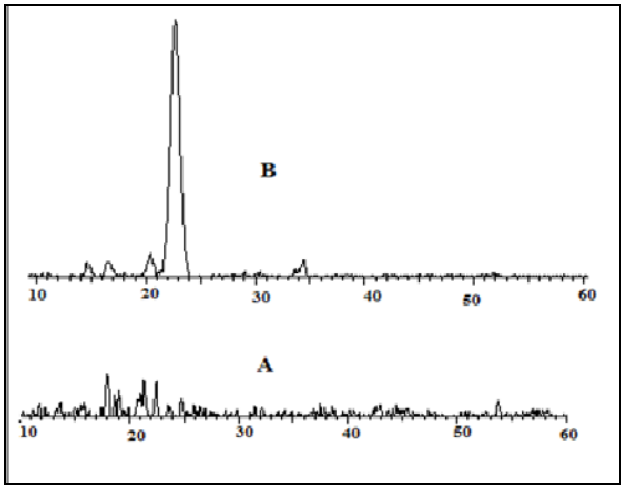

Figure 2: X-Ray Diffraction patterns of A) Cefuroxime axetil; B) Optimized liquisolid system (LS – 4).

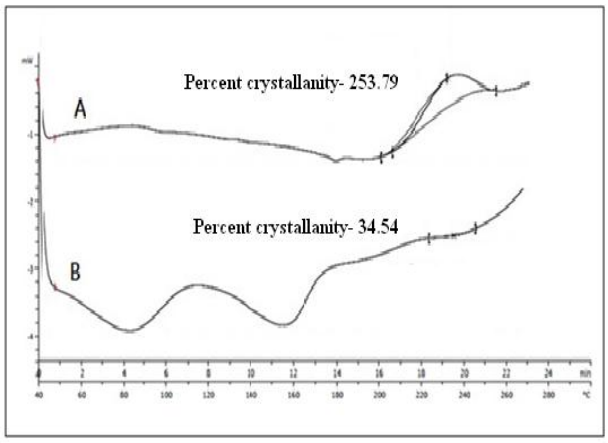

Figure 3: DSC thermogram of A = pure cefuroxime axetil, B = optimized liquisolid system

Post compression studies of liquisolid compacts:

Drug content:

Uniform drug content was observed for all the formulations (98 ± 0.8 to 101 ± 0.6), which is as per the IP specification (95-105%) as shown in Table no. 04.

Disintegration time

The disintegration test revealed that the all the liquisolid tablet were disintegrated within 5 min, which is as per specifications given for the uncoated tablets in the IP as shown in Table no. 04.

Table 3: Results of Flow Properties of Liquisolid Formulations

Formulation no.	Angle of repose Y_2	Bulk density	Tapped density	Housner's ratio	Carr's index
1	25.94±1.07	0.366±0.6	0.391±0.56	1.06±0.18	6.74±0.89
2	19.29±1.13	0.286±0.7	0.318±0.69	1.13±0.25	12.19±1.21
3	23.96±0.74	0.222±0.2	0.241±0.46	1.85±0.34	7.88±0.36
4	27.55±0.98	0.353±0.3	0.404±0.40	1.14±0.35	12.48±1.07
5	29.50±1.02	0.263±0.5	0.313±0.81	1.19±0.21	15.97±1.71
6	26.13±1.45	0.355±0.5	0.404±0.55	1.13±0.17	12.48±0.83
7	26.05±0.93	0.188±0.4	0.213±0.58	1.13±0.39	11.73±1.69
8	30.46±0.39	0.215±0.3	0.255±0.29	1.18±0.19	15.68±0.62
9	22.16±1.37	0.202±0.6	0.285±0.59	1.39±0.40	16.80±1.17
10	26.56±1.53	0.293±0.5	0.371±0.60	1.26±0.21	28.27±1.61
11	26.56±1.53	0.293±0.5	0.371±0.60	1.26±0.21	28.27±1.61
12	26.56±1.53	0.293±0.5	0.371±0.60	1.26±0.21	28.27±1.61
13	23.94±1.50	0.260±0.4	0.300±0.53	1.15±0.13	21.02±1.96
14	27.21±1.30	0.301±0.7	0.338±0.43	1.12±0.25	13.15±0.93
15	19.17±1.40	0.207±0.7	0.213±0.57	1.11±0.17	11.34±0.20
16	22.17±1.17	0.318±0.8	0.363±0.27	1.14±0.19	10.02±0.25
17	26.56±1.53	0.293±0.5	0.371±0.60	1.26±0.21	28.27±1.61

Table 4: Results of Postcompression Parameters of Liquisolid Formulations and Directly Compressed Tablet (Dct)

Formulation no.	Hardness Y_1	Friability	Weight variation	Drug content	Disintegration time	% CDR Y_3
1	3.1	0.56±0.06	280.91±0.45	99.71±0.43	3.46±0.24	99.07
2	3.9	0.56±0.05	191.58±0.30	99.04±0.34	3.14±0.15	92.33
3	3.7	0.67±0.05	165.21±0.27	99.37±0.15	4.15±0.38	96.61
4	3	0.71±0.09	329.78±0.20	99.24±0.17	3.17±0.10	99.92
5	3	0.38±0.02	326.17±0.10	98.81±0.28	4.05±0.31	97.57
6	3.6	0.66±0.02	346.30±0.10	99.05±0.19	2.17±0.17	94.97
7	3.1	0.54±0.04	245.13±0.15	99.11±0.15	4.10±0.09	100.24
8	3.3	0.39±0.02	370.34±0.17	100.41±0.17	2.05±0.12	95.24
9	3.9	0.47±0.03	337.71±0.18	98.60±0.19	3.02±0.80	95.67
10	3.9	0.47±0.03	337.71±0.18	98.60±0.19	3.02±0.80	95.47
11	3.9	0.47±0.03	337.71±0.18	98.60±0.19	3.02±0.80	95.47
12	3.9	0.54±0.05	440.18±0.37	99.27±0.22	4.15±0.15	95.47
13	3.8	0.62±0.03	185.16±0.44	99.80±0.46	6.10±1.04	86.05
14	3.4	0.71±0.09	220.08±0.29	98.87±0.37	3.30±0.17	99.84
15	3.7	0.49±0.07	253.11±0.31	100.27±0.56	3.15±0.22	99.54
16	3.9	0.42±0.08	254.15±0.23	98.60±0.17	4.17±0.80	97.52
17	3.9	0.47±0.03	337.71±0.18	99.80±0.19	3.02±0.58	95.47
DCT	3.6	0.44±0.06	255.14±0.12	99.62±0.23	4.03±0.77	97.45

Friability

All the liquisolid compacts had acceptable friability as none of the tested formulation had percentage loss in tablet's weights that exceed 1% as shown in Table no. 04.

Hardness

Hardness was found to be in the range of 3 ± 0.45 to 4 ± 0.5 kg/cm^2 as shown in Table no. 04.

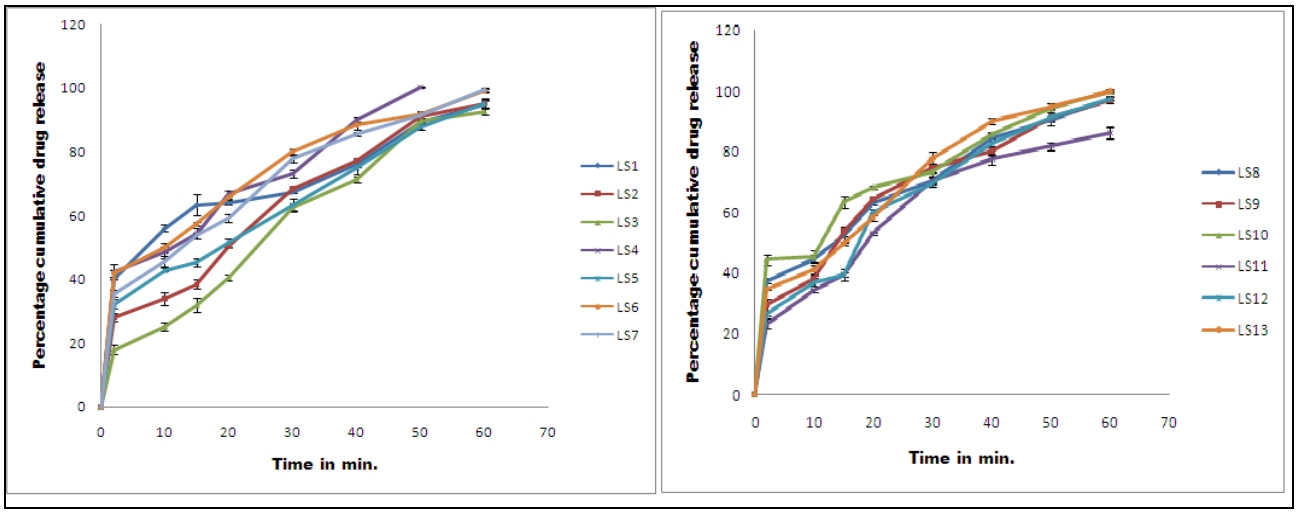

Figure 4: Dissolution profile of Cefuroxime axetil liquisolid formulations A = (LS-1- LS-7) B = (LS-8-LS-13) in 1.2 pH buffer

Weight Variation Test

Weight variation test were performed as per IP. All the tablets were within the range of pharmcopoeial specifications as shown in Table no. 04**.**

In-vitro Dissolution Studies

In-vitro drug release studies were performed in 1.2 pH HCl buffer for all the prepared formulations by using USP dissolution test apparatus- Type II, Rotating Paddle method. The graphs showing drug release profile for formulations are shown in Figure 4. The mean of three determinations was used to calculate the in-vitro dissolution for each formulation batch no burst effect was observed. Complete (100%) drug release was observed within 1 hour, Figure 4, Table no. 04.

The dissolution profile of the optimised cefuroxime axetil liquisolid compacts tablet (LST) formulation LS – 4 with the dissolution profile of cefuroxime axetil directly compressed tablets (DCT) is presented in Figure 5. It was apparent that formulation LS – 4 has the highest dissolution pattern in both the rate and the extent of drug dissolved. The percentage of cefuroxime axetil dissolved of liquisolid tablet (LS – 4) reached at 100.24% after only 50 min, while the DCT showed maximum cefuroxime axetil content dissolved after 90 min.

Effect of Formulations Variables on Angle of Repose

The result of formulations as per design when fitted into various model, a Quadratic model was found to be significant for Angle of repose. In this model factors X_1 (Amount of nonvolatile liquid) significantly affected the Angle of repose, whereas factor X_2 and X_3 (carrier coating ratio and liquid load factor) do not have significant effect on the angle of response. The model equation is as follows:

Angle of repose = $29.94+2.03X_1+1.71X_2+0.10X_3-0.025X_1X_2+1.06X_1X_3+2.26X_2X_3-0.25X_1^2-4.73X_2^2-3.37X_3^2$.

The effect of both the factors X_1 can be explained with the help of the 3D response surface plot as shown in Figures 6. As the Amount of nonvolatile liquid concentration increased the angle of repose increased Figure 6.

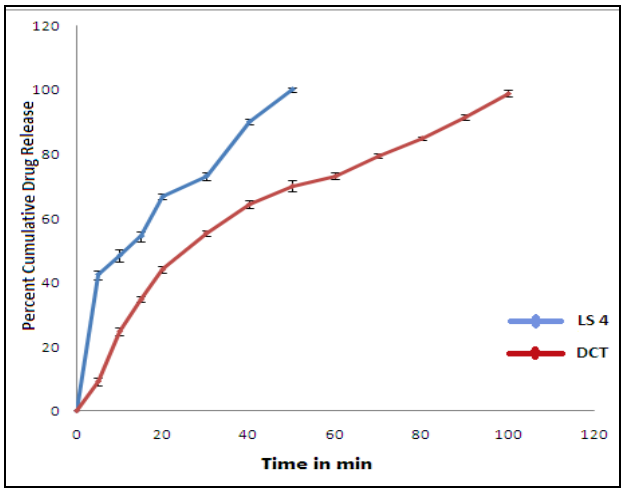

Figure 5: Dissolution profiles of Liquisolid compact tablet (LS-4) and direct compressed tablet (DCT)

Effect of Formulation Variables on Cumulative Percentage Drug Release

The result of formulations as per design when fitted into various model, a linear model was found to be significant for cumulative percent

drug release. In this model factors X_1 and X_2 (Amount of nonvolatile liquid and carrier coating ratio) significantly affected the cumulative percentage drug release, whereas factor X_3 (liquid load factor) do not have significant effect on the response. The model equation is as follows:

Percent cumulative drug release = $+96.20+3.18X_1-1.43X_2+0.19X_3$.

The effect of both the factors X_1 and X_2 can be explained with the help of the 3D response surface plot as shown in Figure 7. As the Amount of nonvolatile liquid concentration increased and carrier coating ratio decreased, the cumulative percent drug release increased Figure 7.

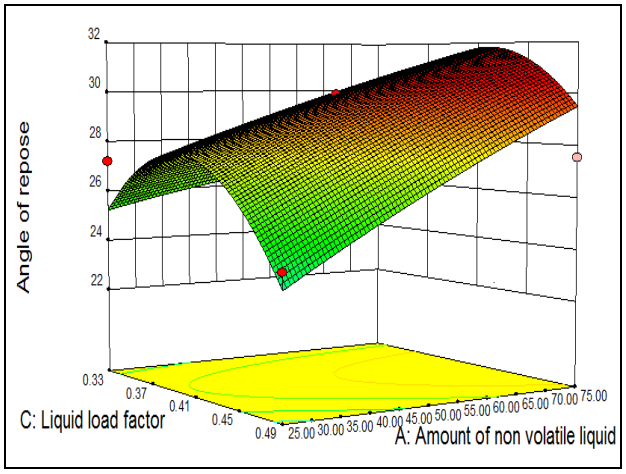

Figure 6: Effect of formulations variables on Angle of repose.

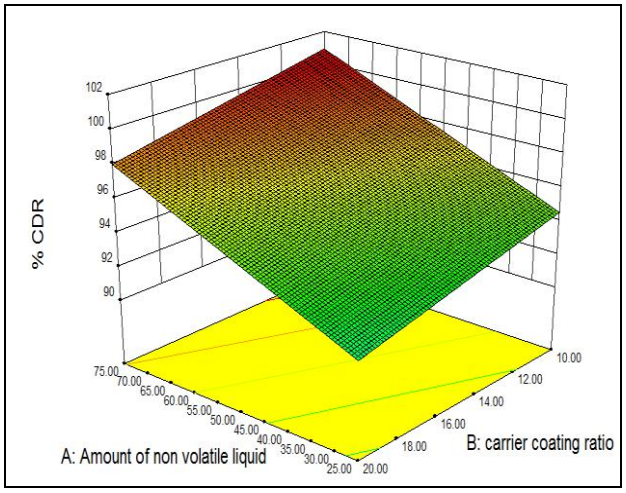

Figure 7: Effect of formulation variables on cumulative percentage drug release.

Effect of Formulations Variables on Hardness

The result of formulations as per design when fitted into various model, a Quadratic model was found to be significant for hardness. In this model factors X_2 and X_3 (carrier coating ratio and liquid load factor) significantly affected the hardness, whereas factor X_1 (Amount of nonvolatile liquid) do not have significant effect on the response. The model equation is as follows:

Hardness = $+ 3.60-0.41X_1 - 0.037X_2 + 0.025X_3 + 0.000X_1X_2 + 0.025X_1X_3 + 0.18X_2 X_3 - 0.10X_1^2 - 0.050X_2^2 - 0.025X_3^2$.

The effect of both the factors X_2 and X_3 can be explained with the help of the 3D response surface plot as shown in Figure 8. As the liquid load factor increased and concentration of carrier coating ratio decreased, the hardness increased.

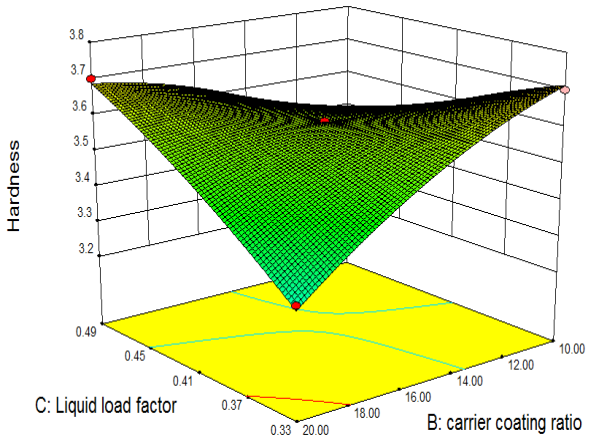

Figure 8: Effect of formulations variables on Hardness

Statistical Analysis

One way ANOVA is applied for the angle of repose, hardness, and in vitro dissolution. Statistical significance of effect of all these dependent variables was done by comparing the mean square against an estimate of the error. It was found that all the independent variables i.e. amount of nonvolatile liquid (A), carrier coating ratio (B), and liquid load factor (C) had < 0.5, demonstrating that they are significantly different from zero. The summary of results of ANOVA for measured responses is shown in Table no. 5.

CONCLUSION

In the present study, the potential of liquisolid system to improve the dissolution properties of water insoluble drug was investigated using cefuroxime axetil as the model drug. Optimization of cefuroxime axetil liquisolid compacts was carried out using Box-Behnken

design by selecting amount of nonvolatile liquid, carrier coating ratio, and liquid load factor as independent variables and angle of repose, hardness, and in vitro dissolution as dependent variable. The results conclusively showed that solubility of water insoluble drug cefuroxime axetil was increased to greater extent thereby improving its dissolution rate. Thus liquisolid technology may be used to improve the release rate of poorly water soluble drugs that will make the dosage form cost effective.

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