Research Article

Formulation and evaluation of Orodispersible liquisolid compacts of Nifedipine using co-processed Superdisintegrants

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Abstract

Objective: The aim of the present study was to enhance the dissolution of a practically insoluble Nifedipine by liquisolid compact technique and to enhance the onset of action by Orodispersible tablet technique. **Materials and methods:** Orodispersible liquisolid compact of Nifedipine were prepared by direct compression method using PEG 400, Microcrystalline cellulose PH 102 and Aerosil 200 as non-volatile solvent, carrier, coating material respectively and co-processed superdisintegrants (Crosspovidone and croscarmellose sodium) in the ratio of 1:1, 1:2, 1:3. The liquisolid compacts were characterized by X-ray powder diffraction, Scanning electron microscopy and FT-IR studies. The statistical analysis for stability studies was carried out by Student's t-test (SPSS SOFTWARE VERSION 16.0) at a level of P = 0.05. **Results and conclusion:** Orodispersible liquisolid compacts of Nifedipine tablets (F3) containing co-processed superdisintegrants in the ratio of 1:3 exhibits quick disintegration time and maximum drug release. No significant difference (P value 0.969 > 0.05) was found in the dissolution rate of the stored formulation when compared with freshly prepared formulation. **Conclusion:** This research work may be useful to formulate Orodispersible tablets using Liquisolid technique which may give rapid onset of action by rapid absorption, maximize efficacy and hence increase patient compliance.

Keywords: Liquisolid compacts, poorly soluble drugs, super-disintegrants, dissolution rate

Introduction

The poor dissolution rate of water insoluble drug is a major impediment to the development of pharmaceutical dosage forms. The oral absorption of drug is most often controlled by dissolution in the gastrointestinal tract. Different methods are employed to improve the dissolution characteristics of poorly water soluble drugs, like solubilization, pH adjustment, co-solvents, micro emulsion, particle size reduction, use of surfactant as a solubilising agent, prodrug approach etc. Amongst these the most promising method for promoting dissolution is the use of the liquisolid system (Munke and Nagarsenker, 2004).

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Liquisolid system refers to formulation by conversion of oily liquid drug and solutions or suspensions of water insoluble solid drugs in non-volatile solvents into dry, non-adherent, free flowing and compressible powder mixtures by blending the suspension or solution with selected carrier and coating materials (Javadzadeh and Nokhodchi, 2008).

In order to improve ease of drug administration, fast disintegrating tablets are widely accepted commercially. Fast or rapid disintegrating tablets include fast dissolution, quick disintegration and results in fast absorption which provide rapid onset of action. Moreover, drug candidates that undergo pre-gastric absorption may show increased oral bioavailability. Fast dissolving tablets provide accurate dosing, easy manufacturing and good stability (Kaushik et al., 2004).

Nifedipine is widely used in the treatment of vascular diseases such as Hypertension, Angina pectoris and Raynaud's phenomenon. It is a class II drug of BCS

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classification; hence it has a low solubility. Since, it is a highly non-polar compound, which absorbed completely from the gastrointestinal tract. Although it is completely absorbed from the gastrointestinal tract, the systemic availability is approximately 45-46% because of high first pass metabolism (Karmarkar et al., 2009).

The rate-limiting step in the absorption of Nifedipine is its dissolution rate in gastrointestinal fluids. If its aqueous solubility is increased it will give higher dissolution rate and improved bioavailability. To overcome the drawbacks, various techniques are employed to enhance the dissolution. Among these the "liquisolid" is a newly developed technique. Therefore, Nifedipine establishes a good candidate for the formulation of liquisolid tablet.

Hence, the present study deals with the dissolution enhancement of Nifedipine by liquisolid technique and also an attempt was planned to formulate fast dissolving tablets of Nifedipine, a poorly water soluble drug for rapid disintegration and rapid onset of action in the management of Hypertension, Angina pectoris and Raynaud's phenomenon using co-processed Superdisintegrants (Srinivas and Gadat, 2006).

Materials and methods

Materials

Nifedipine, Polyethyleneglycol-400, Microcrystalline cellulose PH102, Aerosil 200, Mannitol, Crosspovidone, Croscarmellose sodium, Magnesium stearate, Talc, Mango flavour.

Compatibility studies

Drug-Excipients compatibility studies by FT-IR

Compatibility studies of pure drug and excipients were carried out using Fourier transformed infrared spectrophotometer (Shimadzu, Japan) in the range of 400 - 4000/cm by KBr disc method. A base-line correction was made using dried potassium bromide and then the spectrum of the pure Nifedipine and Nifedipine + Excipients were obtained (Kanagathara et al., 2011).

Solubility studies for the selection of non-volatile solvents

Solubility studies are carried out by preparing saturated solutions of drug in non-volatile solvent and analyzing them spectrophotometrically (Javadzadeh and Nokhodchi, 2008). Saturated solutions are prepared by adding excess of drug to non volatile solvent and shaking them on shaker for specific time period under constant vibration, followed by saturation solution transfer to an orbital shaker for 48 hrs at 25 ˚C. After 48 hrs, the saturated solutions were filtered and analyzed by UV-spectrophotometer at 237 nm.

Calculation of loading factor

Loading factors were calculated for carriers, for the non-volatile solvents PEG 400. By using Lf = W/Q formula (W: Amount of liquid medication and Q: Amount of carrier material), the drug loading factors were obtained and used for calculating the amount of carrier and coating materials in each formulation (Spireas, 2002).

Characterization of Liquisolid compacts

Scanning electron microscopy (SEM)

Morphological Characteristic of drug and powder mass of liquisolid tablets were analyzed using Scanning electron microscopy. The samples were fixed on aluminum stubs with double-sided tape, gold coated sputter and examined in the microscope using an accelerating voltage of 15 kV, at a working distance of 8 mm and magnification of X500, X2000. Study shows complete disappearance of crystal of drugs and confirms that drug is totally solubilized in liquisolid system (Kumar et al., 2013).

Powder X-Ray diffraction (XRD) study

Crystallinity of the drug and the samples were determined using the Philips Analytical XRD with copper target. The conditions were: 40 kV voltages; 30 mA current; at room temperature. The samples were loaded on to the diffractometer and scanned over a range of 2° values from 10 to 80° at a scan rate of 0.05°/min. Generally, disappearance of characteristic peaks of drug in the liquisolid formulation and retaining peaks of carrier material is observed .This indicates that the drug gets converted to amorphous form or in solubilized form in the liquisolid system (Kumar et al., 2014).

Preparation of Co-Processed Superdisintegrants

The co-processed Superdisintegrants were prepared by solvent evaporation method (Gohel, 2013). A blend of crospovidone and croscarmellose sodium (in the ratio of 1:1, 1:2 & 1:3) was added to 10 ml of ethanol. The contents of the beaker (250 ml capacity) were mixed thoroughly and stirring was continued till most of ethanol gets evaporated. The wet coherent mass was granulated through # 44-mesh sieve. The wet granules were dried in a hot air oven at 60º C for 20 minutes. The dried granules were sifted through #44-mesh sieve and stored in airtight container till further use.

Preparation of orodispersible liquisolid tablets of Nifedipine

Various liquisolid ODTs formulas denoted F-I to F-VI as shown in table 1 containing 10 mg of Nifedipine were prepared by dispersing the drug in the non-volatile vehicle (PEG-400). Then a binary mixture of carrier (Avicel PH 102) and coating material (Aerosil 200) was prepared at a ratio of 10:1(R=10) for F-I to F-III and 15:1(R=15) for F-IV to F-VI. The carrier material was added to the admixture

Table 1. Formulation of orodispersible liquisod tablets

Ingredients		F-I	F-II	F-III	F-IV	F-V	F-VI
Nifedipine		10 mg	10mg	10mg	10mg	10mg	10mg
Peg-400		10mg	10mg	10mg	10mg	10mg	10mg
R		10	10	10	15	15	15
Lf		0.205	0.205	0.205	0.138	0.138	0.138
Avicel PH-102		50mg	50mg	50mg	72mg	72mg	72mg
Aerosil 200		5mg	5mg	5mg	4.8mg	4.8mg	4.8mg
SD	1:1	10mg	_	_	10mg	_	_
	1:2	_	10mg	_	_	10mg	_
	1:3	_	_	10mg	_	_	10mg
Mannitol		110.5mg	110.5mg	110.5mg	88.7mg	88.7mg	88.7mg
Magnesium Stearate		2mg	2mg	2mg	2mg	2mg	2mg
Talc		2mg	2mg	2mg	2mg	2mg	2mg
Flavour		0.5mg	0.5mg	0.5mg	0.5mg	0.5mg	0.5mg
Weight of Tablet				200 mg			

R= Excipient ratio; **Lf**= Loading factor; **Avicel PH102**= Carrier material **Aerosil 200**= Coating material **SD**=Co-processed Superdisintegrants (crospovidone: croscarmellose sodium)

of drug and vehicle and triturated well and waited for 10 mins in order to complete absorption of liquefied drug in the porous carrier material .Then, weighed amount of coating material was added and triturated slowly for 15 mins for the complete adsorption of coating material over the porous carrier material. Finally, co-processed superdisintegrant and other excipients were added to the above powder blend and mixed thoroughly. The final powder blend was subjected to direct compression by using 8mm flat upper-scoring punch on Clit single rotary- 16 station punching machine. The formulas F-I to F-III were prepared by using the excipients ratio R=10 and 1:1, 1:2, 1:3 ratio of co-processed Superdisintegrants. The loading factor was kept constant in the above formulas which is equal to 0.205; the formulas F-IV to F-VI were prepared using the excipients ratio R=15 and 1:1, 1:2, 1:3 ratio of co-processed Superdisintegrants. The loading factor was kept constant in the above formula which is equal to 0.138.

Pre compression parameters

The flow properties of the powder are vital for the performance of the tablet. Hence, the flow properties of the powder were analyzed before compression to tablets. The powder mixture of different formulations was evaluated for angle of repose, bulk density, tapped density, compressibility index, Hausners's ratio (Indian pharmacopoeia, 1996).

Bulk density

Accurately weighed 50 gm of blend, previously passed through 20# sieve is transferred into 100 ml graduated cylinder. The powder was carefully levelled without compacting and the unsettled apparent volume was noted.

Bulk density = Weight of the powder/Bulk volume of powder

Tapped density

Accurately weighed 50 gm of the blend was transferred into 100 ml graduated cylinder. Initial volume was observed. The cylinder was tapped initially 500 times from a distance of 1 4 + 2 mm and measured the tapped volume to the nearest graduated units. The tapping was repeated for additional 750 times. Again the tapped volume was measured to the nearest graduated unit**.** The tapped bulk density in gm/ml was calculated by using the following formula.

Tapped density= Weight of powder taken/ Tapped Volume

Compressibility index

The propensity of the powder to be compressed is measured by compressibility and it also helps in measurement of settling property and interparticulate interaction.

Compressibility index (%) = $\rho t - \rho o * 100 / \rho t$

Where ρt = Tapped density gram/ml, ρo = Bulk density gram/ml.

Hausner's ratio

The Hauser's ratio is a number that is correlated to the flowability of a powder or granular material

Hausner's ratio= Tapped density/ Bulk density

Angle of repose

The angle of repose of blend was determined by funnel method. Accurately weighed powder blend was taken in a funnel. Height of the funnel was adjusted in such ways that tip of the funnel just touches the apex of the powder blend. The powder blend was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose is calculated using the following equation;

$$\tan = \theta\ h/r$$

Where, h and *r* are the height and radius of the powder cone.

Post-compression parameters

Thickness and Hardness test

The thickness of the tablets was determined using digital caliper; reading shown was noted. The hardness was tested by using Monsanto tester (Dawahar et al., 2008).

Friability test

The friability of the tablets was determined using Roche friabilator (Lachman et al., 1987). The % friability was then calculated using the formula:

$$\text{Friability} = ([W_o - W]/WO)\ 100$$

Where, Wo =initial weight of tablet; W = after test weight of tablet.

Weight variation test

The test was performed as per USP by weighing 20 tablets individually on electronic balance, calculating the average weight, and comparing the individual tablet weights to the average (Dobetti, 2011).

***In-vitro* dispersion time**

In-vitro dispersion time was measured by following procedure. The tablet was carefully positioned in the center of the petridish containing 6 ml of water and the time required for the tablet to completely disintegrate into fine particles was noted. Three tablets from each formulation were randomly selected and *In-vitro* dispersion time was measured.

***In-vitro* disintegration test**

The test was carried out on 6 tablets using tablet disintegration tester (Kumar et al., 2011). Water at 37 ± 2˚C was used as a disintegration media and the time taken for complete disintegration of the tablet was noted with no passable mass remaining in the apparatus was measured.

Wetting time

A piece of tissue paper was folded twice and placed in small petri dish containing sufficient water. A tablet was kept on the paper and the time for complete wetting of tablet was measured (Patel et al., 2013).

Water absorption ratio

The weight of the tablet prior to placement in the petri dish was noted (Wb) (Rajesh et al., 2011). 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.

Uniformity of dispersion

Two tablets were kept in 100ml water and stirred gently for 2 minutes. The dispersion was passed through 22 meshes. The tablets were considered passing the test if no residue remained on the screen (Kumar et al., 2011).

Drug content determination

Three tablets were selected randomly and average weight was calculated. Tablets were crushed in a mortar and accurately weighed amount of tablet powder was taken from the crushed blend and transferred it in to a 100 ml volumetric flask.10 ml of methanol was added and sonicated for 10 minutes. Then volume was made up to 100 ml with pH 7.4 buffer. The 1mL of resultant solution was diluted to 100mL with buffer (pH 7.4). The absorbance of above solution was measured in UV spectrophotometer at 237nm.

Dissolution studies

The dissolution test for oral disintegrating tablets is the same as that of conventional tablets (Slog et al., 1998). The release rate of Nifedipine from liquisolid tablets was studied using USP II Dissolution Testing Apparatus. The dissolution test was performed using 900 ml of Phosphate buffer pH 7.4, at 37 ± 0.5°C and 50 rpm. A sample (2 ml) of the solution was withdrawn from the dissolution apparatus at 0, 5, 10, 15, 25, 35, 45 minutes intervals and diluted to 10 ml and replaced with 1ml of fresh dissolution medium. The samples were filtered. Absorbances of these solutions were measured at 237nm using UV-Visible spectrophotometer.

Stability studies

Whenever a new formulation is developed, it is very essential to establish that the therapeutic activity of the drug has not undergone any change. To conform this, the selected formulation was subjected to stability studies. Accelerated stability testing studies was performed for 3 months as per

ICH guidelines. The optimized formulations were kept at 40±2 ˚C and 75±5% RH. Tablets were evaluated for physical appearance, hardness, *In-vitro* dispersion time, % drug content and % drug release.

Statistical Analysis

The statistical analysis for stability studies was carried out by Student's t-test (SPSS SOFTWARE VERSION 16.0) at a level of P= 0.05.

Results and discussions

Drug-Excipients compatibility studies by FT-IR

All the reference peaks which are observed in the IR spectrum of Nifedipine were also observed in the IR spectrum of physical mixture of drug and polymers which shown in Figure 1. It was found that Nifedipine was compatible with Superdisintegrants and excipients used in the formulation. The observed peaks are shown in table 2.

Table 2. Drug-Excipients compatibility studies by FT-IR

Assignment	Peak report(cm^{-1})	Peak observed(cm^{-1})
N-H stretch	3400-3250	3332.12
C-H (alkane stretching)	2960-2862	2917.29
O-H (carboxylic acid)	3800-2500	2917.29
C=O stretch (ester)	1730-1630	1688.68
N-O stretch (nitro compound)	1550-1475	1530.59

Vehicle selection

The solubility of Nifedipine was determined in a number of solvents and is reported in table 3. Drug solubility in a non-volatile vehicle is the most important aspect in liquisolid systems. The solubility of the drug contributes to molecular dispersion in a non-volatile solvent which will improve the dissolution rate. Based on the solubility data, PEG 400 was selected as the vehicle for Nifedipine.

Table 3. Solubility of Nifedipine in various Vehicles

Solvents	Solubility (mg/ml) (mean± S.D.)*
PEG 400	3.30±0.035
Propylene glycol	2.88±0.01
Glycerin	0.16±0.005
Polysorbate 80	0.18±0.026

*n=3 S.D = Standard Deviation

Liquid load factor

Loading factors were calculated for different ratio of carriers and coating using PEG 400 as vehicle. The loading factor for the R value 10 and 15 was found to be 0.205 and 0.138 respectively. The data are given in table 4.

Table 4. Liquid load factor

S. No	Liquid vehicles	carrier and coating material ratio	Liquid load factor
1	PEG 400	1:10	0.205
2	PEG 400	1:15	0.138

Characterization of liquisolid compact

Scanning Electron Microscopy

Morphological Characteristic of drug and powder mass of liquisolid tablets were analyzed using Scanning electron microscopy. The scanning electron micrograph of pure Nifedipine in figure 2 (a) showed a needle like crystal shapes whereas liquisolid compact in figure 2 (b) shows the disappearance of needle like crystalline shape of the drug. This indicate that the drug was solubilized in the liquid system and it proves that even though the drug is in solid dosage form it is held within the powder substrate in the

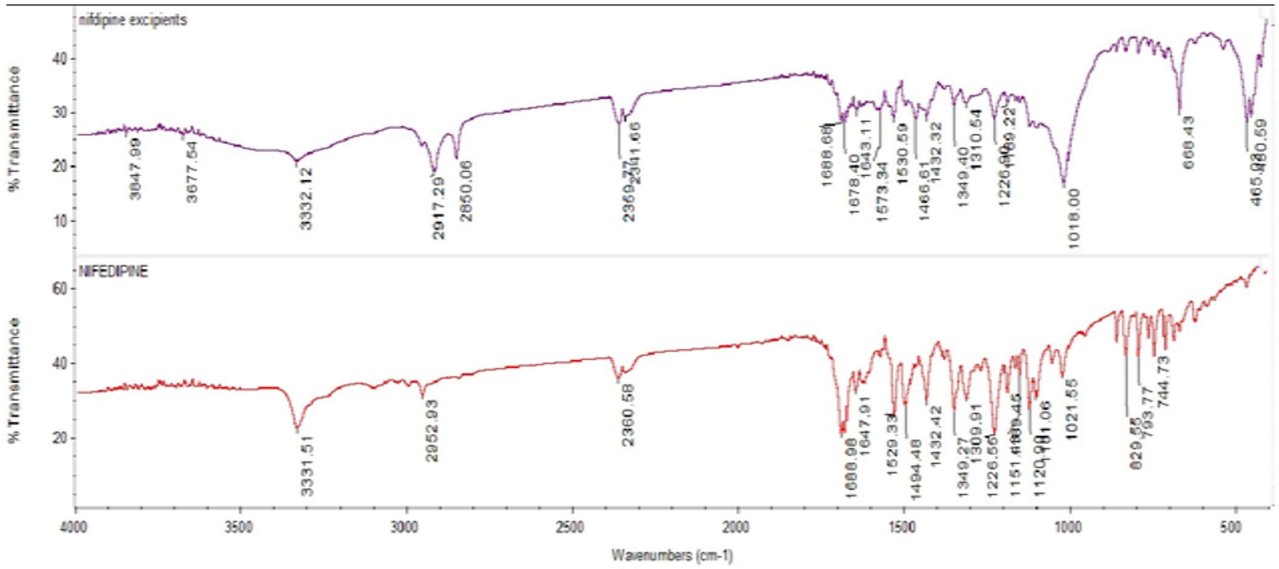

Figure 1. IR spectra of Nifedipine and Nifedipine + Excipients

solution or almost molecules in dispersed state which contributes to the enhancement of the drug solubility.

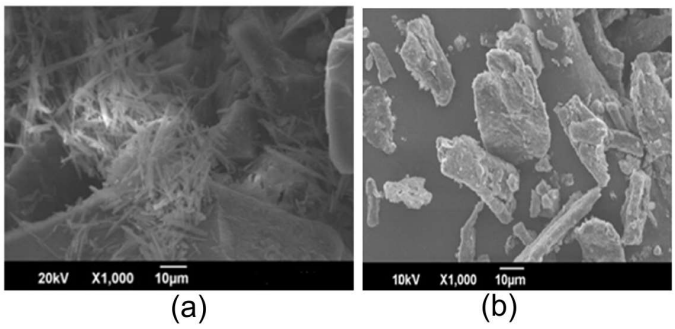

Figure 2. SEM of (a) Nifedipine (b)Liquisolid compact

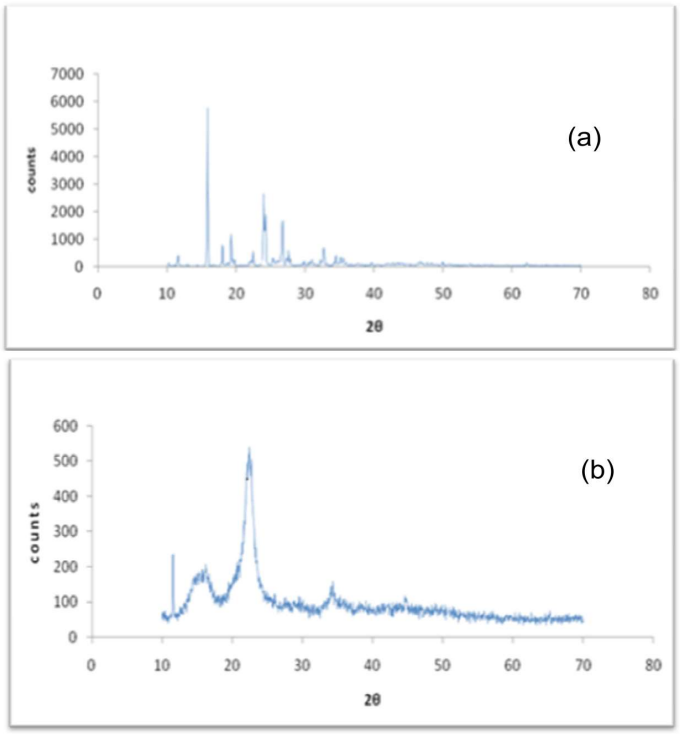

Figure 3. X-ray diffraction of (a) Nifedipine, (b) Liquisolid compact.

X-ray powder diffraction analysis

The X-ray diffraction pattern of pure Nifedipine in Figure 3 (a) showed a characteristic high intensity diffraction peak indicating that the drug is in crystalline form where as a reduced intensity peaks were observed for Liquisolid Compact in figure 3 (b). In the X - Ray diffractogram of Nifedipine, sharp peaks at a diffraction angle (2θ) of 15º, 18º, 19º, 24º, and 26º were present and it suggested that the drug is present in crystalline form. But entirely different low intensity peaks showed by the liquisolid compact. The X-Ray scan showed the absence of characteristics peaks of Nifedipine in liquisolid compacts, indicates that Nifedipine is entirely converted into amorphous or solubilized form.

Evaluation of orodispersible liquisolid compacts of Nifedipine tablets

Pre compression parameters

Angle of repose of all the formulations was found to be ranging from 31.69±0.67 -34.16±1.83, bulk density was found to be 0.802±0.05 - 0.841±0.01, tapped density was in between 0.877±0.01 - 0.937±0.02, Carr's index was found to be within 11.26±0.94 – 12.34±0.81 and Hausner's ratio was found to be within 1.017±0.02 – 1.146±0.04. The results of angle of repose, Carr's index, and Hausners's ratio indicated good flow ability of powders and reported in table 5 and the powders were free flowing, tablets produced were of uniform weight with acceptable weight variation due to uniform filling in the die.

Post compression parameters

Tablet mean thickness was almost uniform in all the formulations. The thickness varies between 4.0±0.010 - 4.02±0.010 mm. The prepared tablets in all the formulations possessed good mechanical strength with sufficient hardness in the range of 3.33±0.25 - 3.58±0.37 kg/cm^2. The friability was found to be between 0.450 - 0.620 %. All the formulated tablets were shown the % friability within the official limits (*i.e.,* not more than 1%). Prepared tablets were evaluated for weight variation and percentage deviation from the average weight of all tablet formulation (F1 – F6) and were found to be within (±7.5)

Table 5. Pre compression parameters

Formulation Code	Angle of repose θ (mean± S.D.)*	Bulk density (g/ml) (mean± S.D.)*	Tapped density (g/ml) (mean± S.D.)*	Carr's Index (%) (mean± S.D.)*	Hausner's ratio (mean± S.D.)*
F1	33.37±1.54	0.802 ±0.05	0.877 ± 0.01	12.16 ± 0.84	1.096 ± 0.05
F2	32.98±1.83	0.806 ±0.02	0.896 ± 0.02	12.00 ± 1.55	1.112 ± 0.05
F3	32.96±1.73	0.820 ±0.01	0.935 ± 0.02	11.94 ± 1.77	1.146 ± 0.04
F4	34.16±1.83	0.832 ±0.01	0.937 ± 0.02	12.34 ± 0.81	1.074 ± 0.01
F5	31.69±0.67	0.841 ±0.01	0.926 ± 0.02	12.3 ± 0.72	1.099 ± 0.03
F6	33.15±1.12	0.834 ±0.00	0.912 ± 0.00	11.26 ± 0.94	1.017 ± 0.02

n=3* S.D=Standard Deviation

Table 6. Post compression parameters of orodispersible liquisolid compacts tablets

Formulations	*Hardness Kg/cm^2 (mean± S.D.)*	Friability %	*Thickness Mm (mean± S.D.)*	*% weight Variation (mean± S.D.)*
F1	3.41±0.20	0.490	4.01±0.022	0.014±0.37
F2	3.33±0.25	0.620	4.01±0.012	0.047±0.49
F3	3.58±0.37	0.450	4.01±0.014	0.048±0.43
F4	3.50±0.44	0.510	4.02±0.010	0.022±0.52
F5	3.58±0.09	0.480	4.01±0.005	0.037±0.34
F6	3.56±0.20	0.590	4.00±0.015	0.044±0.13

n=3* S.D=Standard Deviation

Table 7. Results of *In-vitro* dispersion time, wetting time and water absorption ratio of orodispersible Nifedipine tablet

Formulations	**In-vitro* dispersion time (sec) (mean± S.D.)*	*Disintegration Time (sec) (mean± S.D.)*	*Wetting time (min) (mean± S.D.)*	*Water absorption Ratio (%) (mean± S.D.)*	Uniformity of Dispersion
F1	86.16±1.52	89.00±2.00	2.48±0.23	68.15±0.89	Passes
F2	69.00±1.00	72.33±2.51	2.53±0.58	66.31±0.91	Passes
F3	45.33±1.15	49.33±1.52	1.56±0.45	73.56±1.70	Passes
F4	66.16±1.52	65.00±1.00	2.58±0.38	65.59±0.86	Passes
F5	58.22±1.23	52.20±1.20	2.14±0.16	69.33±1.20	Passes
F6	47.20±1.30	51.30±1.22	1.56±0.32	73.20±1.08	Passes

n=3* S.D=Standard Deviation

the prescribed official limits. The data are given in table 6.

The *in-vitro* dispersion time was found to be in the range of 45.33±1.15 - 86.16±1.52 sec and shown in figure 4 (a) and figure 4 (b). The mean of the disintegration times for all investigated tablets was less than 2 min, which fulfil the pharmacopoeial requirement. The disintegration time was found to be in the range of 49.33±1.52 - 89.00±2.00 sec.

In this study, the disintegrating effect of co-processed Superdisintegrants was studied by changing different ratio. The formulation F1 with 10 mg of co-processed Superdisintegrants in the ratio of 1:1 showed 89.00±2.00 sec and with 10 mg of co-processed Superdisintegrants in the ratio of 1:3 for formulation F3 showed lesser disintegration time of 49.33±1.52 sec. The results also suggested that co-processed Superdisintegrants showed faster disintegration time, due to the rapid uptake of water from the medium, swelling and burst effect. The wetting time of tablets was in the range of 1.56±0.45 - 2.58±0.58 min, which complies with the official specifications. The water absorption ratio was found to be in the range 68.15±0.89 – 73.56±1.70 % and data are given in table 7.

Estimation of % drug content

The drug content of the liquisolid compacts F1 to F6 were found to be in the range of 96.12 – 99.15 ± 0.57%. The %drug content of F1 to F6 of Nifedipine liquisolid compact was shown in table 8.

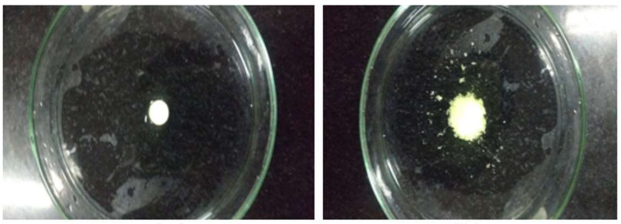

Figure 4.*In-vitro* dispersion time at (a) 0 sec (b) at 45.33 sec of F3 formulation.

Dissolution studies

Among the six formulations F3 has the maximum dissolution rate. It shows 52.33% percentage drug release in the first 10min and 100% release within 35min. From the above results it is clear that the increase in the amount of co-processed superdisintegrants, increased in the dissolution rate of the drug. It is because of increased aqueous solubility, and increased wetting property of the

Table 8. Estimation of %drug content

S. No	Formulation Code	Drug content (%) (mean± S.D.)*
1	F1	96.12 ± 0.00
2	F2	96.30 ± 0.42
3	F3	99.15 ± 0.57
4	F4	96.15 ± 0.98
5	F5	98.53 ± 0.52
6	F6	96.20 ± 0.81

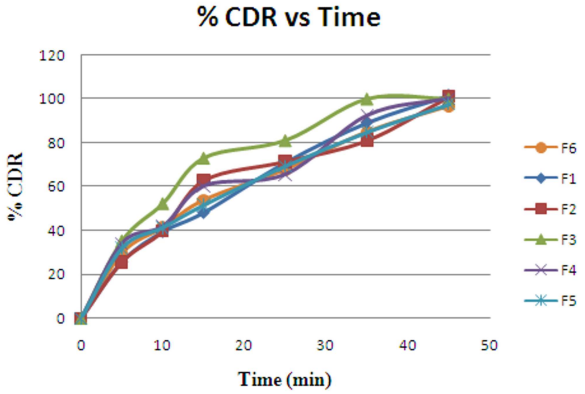

Figure 5. Dissolution studies of orodispersible liquisolid compacts of Nifedipine

drug. The percentage of drug release of F1 – F6 shows 101.67%, 101.02%, 100%, 100.3%, 97.63%, and 96.69% respectively. Among the different formulations, F3 contains the co-processed superdisintegrants in the ratio of 1:3 and excipient ratio of R=10 and Liquid load factor of Lf=0.205 achieved more than 70% of drug within 15 mins. These results suggests that the co-processed superdisintegrants in the ratio of 1:3 and excipient ratio of R=10 have faster disintegrating and dissolution effect. Dissolution studies of orodispersible liquisolid compacts of Nifedipine was shown in figure 5 and table 9.

Table 9. Dissolution studies of orodispersible liquisolid compacts of Nifedipine

Time	% Cumulative Drug Release					
	F1	F2	F3	F4	F5	F6
0 min	0	0	0	0	0	0
5 min	25.81	25.72	35.32	34.3	32.04	29.71
10 min	39.54	39.9	52.33	42.03	41.39	41.42
15 min	48.23	62.8	73.06	60.34	51.66	53.84
25 min	71.08	71.43	81.06	65.7	69.51	67.85
35 min	89.27	81.12	100	92.6	85	85
45 min	101.67	101.02		100.3	97.63	96.69

Table 10. Accelerated stability study of F3 formulation

Storage condition	Evaluation Parameters	Duration in months	
		0	3
40±2 °C and 75%±5% RH	Hardness (mean± S.D.)*	3.58±0.37	3.58±0.37
	In-vitro dispersion time (mean± S.D.)*	45.33±1.15	45.33±1.15
	Drug content (%)(mean± S.D.)*	99.15 ± 0.57	99.00±0.41
	% of drug release	100	99.93

* n=3 S.D=Standard Deviation

Stability studies

Accelerated stability studies for the optimized tablets formulation F3 were carried out at a temperature of 40±2 °C and 75±5% RH for a period of 3 months. Tablets were evaluated for physical appearance, hardness, *In-vitro* dispersion time, % drug content and % of drug release. The results are shown in table 10. No significant difference (P value 0.969 > 0.05) was found in the dissolution rate of the stored formulations when compared with freshly prepared formulation. Tablets have not shown any significant change during storage. Hence, it was concluded that the tablets have good stability during their shelf life.

Conclusion

Orodispersible liquisolid compacts prepared with PEG 400 and co-processed superdisintegrants enhanced the dissolution rate of Nifedipine to a greater extent. The tablets prepared with co-processed superdisintegrants showed highest dissolution rate. This may be attributed to rapid uptake of water with vigorous swelling ability of co-processed superdisintegrants. Hence, the combined effect of liquisolid compact technique and inclusion of different ratio of co-processed superdisintegrants is useful in enhancement of dissolution rate of Nifedipine. It can be said that liquisolid technique with co-processed superdisintegrants is a promising strategy in improving dissolution of insoluble drugs and formulating immediate release solid dosage forms.

Conflict of interest

The authors have no conflict of Interest.

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