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Original Article

FORMULATION AND *IN-VITRO* EVALUATION OF EFAVIRENZ LIQUISOLID COMPACTS

SAI SRUTHI R, SHAMILI KAPARTHI, P. R. SATHESH BABU*, C. V. S. SUBRAHMANYAM

Gokaraju Rangaraju College of Pharmacy, Osmania University, Nizampet, Hyderabad 500090, India
Email: shamiliscintillating@gmail.com

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ABSTRACT

Objective: The present research is aimed to enhance the dissolution rate of Efavirenz using liquisolid compact technology.

Methods: About 16 different formulations were developed using factorial design with carriers (Neusilin and Fugicalin), binder (PVP K-30) and vehicle (polyethylene glycol 300) as independent variables and aerosil 200 is used as coating material. The *In-vitro* drug release from the LSC has used a dependent variable. The empirical method by Spireas and Bolton was applied to calculate the amounts of carrier and coating materials and obtained the improved flow characteristics and hardness by changing the proportion of carrier and coating materials.

Results: A 2^3 factorial design is used and developed LSC using Neusilin (LSC-N1 to LSC-N8) and Fugicalin (LSC-F1 to LSC-F8). The physicochemical evaluation of all formulations exhibited well within the specification limits with respect to weight variation, hardness, friability and content uniformity. The *In-vitro* drug release from these LSC was evaluated in 0.1 N HCl and the optimized formulation (LSC-N8) was compared with pure drug (capsule) and physical mixture (tablet). The release studies proved that the liquisolid tablets results in higher release profile than pure drug and physical mixture due to increase in surface and wetting properties of the drug.

Conclusion: LSC technique confirmed the enhanced dissolution rate of Efavirenz, which in turn helps in improving bioavailability.

Keywords: Liquisolid compacts, Efavirenz, Neusilin, Fujicalin, Factorial design.

INTRODUCTION

The active ingredient in a solid dosage form must undergo dissolution before it is available for absorption from the gastrointestinal tract [1]. The poor dissolution rate of the water-insoluble drug is a substantial problem confronting the pharmaceutical industry. The absorption rate of a poorly water-soluble drug from the solid oral dosage form is poor due to the low dissolution rate of the drug. Hence, the dissolution rate is the rate determining step in drug absorption.

Various methods such as crystallization by solvent change, preparation of inclusion complexes with β-cyclodextrins, formation of water-soluble salts, micellar solubilization, solid dispersion, lyophilization, microencapsulation, liquisolid technique and the inclusion of drug solutions or liquid drugs into soft gelatin capsules are some of the techniques that have been reported to enhance the dissolution characteristics of water-insoluble drugs [2]. The technique of liquisolid compacts is one of the most promising techniques. Liquisolid concept is used to enhance the solubility of poorly water soluble drugs at least for the first two hours (active absorption phase) and thereby increasing drug dissolution and absorption rate of drugs.

The liquisolid technique as described by Spireas is a novel concept, where a liquid may be transformed into a free-flowing, readily compressible and apparently dry powder by simple physical blending with selected carrier and coating material. The liquisolid powder is a free flowing and a compressible powder form of liquid medication [3]. The term liquid medication implies liquid drug and solution or suspension of water insoluble solid drug carried in suitable non-volatile liquid vehicles. Using formulation technique, a liquid medication can be converted into a dry-looking, non-adherent, free flowing, and readily compressible powder by blending with selected powder excipients referred to as the carrier and coating materials. Various grades of cellulose, starch, lactose silica powder may be used as the coating (or covering) material [3]. In liquisolid compact, the drug is in a tablet or encapsulated dosage form, and it is held in a solubilized liquid state, which consequently contributes to increased drug wetting properties, thereby enhancing drug dissolution. In liquisolid formulation, the drug is in either solubilized or molecularly dispersed state in the liquid vehicle, which is absorbed into or onto the carrier and coating material respectively. Hence, increased surface area of the drug in powder form and enhanced dissolution of drug [2].

Spireas *et al.* proposed the new mathematical model to retain good flow behavior and compressibility to design the liquisolid formulation technique. This technique requires a suitable drug candidate, non-volatile solvent, and carrier and coating materials. The basic properties of powder are proposed according to Spireas *et al.* is "Flowable liquid retention potential" (value) and "compressible liquid retention potential" (ψ value). Flowable liquid retention potential is the maximum weight of liquid (solvent) that can be retained per unit weight of the powder (excipient) material to produce good flow. Compressible liquid retention potential is the compression force applied to produce tablets with acceptable strength without squeezing out any liquid during compression. Excipient ratio (R) is defined as carrier to coating ratio quoted as given by equation (1)

$$R = Q/q \quad (1)$$

Where, Q = Carrier material and q = Coating material.

Liquid load factor (L_f) is defined as the weight of liquid medicament (W) to the weight of carrier (w). The equation is given below (2)

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

The $\emptyset$ value is for calculating excipients quantities as shown in the equation (3).

$$L_f = \boldsymbol{\emptyset} + \emptyset\,(1/R) \quad (3)$$

Where, $\boldsymbol{\emptyset}$ and $\emptyset$ are values of carrier and coating material [4].

Efavirenz, chemically (4S)-6-chloro-4-(2-cyclopropylethynyl)-4-(trifluoromethyl)-2, 4-dihydro-1H-3, 1-benzoxazin-2-one is an Anti-HIV agent. Efavirenz is an official drug and appears as a white or almost white crystalline powder. It is freely soluble in methanol, chloroform and very slightly soluble in water and ethanol. Efavirenz has a melting point of 138 °C to 140 °C; log P value of 4.6 and got a

pKa of 12.52. The dose of efavirenz ranges between 600 mg orally once a day [5].

Objectives

The main aim of present study was to enhance the dissolution rate of Efavirenz, a BCS class-II (low soluble and high permeable drug) by developing the liquisolid tablets using different carriers and coating materials with different liquid loading factors and excipient ratios.

The objectives of the present investigation include the following:

1. To identify best non-volatile solvent using solubility studies for Efavirenz.

2. To study the effect of different carriers and coating materials on dissolution rates of Efavirenz liquisolid compacts.

3. To develop various formulations of Efavirenz liquisolid compacts using the design of experiments.

4. To evaluate the developed Efavirenz liquisolid compact formulations for pre-compression (Angle of repose, Bulk density, Tapped density, Carr's index, Hausner's ratio) and post-compression parameters (Weight variation, Friability, Hardness, Disintegration time, Drug content uniformity, *In-vitro* dissolution studies).

MATERIALS AND METHODS

Efavirenz is a gift sample (Hetero Pharmaceuticals, Hyderabad), Neusilin and Fujicalin are free samples (Gangwal Chemicals Pvt Ltd). Aerosil 200, PVP K-30, Cross caramellose sodium, Magnesium stearate, Lactose, Propylene glycol (PG), Glycerine, Tween 80, PEG 400, PEG 300 are procured from S. D. Fine Chem Limited, Mumbai and used in the study.

Experimental methodology

Estimation of efavirenz

Efavirenz estimation was made in 0.1N hydrochloric acid (pH 1.2) solution at λ_{max} of 247 nm by UV spectrophotometry (UV-1700, Shimadzu, Japan). The calibration curve was obeyed Beer Lambert's law in the concentration range of 0-40 µg/ml (R^2 = 0.997) [3].

Characterization of efavirenz

The efavirenz purity was characterized by melting point, FT-IR studies, DSC studies and XRD studies. The micrometric properties of efavirenz were determined by the angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio.

Drug-excipient compatibility studies

The excipients used in the formulation were selected from drug-excipients compatibility studies using spectral interference and Fourier Transform Infrared (FTIR) Spectroscopy analysis.

Saturation solubility studies

The solubility studies were performed for the selection of best non-volatile solvents. Excess of efavirenz was placed in ten ml of five different non-volatile solvents (propylene glycol, Tween 80, PEG 300, PEG 400, and glycerine) and these dispersions were stirred in orbital shaker bath for 72 h at 25 °C. The saturated solutions were filtered after 72 h using Whattman filter paper (0.22 µm) and the filtrate was analyzed spectrophotometrically at 247 nm. The studies were conducted triplicate [6, 7].

Determination of the flowable liquid retention potential

In constant weight of carrier/coating material, increasing amount of solvent was incorporated and on each addition, the angle of slide was determined. The Flowable liquid retention potential (Ø-value) of each liquid/powder admixture was calculated using the following equation (4).

$$\emptyset - value = \frac{\text{weight of liquid}}{\text{weight of solid}} \quad \ldots\ldots (4)$$

The Ø-values were plotted against the corresponding angle of the slide to identify optimal flow properties. The angle of slide value of 33° corresponding to the liquid/powder admixture is represented as the ideal Flowable liquid-retention potential [8].

Table 1: Absolute values of levels of variables employed in factorial design

S. No.	Variables		Levels	
	Absolute	Coded	-1	+1
1	Concentration of drug in the liquid vehicle (% w/w)	X_1	50	75
2	Concentration of PVP-K30 in the formulation (% w/w)	X_2	2	5
3	Concentration of super disintegrant in the formulation (% w/w)	X_3	2.5	5

Table 2: Plan of experiments with coded values of variables of efavirenz liquisolid compacts formulation using 2^3design [9]

S. No.	Run order	Drug concentration in the liquid vehicle (% w/w)	Concentration of PVP-K30 in the formulation (% w/w)	Concentration of cross caramellose sodium in the formulation (% w/w)
1	LSC-1	-1	-1	-1
2	LSC-2	+1	-1	-1
3	LSC-3	-1	+1	-1
4	LSC-4	+1	+1	-1
5	LSC-5	-1	-1	+1
6	LSC-6	+1	-1	+1
7	LSC-7	-1	+1	+1
8	LSC-8	+1	+1	+1

Formulation development

The liquisolid compacts of efavirenz were developed by using 2^3 factorial design, i.e., 3 variables and 2 levels. The variables include the concentration of drug in the liquid vehicle (% w/w), concentration of binding agent (PVP K-30) in the formulation (%w/w) and concentration of super disintegrant (cross caramellose sodium) in the formulation (%w/w).

The factorial design was applied at lower and higher levels using two different carries (Neusilin and Fugicalin) and developed eight formulations for each carrier. The absolute levels of variables used in the study are given in the table 1 and the plan of experiments with coded levels of variables is given in the table 2.

Neusilin and Fujicalin were selected as two different carriers and the above-mentioned variables, and respective levels were assessed individually on both the carriers employed in the study. Using the design of experiments, eight formulations for each of Neusilin (LSC-1N to LSC-8N) and Fugicalin (LSC-1F to LSC-8F) were developed using direct compression technique. Formulations LSC-N1 to LSC-N8 were formulated using neusilin as carrier and formulations LSC-F1 to LSC-F8 were formulated using fujicalin as carrier.

Evaluation of liquisolid system

Flow property

Flow property of liquisolid admixture was accessed by measuring the angle of repose, Carr's index and Hausner's ratio. Each study was carried out in triplicate. The angle of repose was calculated by a fixed height cone method. Carr's index & Hausner's ratio were determined using bulk density apparatus as reported in the literature [10, 11].

Weight variation

Weight variation was calculated as per method described in USP. Twenty tablets were selected at random and their average weight was determined using an electronic balance. The tablets were weighed individually and compared with average weight. The requirements are met if the weights of not more than 2 of tablets differ by more than the percentage listed in the table 3 and no tablets differ in weight by more than double that percentage [12, 13].

Table 3: Acceptance criteria for weight variation [14]

Average weight of tablet (mg)	%±deviation allowed
130 or less	10
More than 130 & less than 324	7.5
324 and above	5

Tablet thickness

Thickness and diameter of formulation trials were measured using a digital hardness tester. 10 tablets of each trial formulation were taken and measured individually at frequent intervals [15].

Hardness

The hardness of the liquisolid tablets was evaluated using a Monsanto hardness tester. The tablet to be tested was placed between the spindle and the anvil. The desired pressure needed to hold the tablet in position was applied by moving the screw knob in a clockwise direction. The scale was moved so that the indicator was fixed at zero. The pressure was applied until tablet breaks. The reading was noted, indicating the pressure that was needed to break the tablet. The mean hardness of each batch was determined and expressed in kg/cm^2 [16].

Disintegration time

Disintegration test was carried out using USP tablet disintegration test apparatus (TGR56, Electro lab, India) using of 0.1N hydrochloric acid at room temperature (37±2 ^{0}C). Disintegration apparatus with a basket rack assembly containing six open-ended tubes and 10-mesh screen on the bottom was used. A tablet was placed in each tube of the basket and the time for complete disintegration of the six tablets was recorded [17].

Content uniformity

Ten tablets from each formulation were powdered. The powdered sample equivalent to 6 mg of drug was transferred to a 100 ml volumetric flask containing 5 ml of 0.1N hydrochloric acid solution. The contents were shaken up to 30 min and made up to mark with HCl. The solution was further diluted with 0.1N Hydrochloric acid solution if required. The drug content was determined by measuring the absorbance at 247 nm [18, 19].

***In-vitro* drug releases study**

In vitro drug release of the samples was carried out using USP-type II dissolution apparatus (paddle type). The temperature of the medium was maintained at 37±0.5 °C. The apparatus was allowed to run for 50 RPM. Aliquots of samples were withdrawn at various intervals. The samples were filtered through Whatman filter. Fresh dissolution medium (0.1N HCl solution) was replaced every time with the same quantity of the sample. Collected samples were analyzed at λ_{max} of 247 nm. The percentage cumulative drug release (% CDR) was calculated [20, 21].

RESULTS AND DISCUSSION

Characterization of efavirenz

Melting point

The melting point of efavirenz was determined by capillary tube method and it was found to be 138 °C. This value is same as that of the literature citation 138-140 °C (B. P 2008).

FT-IR spectrum of pure drug

The FT-IR spectrum for the pure drug was recorded and the characteristic bands are observed in the graph (fig. 3). A perusal to the FT-IR spectrum, it was confirmed the presence of all characteristic bands for the efavirenz [22].

Differential scanning calorimetry

The DSC spectrum for the pure drug was recorded in the fig. 1. A perusal to the DSC of the drug, the peak onset was found to be 138 °C. This value is matching with the melting point obtained from open capillaries. Thus indicates the purity and confirmation of efavirenz [13].

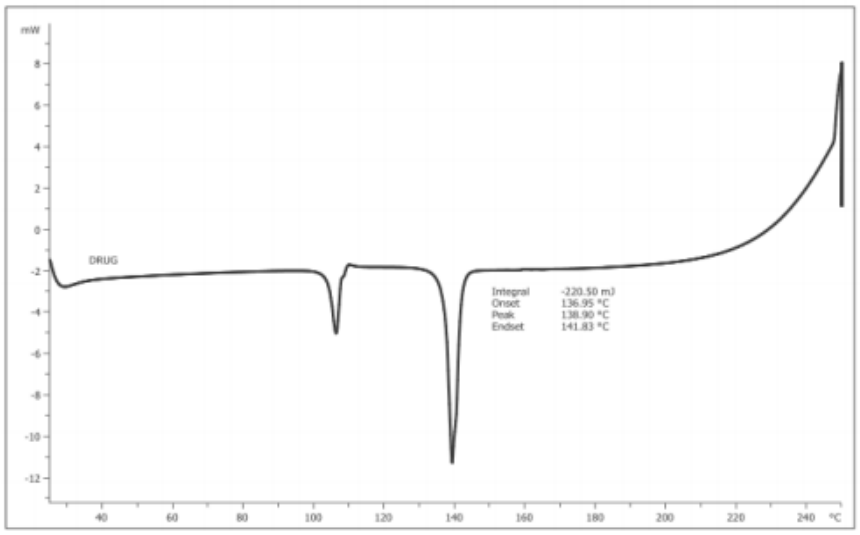

Fig. 1: DSC thermogram of efavirenz

XRD of pure drug

The purity and crystallinity of efavirenz was identified using XRD studies. The XRD graph of efavirenz was recorded in the fig. 2. The XRD studies confirm the crystalline nature of the drug. A perusal to the fig. 2, characteristic peaks of the drug were present at 20.20° and 21.35°, which confirmed the crystalline nature of drug.

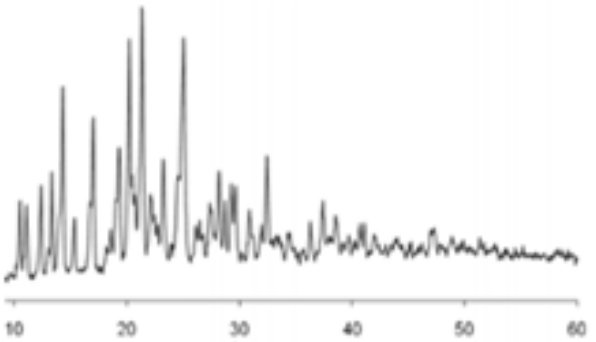

Fig. 2: XRD graph of efavirenz

Flow properties

The flow properties of the pure drug were determined. It is observed that angle of repose; compressibility index and Hausner's ratio were indicating good flow properties of the pure drug (efavirenz). Thus, the drug is suitable for direct compression.

Drug–excipient compatibility studies

Spectral interference analysis

The absorbances of the solutions containing drug (10 µg/ml) and for a drug with the excipient mixture in 0.1 N HCl solutions were measured at 247 nm to determine the influence of excipients on drug substance (table 4).

Table 4: Data obtained in the spectral interference analysis

S. No.	Sample	Absorbance
1	Drug solution without additive	0.481
2	Drug solution with Aerosil 200	0.485
3	Drug solution with Fujicalin	0.481
4	Drug solution with Neusilin	0.501
5	Drug solution with PVP K-30	0.499
6	Drug solution with PEG 300	0.505

The absorbances of the solutions (drug and additive) were almost closer to the absorbance of the drug solution. Thus, the analysis revealed that drug has no interference with the excipients used in the formulation.

FT-IR studies

The FT-IR studies were carried out to identify the compatibility of the excipients with the drug used in the formulation. The IR spectra obtained for the pure drug and for various mixtures (drug+excipient) are given in the fig. 3. From the fig. 3 it was found that, there was no significant change in the band peaks of drug-excipient mixtures with respect to a pure drug, giving *prima-facie* evidence that there is no incompatibility of excipients with the drug.

Saturation solubility study

The solubility studies for efavirenz in different solvents showed a varied solubility as shown in the fig. 4. The maximum solubility of the drug was observed in PEG 300 (74.87 mg/ml) among the various solvents used in the study. Hence, PEG 300 was selected as a non-solvent in the formulation of liquisolid compacts of efavirenz.

Flowable liquid retention potential (Φ–value)

This test is performed at 3 different ratios of carrier and coating material (i.e., R at 15, 20, and 25).

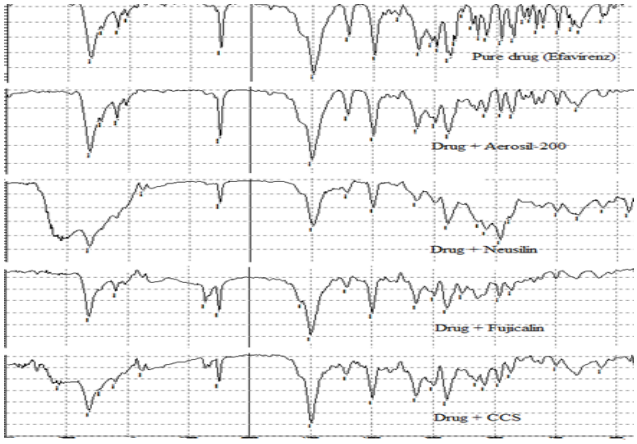

Fig. 3: Overlay of FT-IR spectrum of efavirenz and mixture of efavirenz with excipients

Formulation development

Using 2^3 factorial designs, eight formulations for each of Neusilin and Fujicalin were developed as per the design of experiments given in table II. The liquisolid compacts were prepared using direct compression technique. The prepared tablets were subjected to various evaluation tests as mentioned in the methods and materials section.

Evaluation of liquisolid tablets

Flow properties

Bulk density

It is the ratio of given mass of powder and its bulk volume determined by measuring the volume of known mass powder sample that has been passed through the screen into graduating cylinder.

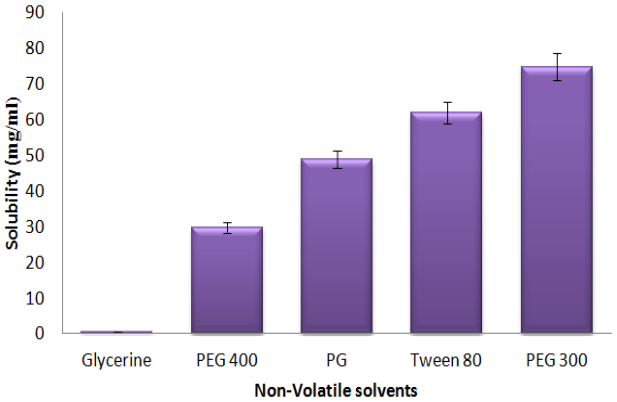

Fig. 4: Solubility studies of efavirenz in different solvents

Bulk density was determined according to USP method I. The powder sample under test was screened through sieve no 18 and an appropriate amount of pure drug and the formulation blend were accurately weighed and filled in a 100 mL graduated cylinder and the powder were leveled and the unsettled volume (V_o) was noted. Bulk density (D_b) was calculated in g/ml by the formula:

$D_b = M/V_o$

Where, M = mass of powder taken

V_o = unsettled apparent volume

Limits: It has been stated that the bulk density values having less than 1.2 g/cm^3 indicates good packing and values greater than 1.5 g/cm^3 indicates poor packing.

Table 5: *Flowable liquid load factor (ϕLf)* for various R values

R	1/R	Flowable liquid load factor(ϕL_f)	
		Neusilin	Fujicalin
25	0.04	0.791	0.510
20	0.05	0.880	0.612
15	0.06	1.020	0.751

The ϕ values obtained for 3 different ratios are given in the table 5. The ratio R=20 is selected for the formulation of efavirenz liquisolid compacts. Further, the compressible liquid retention potential for R=20 is determined and obtained as 0.880 (Neusilin: Aerosil 200) and 0.612 (fujicalin: aerosil 200) admixtures.

Tapped density

After carrying out the procedure as given in the measurement of bulk density, the cylinder containing the sample was tapped using a mechanically tapped density tester (Electro lab). The cylinder was tapped until no change in volume and then tapped volume V_t was measured to the nearest graduated unit. The tapped density was calculated, in grams per mL, using the formula:

$D_t = M/V_t$

Where, M = weight of sample powder

V_t= final tapped volume

Compressibility index (% Compressibility)

Carr's compressibility index, i.e., % compressibility indicates the flow property and packing ability of the tablet. It is determined by measuring both the bulk and tapped density of a powder. When the % compressibility ranges from 5 to16, the materials have acceptable flow property and packing ability. Compressibility Index was calculated using following equation:

$CI\ (\%) = (D_t - D_b)/D_t] \times 100$

Where, D_t = Tapped density

D_b = Bulk density

Hausner's ratio

The Hausner's ratio indicates the flowability and packing ability of the tablet. When the Hauser's ratio is close to 1, materials have acceptable flow and packing ability. Hausner's ratio was calculated using the formula:

Hausner's ratio = D_t/D_b

Where, D_t = Tapped density

D_b = Bulk density

Table 6: Correlation of compressibility index and Hausner's ratio with flow properties

Compressibility Index	Flow character	Hausner's ratio
1–10	Excellent	1.00–1.11
11–15	Good	1.12–1.18
16–20	Fair	1.19–1.25
21–25	Passable	1.26–1.34
26–31	Poor	1.35–1.45
32–37	Very poor	1.46–1.59
≥ 38	Very, very poor	≥ 1.60

The bulk density and tapped bulk density for all the formulations were conducted and the data were used to determine Carr's index and Hausner's ratio. The percentage compressibility for all the formulation blends of LSC-N1 to LSC-N8 and LSC-F1 to LSC-F8 lies in the range of 10.23 to 14.67 and 10.58 to 18.25 respectively. The Hausner's ratio for all the formulation blends of LSC-N1 to LSC-N8 and LSC-F1 to LSC-F8 lies within the range of 1.11 to 1.17 and 1.13 to 1.22 respectively, indicated good flow properties of the blend. Further, there flow properties were confirmed by angle of repose for all formulation blends.

Weight variation test

Weight variation was calculated as per method described in USP. Twenty tablets were selected at random and their average weight was determined using an electronic balance. The tablets were weighed individually and compared with average weight. The requirements are met if the weights of not more than 2 tablets differ by more than the percentage listed in the table 7 and no tablets differ in weight by more than double that percentage.

Thickness

Thickness and diameter of formulation trials were measured using a digital hardness tester. 10 tablets of each trial formulation were taken and measured individually at frequent intervals.

The thickness of formulations LSC-N1 to LSC-N8 was found to be in the range of 3.98 mm to 4.14 mm and the formulations LSC-F1 to LSC-F8 was found to be in the range of 4.46 mm to 4.57 mm.

Table 7: Acceptance criteria for weight variation

Average weight of tablet (mg)	%±deviation allowed
130 or less	10
More than 130 & less than 324	7.5
324 and above	5

As per the USP limits the % deviation for an uncoated tablet of weight for 324 mg and above is±5 %. The percentage deviation of all tablet formulations was found within±5 % and hence all the liquisolid batches pass the weight variation test as per USP.

Hardness

10 tablets from each batch were selected and hardness was measured using hardness tester to find the average tablet hardness or crushing strength.

The hardness of the formulations LSC-N1 to LSC-N8 & LSC-F1 to LSC-F8 was found to be in the range of 4.8–5.08 and 4.04–4.97 kg/cm^2 respectively. The acceptable hardness should be equal to or more than 4.5 kg/cm^2.

Disintegration time

Disintegration test, measured using USP tablet disintegration test apparatus (TGR56, Electro lab, India) using 900 ml of distilled water at room temperature (37±2 ^{0}C). For a drug to be absorbed from a solid dosage form after oral administration, it must first be in solution, and the condition is break up of the tablet, a process called disintegration. The disintegration test is a measure of the time required under a given set of conditions for a group of tablets to disintegrate into particles which will pass through a 10 mesh screen. Generally the test is useful as a quality assurance tool for dosage forms.

The USP device to test disintegration uses 6 glass tubes that are 3 inches long; open at the top and 10 mesh screens at the bottom end. To test, 1 tablet is placed in each tube and the basket rack is positioned in a 900 ml beaker of water, simulated gastric fluid or simulated intestinal fluid at 37±2 °C such that the tablet remains 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28-32 cycles per minute. Floating of the tablet can be prevented by placing perforated plastic discs on each tablet. According to the test, the tablet must disintegrate, and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass. If 1 or 2 tablets fail to disintegrate, the test is repeated using 12 tablets.

The tablet disintegration time ranges from 150 to 226 seconds for LSC-N1 to LSC-N8 formulations and 130 to 224 s for LSC-F1 to LSC-F8. The disintegration time was found to within the acceptable range. It is clearly evident that as the concentration of disintegrant increased, the disintegration time decreased.

Content uniformity

Ten tablets from each formulation were powdered. The powdered sample equivalent to 100 mg of drug was transferred to a 100 ml volumetric flask containing 100 ml of methanol. The contents were shaken up to 30 min. The solution was further diluted with 1% SLS solution. The drug content was determined by measuring the absorbance at 247 nm.

Drug content for formulations LSC-N1 to LSC-N8 was found to be in the range of 98.16-99.12%. In the case of LSC-F1 to LSC-F8 was found to be in the range of 98.12-99.23%.

***In-vitro* dissolution studies**

All the prepared liquisolid compacts of efavirenz using neusilin (LSC-N1 to LSC-N8) and fujicalin (LSC-F1 to LSC-F8) were subjected for *in-vitro* drug release studies. The dissolution studies were conducted simultaneously for the pure drug (100 mg in capsule) and for the physical mixture (tablet) in 0.1 N hydrochloric acid solution using Type-II apparatus. All the studies were conducted in triplicate at 50 rpm and at 37±0.5 °C.

All the liquisolid compacts showed that the drug release was more than 80 % in 30 min for all the LSC formulations LSC-N1 to LSC-N8 prepared with Neusilin. Further, the formulation LSC-N8 showed almost complete release in 45 min. The drug release from the physical mixture and pure drug were limited to the extent of 31.5 and 28.0 % respectively in 35 min. Thus, the *in-vitro* dissolution studies indicated the importance of liquisolid compacts to enhance the solubility and dissolution rates.

The release data obtained for the best formulations (LSC-N8 and LSC-F8) along with pure drug and physical mixture were tabulated as a ready reference in table 8 and the data was plotted in the fig. 5.

Table 8: *In-vitro* dissolution data obtained for LSC-N8, pure drug and physical mixture

Time (min)	Percentage cumulative drug release* (AM±SD)		
	LSC-N8	Physical mixture	Pure drug
0	0.00±0.00	0.00±0.00	0.00±0.00
5	54.60±0.03	9.0±0.05	2.5±0.04
10	62.01±0.08	15.0±0.09	7.8±0.11
15	72.70±0.45	20.0±0.24	15.0±0.23
20	80.02±0.06	22.0±0.09	19.0±0.98
25	88.90±0.66	28.0±0.08	22.00.08
30	94.08±0.32	31.5±0.32	25.0±0.15
35	99.98±0.09	34.6±0.06	28.0±0.07

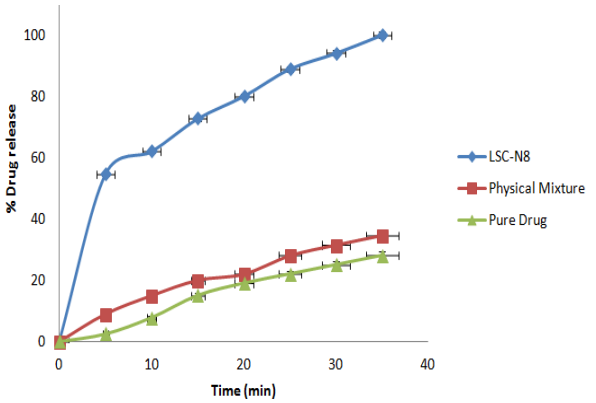

Fig. 5: Comparative *in-vitro* dissolution profile of the optimized formulation LSC-N8, pure drug and physical mixture

CONCLUSION

Efavirenz being a poorly water soluble drug can be made to provide a better treatment if the drug is released effectively and this is achieved by formulating the drug as liquisolid compacts. A 2^3 factorial design was employed and developed 8 different formulations for each of neusilin and fuji calin as carrier materials. The PEG 300 was chosen as the best non-solvent based on the saturation solubility studies. Angle of slide studies was considered and selected a ratio of 20. The prepared liquisolid compacts were evaluated for various physicochemical studies and *in-vitro* release studies, which indicated the formulations shower improved drug release in comparison to pure drug and physical mixture.

ACKNOWLEDGEMENT

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CONFLICT OF INTERESTS

Declared None

REFERENCES

1. Appa RB, Shivalingam MR, Kishore RYV, Somesekhara Rao, Rajesh K, Sunitha N. Formulation and evaluation of aceclofenac solid dispersions for dissolution rate enhancement. Int J Pharm Sci Drug Res 2010;2:146–50.
2. Charman SA, Charman WN. Oral modified release delivery systems-Modified Release Drug Delivery Technology; New York: 2003. p. 1-9.
3. Christian L, Jennifer D. Improving drug solubility for oral delivery using solid dispersions. Eur J Pharm Biopharm 2000;50:47-60.
4. Darwish AM, El-Kamel AH. Dissolution enhancement of glibenclamide using liquisolid tablet technology. Acta Pharm 2001;51:173-81.
5. Fahmy RH, Kassem MA. Enhancement of famotidine dissolution rate through liquisolid tablets formulation: *In vitro* and *in vivo* evaluation. Eur J Pharm Biopharm 2008;69:993-1003.
6. Jagan Mohan Vatyam, Ch S Vijaya Vani, V Umamaheshwara Rao. Enhancement of solubility and dissolution rate of efavirenz using liquisolid compact technique. Int J Pharm 2014;4:150-6.
7. Javadzadih Y, Stahi MR, Asnaashari S, Nokhodchi A. Liquisolid technique as a tool for enhancement of poorly water-soluble drugs and evaluation of their physicochemical properties. Acta Pharm 2007;57:99–109.
8. Kang MJ, Jung SY, Song WH, Park JS, Choi SU, Oh KT, *et al*. Immediate release of efavirenz from Fujicalin®-based fast-dissolving self-emulsifying tablets. Drug Dev Ind Pharm 2011;31:1298-305.
9. Kavitha K, Kotha NS, Lova Raju, NS Ganesh, B Ramesh. Effect of dissolution rate by liquisolid compact approach: an overview. Scholar Res Library 2011;3:71-83.
10. Matsunaga H, Eguchi T, Nishijima K, Enomoto T, Sasaoki K, Nakamura N. Solid state characterization of candesartan cilexetil (TCV-116): Crystal structure and molecular mobility. Chem Pharm Bull 1999;47:182-6.
11. Naveen C, Shastri N, Tadikonda RR. Use of the liquisolid compact technique for improvement of the dissolution rate of valsartan. Acta Pharm Sin B 2012;2:502-8.
12. Neelam Sreedhar, Sonu Bhatia. Solubility enhancement of cox-2 inhibitors using various solvent systems. AAPS PharmSciTech 2003;4:E33.
13. Nokhodchi A. The effect of type and concentration of vehicles on the dissolution rate of a poorly soluble drug (indomethacin) from liquisolid compacts. J Pharm Sci 2010;12:18-25.
14. Pratik Kumar A. Commercial telmisartan tablets: a comparative evaluation with innovator brand micardis pratik Kumar A. Int J Pharm Sci Res 2010;1:282-92.
15. Rajesh K, Raja Lakshmi R, Uma Maheswari J, Ashok Kumar C. Liquisolid technique a novel approach to enhance solubility and bioavailability. Int J Biopharm 2011;2:8-13.
16. Sanjeev Raghavendra Gubbi, Ravindra Jarag. Formulation and characterization of atorvastatin calcium liquisolid compacts. Asian J Pharm Sci 2010;5:50-60.
17. Sharma D. Solubility enhancement-eminent role in poorly soluble drugs. Res J Pharm Technol 2009;2:220-4.
18. Spireas S, Bolton M. Liquisolid systems and methods of preparing same. U. S. Patent; 1999. p. 968, 550.
19. Tiong N, Elkordy AA. Effects of liquisolid formulations on the dissolution of naproxen. Eur J Pharm Biopharm 2009;73:373-84.
20. Vijay kumar Nagabandi, Ramarao Tadikonda, Jayaveera KN. Formulation development and evaluation of liquisolid system to improve the dissolution rate of Ketoprofen. Int J Biomed Res 2011;2:530-41.
21. Vijay N, Ramarao T, Jaya Veera K. Liquisolid compacts a novel approach to enhance bioavailability of poorly soluble drugs. Int J Pharm Biol Sci 2011;1:89-102.
22. Wen X, Tan F, Jing Z, Liu Z. Preparation and study the 1:2 inclusion complex of carvedilol with beta-cyclodextrin. J Pharm Biomed Anal 2004;34:517-23.