



Research Article

COMPARATIVE STUDY ON EFFECT OF DIFERENT TECHNIQUES USED IN THE FORMULATION OF FELODIPINE FAST DISSOLVING TABLETS

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ABSTRACT

Felodipine which is used in the present study is a dihydropyridine derivative, that is chemically described as ethyl methyl-4-(2,3-dichlorophenyl)-1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate, widely accepted for its excellent antihypertensive and antianginal properties since it is calcium antagonist compound (calcium channel blocker). Felodipine is practically insoluble in water and its dissolution rate is limited by its physicochemical properties. Felodipine fast dissolving tablets (FDT) have been prepared by direct compression method. Effect of method of preparation (i.e. solid dispersion and sublimation) on dissolution rate, disintegration time and wetting time was studied. Effect of superdisintegrants (such as croscarmellose sodium, and crospovidone) on wetting time, disintegrating time, drug content, *in vitro* release, and stability parameters have been studied. The prepared tablets were characterized by XRD, and FTIR Studies. Tablets prepared by solid dispersion with mannitol showed higher hardness than other tablets prepared by solid dispersion with PVP and PEG. Friability of tablets ranged between 0.21-0.64%. Drug content of tablets ranged between 95.91-102.00%. XRD analysis revealed that there was a formation of amorphous form in all solid dispersions. FT-IR studies revealed that, there was no incompatibility of the drug with the excipients used. Disintegration time of tablets prepared by solid dispersion using mannitol, increased significantly (p<0.05). From this study, it can be concluded that dissolution rate of felodipine could be enhanced by tablets containing solid dispersion by direct compression technique. Tablets containing solid dispersion with PVP of ratio 1:4 (P3), with PEG of ratio 1:4 (E3) and with mannitol of ratio 1:9 (M4) yielded best results in terms of dissolution rate.

Key words: Fast dissolving tablets, Felodipine, Croscarmellose sodium, Crospovidone and Sodium starch glycolate.

INTRODUCTION

Felodipine which is used in the present study is a dihydropyridine derivative, that is chemically described as ethyl methyl-4-(2, 3-dichlorophenyl)-1, 4-dihydro-2, 6-dimethyl-3,5-pyridinedicarboxylate, widely accepted for its excellent antihypertensive and antianginal properties since it is calcium antagonist compound (calcium channel blocker). Felodipine is practically insoluble in water and its dissolution rate is limited by its physicochemical properties¹. For poorly soluble orally administered drugs the rate of absorption is often controlled by the rate of dissolution. The rate of dissolution can be increased by increasing the surface area of available drug by various methods (micronization, complexation, solid dispersion etc). Another prerequisite for the fast dissolution may be the disintegration time of tablets. Because, faster disintegration of tablets delivers a fine suspension of drug particles and thus, greater dissolution of the drug².

The rate of dissolution can be increased by increasing the surface area of available drug by various methods [micronization, complexation, and solid dispersion (SD)]². The dissolution of a drug can also be influenced by disintegration time of the tablets. Faster disintegration of tablets delivers a fine suspension of drug particles resulting in a higher surface area and faster dissolution.

Now a day fast dissolving tablets are gaining more importance in the market. Currently these tablets are available in the market for treating many disease conditions. More is concerned on hypertension³, migraine⁴, dysphasia⁵, nausea and vomiting⁶, Parkinson's disease⁷, schizophrenia⁸, pediatric emergency⁹. These conditions are those which require the drug to be formulated as fast dissolving tablets. Some patient prefers fast dissolving tablets to conventional tablets best of ease of administration, swallowing, pleasant taste and the availability in several flavors¹⁰.

The pediatric and geriatrics patients are of particular concern. To overcome this, dispersible tablets¹¹ and fast-disintegrating tablets¹² have been developed. Most commonly used methods to prepare these tablets are; freeze-drying/Lyophilization¹³ tablet molding¹⁴ and direct-compression methods¹⁵. Lyophilized tablets show a very porous structure, which causes quick penetration of saliva into the

pores when placed in oral cavity^{13, 16}. The main disadvantages of tablets produced are, in addition to the cost intensive production process, a lack of physical resistance in standard blister packs and their limited ability to incorporate higher concentrations of active drug¹¹. Moulded tablets dissolve completely and rapidly. However, lack of strength and taste masking are of great concern¹⁷. Main advantages of direct compression are low manufacturing cost and high mechanical integrity of the tablets¹⁸. Therefore, direct-compression appears to be a better option for manufacturing of tablets. The fast disintegrating tablets prepared by direct compression method, in general, are based on the action established by superdisintegrants such as croscarmellose sodium, and crospovidone. The effect of functionality differences of the superdisintegrants on tablet disintegration has been studied¹⁹. The objective of the present work to develop felodipine fast dissolving tablets by croscarmellose sodium and crospovidone are used as superdisintegrants. Effect of method of preparation (i.e. SD and sublimation) on dissolution rate, disintegration time and wetting time was studied. The compositions of which are given in [Table 1 and 2].

MATERIAL AND METHODS

Felodipine as procured as a gift sample from Cipla Ltd, Bangalore, India.. Superdisintegrants (Maruti Chem. Ahmadabad), Aspartame (Aan Pharma Pvt Ltd., Rakanpur-Gujarat). Sodium lauryl sulphate, D.C. Mannitol, Micro crystalline cellulose, Talc, and Mg. stearate purchased from S.D. fine chem., Mumbai.

Preparation of tablets by direct compression method: Tablets containing 5 mg of felodipine were prepared by direct compression method and the various formulae used in the study are shown in [Table 1]. The drug, diluents and superdisintegrants were properly mixed together (in a plastic container). Aerosil and magnesium stearate were passed through mesh number 60, mixed, and blended with initial mixture in a plastic container. The tablets were prepared by direct compression method by manual feeding using 7 mm bi concave punches on a 'Rimek mini press 1' a 10 station rotary compression machine.

Preparation of tablets by sublimation technique: The tablets containing 5 mg of Felodipine were prepared by sublimation method

and formulae used are shown in [Table 2]. The drug, directly compressible diluents, super disintegrants and camphor were properly mixed together (in a plastic container). Aerosil, magnesium stearate and talc were passed through mesh no. 60, mixed and blended with initial mixture in a plastic container. The tablets were prepared by direct compression method by manual feeding using 7 mm bi concave punches on a 'Rimek mini press 1' a 10 station rotary compression machine.

After compression the tablets were heated by vacuum drying technique at 50° C until a constant weight was obtained to ensure the complete removal of sublimable component. The sublimable component was removed to make the tablet porous.

Preparation of SD of Felodipine: SD of Felodipine were prepared by solvent evaporation and melt method. Drug was weighed and taken in a china dish, dissolved in methanol and then carrier was added (PVP, PEG and Mannitol in ratio of 1:1, 1:2, 1:4 and 1:9). The solvent was evaporated at room temperature and dried in hot air oven at 50° C for 4 hours. The resultant mass was passed through sieve no. 60 and stored in desiccator.

Drug content of SD: 10 mg of 1:1 SD, 15 mg of 1:2 solid dispersions, 20 mg of 1:4 solid dispersions and 50 mg of 1:9 solid dispersions were weighed and transferred to 250 ml of volumetric flask. Dissolved in phosphate buffer pH 6.5 containing 0.1% sodium lauryl sulphate and the volume were made up with the same. An aliquot of the filtrate was diluted and analyzed spectrophotometrically (UV-1700, Shimadzu Corporation, Japan) at 362 nm.

Preparation of tablets containing SD of Felodipine: The SD equivalent to 5 mg of drug was taken. Then mixed with directly compressible diluents and superdisintegrants in a plastic container. Magnesium stearate and aerosil were passed through sieve no. 60, mixed and blended with initial mixture in the plastic container followed by compression of the blend.

Evaluation of Felodipine tablets: The prepared tablets were evaluated for hardness, thickness and diameter, friability, disintegration time, wetting time, drug content, in-vitro dissolution studies, and stability studies. Pfizer hardness tester was used for the determination of the hardness of tablets. Tablet was placed in contact between the plungers, and the handle was pressed, the force of the fracture was recorded. The thickness and diameter of 4 tablets (2 tablets from each batch) were recorded during the process of compression using calipers (Mitotoyo; Japan). The friability of tablets was determined using Roche friabilator (Cambel Electronics, Mumbai, India). Two tablets were accurately weighed and placed in

the friabilator and operated for 100 revolutions. The tablets were de-dusted and reweighed. Percentage friability was calculated using the following formula.

$$F = (1 - W_0 / W) \times 100$$

Where, W_0 is the weight of the tablets before the test and W is the weight of the tablet after the test. Six tablets were tested from each formulation. In the disintegration time²⁰ study tablet was put into 100 ml distilled water at $37 \pm 2^\circ$. Time required for complete dispersion of a tablet was measured with the help of digital tablet disintegration test apparatus and in wetting time²¹ study a piece of tissue paper folded twice was placed in a small Petri dish (internal diameter = 6.5cm) containing 5 ml of distilled water. A tablet was placed on the paper, and the time for complete wetting of the tablet was measured in seconds. For the determination of drug content tablets were weighed individually, pulverized, and diluted to 250ml with sufficient amount of phosphate buffer pH 6.5 containing 0.1% SLS. After that an aliquot of the filtrate was diluted and analyzed spectrophotometrically (UV-1700 Shimadzu Corporation, Japan) at 362 nm.

The *in vitro* dissolution study was carried out in the USP dissolution test apparatus (Electrolab TDT - 08 L Dissolution tester USP) type 2 (paddle). 900 ml of the dissolution medium (phosphate buffer pH 6.5 containing 0.1% SLS) was taken in vessel and the temperature was maintained at $37 \pm 0.5^\circ\text{C}$. The speed of the paddle was set at 50 rpm. 5 ml of the dissolution medium was withdrawn and the same amount of fresh medium was replenished to the dissolution medium. The sample withdrawn was filtered and diluted with phosphate buffer pH 6.5 containing 0.1% SLS prior to analysis in the UV spectrophotometer (UV-1700 Shimadzu Corporation, Japan) at 362 nm. The stability study of the tablets was carried out according to ICH guidelines at $40 \pm 2^\circ\text{C}/75 \pm 5\% \text{RH}$ for three months by storing the samples in stability chamber (Lab-Care, Mumbai).

Characterization of felodipine tablets

FTIR Studies: IR spectra for drug, excipients and formulations P3, E3 and M4 were recorded in a Fourier transform infrared (FTIR) spectrophotometer (FTIR 1615, Perkin Elmer, USA) with KBr pellets.

XRD Studies: X-ray diffraction analysis of pure drug Felodipine, PVP, PEG, Mannitol and formulations P3, E3 and M4 were performed. This was done by measuring the 2θ ranges from 10-50 on a PW 3710 X ray generator diffractometer. The X-ray diffraction patterns were recorded automatically using rate meter with time per step is 0.500 sec. and scanning speed of 20/ minute.

Table 1: Formulae used in the preparation of tablets using PVP, PEG, and mannitol SD

Formulation code	Amount of PVP SD Equivalent to 5 mg of drug	Amount of PEG SD Equivalent to 5 mg of drug	Amount of Mannitol SD Equivalent to 5 mg of drug	Lactose	CCS	MCC
P	25.4	-	-	100.1	-	20
P1	10.16	-	-	109.34	6	20
P2	15.24	-	-	104.26	6	20
P3	26.31	-	-	93.19	6	20
P4	52.63	-	-	66.87	6	20
E	-	25.4	-	100.1	-	20
E1	-	10.16	-	109.34	6	20
E2	-	15.24	-	104.26	6	20
E3	-	24.80	-	94.70	6	20
E4	-	50.81	-	68.69	6	20
M	-	-	52	73.5	-	20
M1	-	-	9.92	109.58	6	20
M2	-	-	15.62	103.88	6	20
M3	-	-	26	93.5	6	20
M4	-	-	52	67.5	6	20

** All the formulations contain 1.5 mg of magnesium stearate, talc, and aerosil.

RESULTS AND DISCUSSION

The values of pre-compression parameters evaluated were within prescribed limits and indicated good free flowing property. [Table 3] shows the precompression parameters of powder blend. The data obtained from post-compression parameters such as hardness, friability, thickness, drug content, wetting time, and *in vitro*

disintegration. In all the formulations, hardness test indicated good mechanical strength, friability is less than 1%, indicated that tablets had a good mechanical resistance. Thickness of the tablets range from 3.28 to 3.95 mm. Tablets prepared with mannitol showed highest thickness because of their least density. The results are shown in [Table 4]. Drug content was found to be high ($\geq 99.1\%$) and uniform in all the tablet formulations results are shown in [Table 5].

The disintegration time of the formulations were shown in [Table 5]. Tablets prepared with PVP (P1, P2, P3), PEG (E1, E2, E3) and mannitol (M1, M2, M3, M4) disintegrated rapidly while tablets prepared with PVP (P and P4), with PEG (E and E4) and with mannitol (M) did not disintegrate in specified limit of time for fast dissolving tablet. This may be due to more hardness of the tablets as these carriers act as strong binders at higher level with in the tablets. During compression, the carrier could plasticize, soften or melt, filling the pores within tablets and thus making them non-disintegrating. It is also possible that the soften and melted carriers coat the disintegrants and other ingredients used in tablets, and such a coating along with the reduction of porosity of tablets makes disintegration difficult. As the method of preparation of tablets changed to sublimation, the disintegration time decreased significantly regardless of the diluents used. It is because tablets

prepared by sublimation method rapidly exhibits high pores and disintegrate the tablet rapidly. Above results shows that tablets prepared with 4 % superdisintegrant and 40 % camphor (sublimation method) showed least disintegration time in comparison with the all other formulations because of their lowest hardness and the porous structure is responsible for faster water uptake, hence it facilitates wicking action of crospovidone in bringing about faster disintegration ²².

The results of wetting time studies are shown in [Table 5]. Wetting time of formulations P, P4, E, E4, M and C were significantly higher than other formulations. Wetting times of the formulations C1 to C5 were significantly lower than all remaining formulations. It is because of highest porosity of the tablets ²². Drug content of tablets ranged between 95.91 to 102.00 %. Results are shown in [Table 6].

Table 2: Formulae used in the preparation of tablets using sublimation method

Formulation code	Felodipine	Spray dried lactose	Crosspovidone	Directly compressed MCC	Camphor
C	5	105.50	-	30	-
C1	5	97.00	6	30	4.5
C2	5	94.00	6	30	7.5
C3	5	86.50	6	30	15
C4	5	71.50	6	30	30
C5	5	41.50	6	30	60

** All the formulations contain 1.5 mg of magnesium stearate, and 3 mg of talc, and aerosil.

Table 3: Precompressional parameters

Formulation	Angle of Repose (θ)(\pm SD), n=3	Compressibility (%) (\pm SD), n=3	Hausner's Ratio (\pm SD), n=3
P	23.65 (2.22)	16.66 (4.22)	1.37 (0.06)
P1	24.21 (3.52)	29.57 (0.060)	1.32 (0.05)
P2	23.70 (0.28)	23.80 (1.34)	1.31 (0.02)
P3	22.49 (1.12)	23.60 (2.60)	1.35 (0.04)
P4	34.06 (0.95)	27.22 (1.67)	1.32 (0.03)
E	23.38 (0.25)	23.00 (2.30)	1.24 (0.02)
E1	32.90 (1.30)	20.00 (2.50)	1.25 (0.07)
E2	22.18 (1.45)	27.41 (2.10)	1.37 (0.02)
E3	30.10 (1.91)	23.85 (0.60)	1.30 (0.00)
E4	28.72 (0.50)	18.62 (0.32)	1.22 (0.09)
M	24.68 (1.80)	27.41 (0.75)	1.37 (0.02)
M1	22.76 (0.35)	23.80 (4.60)	1.31 (0.06)
M2	24.58 (0.90)	27.41 (0.60)	1.37 (0.01)
M3	23.70 (3.00)	23.80 (0.50)	1.28 (0.02)
M4	25.60 (2.80)	22.80 (0.64)	1.30 (0.01)
C	33.80 (0.51)	16.66 (5.00)	1.20 (0.03)
C1	22.99 (0.72)	22.61 (3.42)	1.57 (0.05)
C2	22.12 (1.52)	25.80 (2.26)	1.34 (0.04)
C3	22.49 (2.20)	20.00 (1.20)	1.25 (0.05)
C4	23.90 (4.20)	22.80 (0.60)	1.20 (0.02)
C5	22.59 (0.89)	25.45 (1.22)	1.34 (0.03)

Note: Values in parenthesis are standard deviation (\pm SD)

Table 4: Post compressional parameters of tablets

Formulation	Hardness test (kg/cm ²) (\pm SD), n=6	Friability (%) (\pm SD), n=10	Thickness (mm) (\pm SD), n=4
P	4.50 (0.28)	0.26 (0.04)	3.50 (0.00)
P1	3.55 (0.10)	0.30 (0.04)	3.65 (0.050)
P2	3.55 (0.15)	0.32 (0.02)	3.48 (0.058)
P3	3.50 (0.20)	0.33 (0.04)	(0.060)
P4	6.05 (0.31)	0.33 (0.02)	3.42 (0.055)
E	3.08 (0.20)	0.26 (0.02)	3.75 (0.050)
E1	4.50 (0.25)	0.32 (0.05)	3.80 (0.100)
E2	5.09 (0.40)	0.26 (0.06)	3.84 (0.060)
E3	4.50 (0.35)	0.24 (0.00)	3.82 (0.072)
E4	3.57 (0.32)	0.46 (0.01)	3.68 (0.075)
M	4.00 (0.45)	0.42 (0.04)	3.95 (0.050)
M1	3.55 (0.10)	0.30 (0.04)	3.88 (0.058)
M2	4.50 (0.15)	0.50 (0.02)	3.93 (0.090)
M3	4.08 (0.40)	0.33 (0.03)	3.70 (0.060)
M4	4.50 (0.35)	0.26 (0.06)	3.75 (0.072)
C	4.50 (0.12)	0.40 (0.02)	3.28 (0.050)
C1	3.09 (0.20)	0.21 (0.01)	3.75 (0.075)
C2	3.00 (0.25)	0.33 (0.03)	3.68 (0.078)
C3	2.50 (0.30)	0.28 (0.00)	3.53 (0.058)
C4	2.08 (0.35)	0.30 (0.01)	3.48 (0.055)
C5	2.00 (0.20)	0.64 (0.02)	3.52 (0.055)

Note: Values in parenthesis are standard deviation (\pm SD)

Table 5: Disintegration time and wetting times of tablet formulations

Formulation	Disintegration time (sec) (\pm SD), n=6	Wetting time (sec) (\pm SD), n=6
P	420 (10.50)	160 (7.70)
P1	48 (2.00)	35 (3.75)
P2	42 (3.44)	40 (2.20)
P3	50 (2.90)	48 (2.50)
P4	420 (5.50)	600 (8.50)
E	480 (1.70)	180 (4.40)
E1	52 (2.45)	42 (3.27)
E2	50 (2.00)	40 (3.16)
E3	48 (3.50)	45 (3.11)
E4	360 (4.12)	660 (5.12)
M	120 (2.75)	75 (4.42)
M1	62 (1.60)	40 (3.30)
M2	52 (2.22)	30 (2.20)
M3	46 (2.45)	35 (2.00)
M4	45 (2.00)	30 (1.50)
C	600 (9.00)	250 (5.50)
C1	40 (7.00)	25 (6.00)
C2	30 (1.00)	22 (2.20)
C3	25 (2.00)	20 (2.00)
C4	20 (2.10)	18 (1.50)
C5	12 (2.00)	08 (2.00)

Table 6: Dissolution parameters ($t_{50\%}$ and $t_{90\%}$) and drug content of felodipine tablets.

Formulation	$t_{50\%}$ (min)(\pm SD), n=4	$t_{90\%}$ (min)(\pm SD), n=4	Drug content (%) (\pm SD), n=6
P	7.42 (0.12)	28.33 (0.30)	99.00 (1.97)
P1	1.34 (0.25)	10.07 (0.25)	96.15 (2.20)
P2	1.32 (0.14)	8.52 (0.19)	96.15 (1.50)
P3	1.17 (0.40)	6.12 (0.26)	96.00 (1.55)
P4	18.34 (0.32)	41.15 (0.22)	98.00 (3.00)
E	9.53 (0.05)	41.34 (0.25)	95.10 (0.50)
E1	4.54 (0.95)	20.48 (0.35)	96.50 (2.15)
E2	1.30 (0.80)	12.05 (0.19)	97.00 (2.14)
E3	1.37 (0.05)	8.20 (0.15)	98.55 (2.50)
E4	1.37 (0.11)	17.28 (0.10)	95.91 (3.00)
M	3.50 (0.22)	25.00 (0.25)	98.55 (2.20)
M1	1.44 (0.04)	10.19 (0.09)	98.55 (0.60)
M2	1.19 (0.22)	8.23 (0.42)	96.00 (1.20)
M3	1.09 (0.06)	4.40 (1.02)	100.96 (0.75)
M4	1.13 (0.20)	3.60 (1.00)	96.15 (1.20)
C	19.14 (0.15)	59.00 (0.40)	102.00 (2.27)
C1	5.02 (0.14)	7.06 (0.45)	97.35 (1.50)
C2	3.05 (1.00)	5.19 (0.30)	98.00 (3.30)
C3	1.46 (1.00)	3.32 (0.30)	98.07 (0.90)
C4	1.40 (0.60)	2.18 (0.06)	99.00 (2.20)
C5	0.36 (0.20)	0.58 (0.07)	98.55 (1.50)

Note: Values in parenthesis are standard deviation (\pm SD)

[Figures 1 to 5] shows the dissolution profiles of tablets prepared from SD of Felodipine with PVP, PEG and MANNITOL. [Table 6] shows the $t_{50\%}$ and $t_{90\%}$ values of release profiles of tablets. These values changed with change of carriers and method of preparation of tablets. The dissolution rate of tablets prepared with SD of Felodipine in the ratio 1:1, 1:2, 1:4 (P1, P2, P3) with PVP, in the ratio 1:1, 1:2, 1:4 (E1, E2, E3) with PEG and in the ratio 1:1, 1:2, 1:4, 1:9 (M1, M2, M3, M4) with mannitol increased significantly ($P < 0.05$) than P, E and M respectively. This may be due to the use of croscarmellose sodium, which causes swelling to 4-8 folds in 10 seconds²³ and due to particle size reduction and improved wettability²⁴. In addition to micronization, conversion of drug to amorphous form during the preparation might have also contributed to the increased dissolution rates observed with the solid dispersions²⁵. However, tablets prepared with PVP SD in the ratio 1:9 (P4) and with PEG SD in the ratio 1:9 (E4) did not further enhance the dissolution rate unlike solid dispersions. In practice the effect of micronization is often disappointing, especially when the drugs are encapsulated or tableted²⁶⁻²⁸.

This phenomenon was attributed to the agglomeration tendency of micronized, poorly soluble, hydrophobic drugs, which effect results in a decreased effective surface area for dissolution²⁹. The $t_{50\%}$ and $t_{90\%}$ values indicate that the dissolution rate of tablets (P1, P2, P3, E1, E2, E3, M1, M2, M3, M4) increased significantly ($p < 0.05$) than dissolution rate of tablets P, E and M respectively.

[Table 7] shows the parameters of tablets after stability studies. The increase ($P < 0.05$) in the disintegration time was observed in case of tablets prepared with mannitol SD. This may be due to increase in the hardness of the tablets during storage^{30,5}. Decrease ($P < 0.05$) in the disintegration time was observed in tablets prepared by camphor sublimation method. Since during the preparation of tablets by camphor sublimation method, only 6 hours at 60°C was used, where as 90 days and 45°C were used during stability studies. The long storage of 90 days at 45 °C might have removed trace amount camphor that was not removed during the short period of preparation. No change was observed in the disintegration time of tablets prepared with PVP and PEG SD. No significant change in the thickness was observed in all the tablets and drug content of all formulation was within the acceptable limits. In [Figure 6] shows the IR spectrum of the pure drug and formulations. The felodipine used in the present study shows characteristic absorption bands in the following IR region.

IR (KBR) cm^{-1}

3370 (NH Stretching), 3069 (Aromatic CH stretching), 2840, 2948 (CH stretching of CH_2 and CH_3 Groups), 1700, 1688 (C=O stretching), 1644 (NH Bending), 1621, 1495, 1460 (C = C ring stretching), 1099 (C O C stretching), 727, 801 (Substituted benzene ring), 564 (Cl stretching).

The IR spectrum of the formulation P3 shows the characteristic absorption bands in the following IR region.

It is quite interesting to note that, the spectrum contains very broad peaks in the range 3200 to 3500 and a very sharp peak almost merged with the broad peak at 3370 indicating the presence of OH of PVP and NH of Felodipine. Further it has the aromatic CH peak from 3050 and CH stretching of PVP in the range 2836 to 2978. The spectrum shows the presence of carbonyl group of drug at 1700 and 1688, NH bending 1643 and C=C ring stretching at 1617, 1496 and 1443. Since all the major peaks of the pure drug and PVP are present without any change in their positions in the spectrum of the formulation P3. It may be concluded that the drug and polymer have retained their identity without losing their properties and not going in to a chemical interaction with each other. Thus the conclusion from the IR spectra of the drug and formulation is that there is no interaction between drug and polymer.

Similarly the IR spectra of formulations E3 and M4 reveal that the pure drug Felodipine has not gone into the interaction with PEG in the formulation E3 and Mannitol in the formulation M4.

One of the common approaches to improve the bioavailability of poorly water soluble drugs is to enhance their dissolution rate by formation of amorphous dispersions and, preferably molecular dispersions³¹. X-ray diffraction patterns of formulation P3, E3 and M4 revealed that felodipine a crystalline material shows characteristic peaks at 2θ 10.20, 10.35, 10.77, 13.16, 14.64, 16.20, 17.71, 20.48, 23.34, 24.49, 25.40, 26.47, 27.55, 29.25, 31.99, 33.89, 36.87, 39.55, 43.11, 44.64, and 47.61. However the XRD patterns of its solid dispersion in PVP, PEG and mannitol shows the typical profiles of amorphous material as observed from the values. A peak corresponding to felodipine crystals completely disappeared in SD prepared with PVP, PEG and mannitol. These results indicate that drug was dispersed in amorphous form in the solid dispersions of PVP, PEG and mannitol (Figures 7-9).

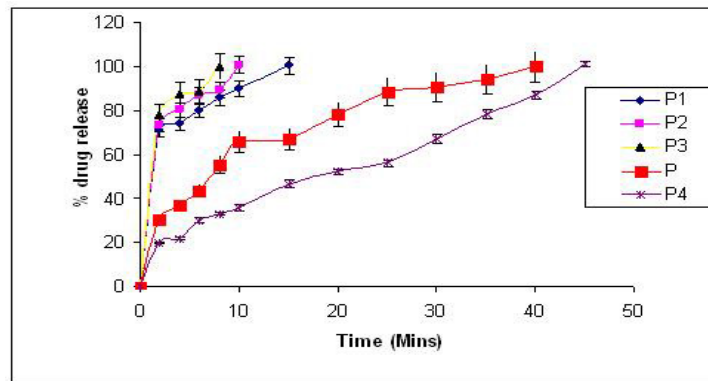


Fig 1: Dissolution profiles of formulations containing PVP SD

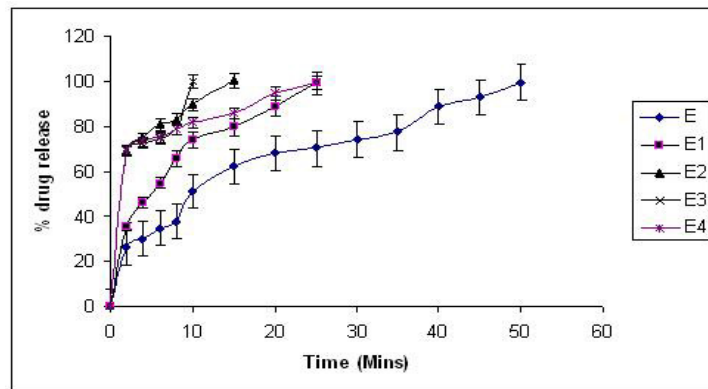


Fig 2: dissolution profiles of formulations containing PEG SD

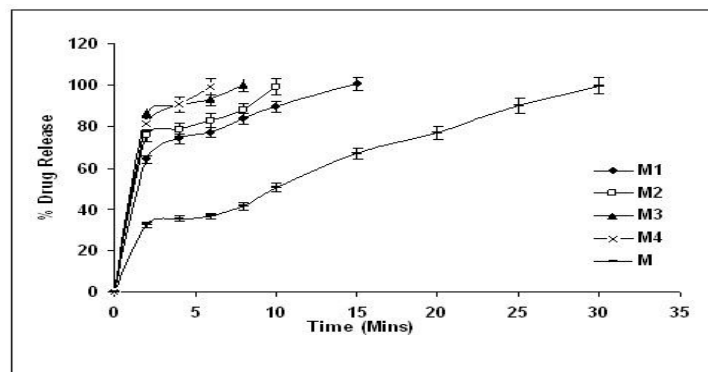


Fig 3: Dissolution profiles of formulations containing mannitol SD

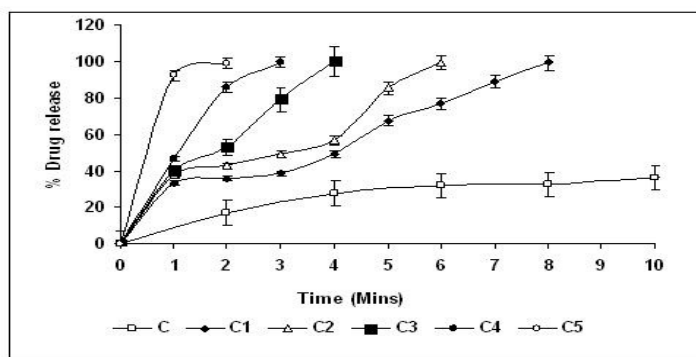


Fig 4: Dissolution profiles of formulations prepared by sublimation method

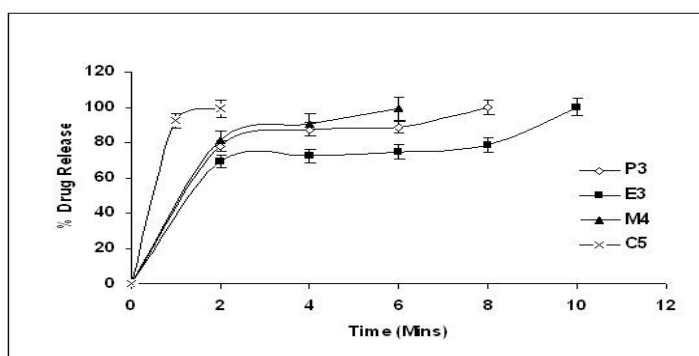


Fig 5: dissolution profiles of best formulations

Table 7: Results of stability studies

Formulation	Disintegration Time (sec)(\pm SD), n=6	Thickness (mm)(\pm SD), n=10	% drug content (\pm SD), n=4
P	450 (10.15)	3.50 (0.052)	99.00 (0.62)
P1	50.00 (6.33)	3.62 (0.050)	96.00 (0.72)
P2	44.00 (4.11)	3.45 (0.051)	95.36 (1.35)
P3	48.00 (3.92)	3.48 (0.062)	94.72 (0.72)
P4	490.0 (4.56)	3.38 (0.039)	97.62 (1.55)
E	500 (3.78)	3.68 (0.084)	94.65 (0.58)
E1	55.00(2.35)	3.78 (0.081)	95.75 (0.42)
E2	52.00 (4.15)	3.80 (0.045)	97.00 (0.62)
E3	50.00 (5.95)	3.78 (0.080)	97.31 (0.75)
E4	400.0 (4.72)	3.65 (0.072)	94.91 (1.31)
M	320.0 (3.15)	3.88 (0.059)	97.92 (2.27)
M1	108.0 (4.90)	3.68 (0.048)	97.52 (2.21)
M2	95.00 (2.72)	3.72 (0.052)	95.57 (2.00)
M3	85.00 (3.57)	3.68 (0.055)	99.65 (1.55)
M4	75.00 (3.50)	3.72 (0.065)	95.15 (1.32)
C	650.0 (8.00)	3.18 (0.062)	100.0 (0.05)
C1	41.00 (3.45)	3.68 (0.059)	97.00 (0.48)
C2	28.00 (3.11)	3.58 (0.050)	98.00 (0.58)
C3	24.00 (2.92)	3.55 (0.058)	97.57 (0.48)
C4	18.00 (2.56)	3.42 (0.058)	98.92 (1.31)
C5	14.00 (3.61)	3.48 (0.050)	98.00 (0.90)

Note: Values in parenthesis are standard deviation (\pm SD).

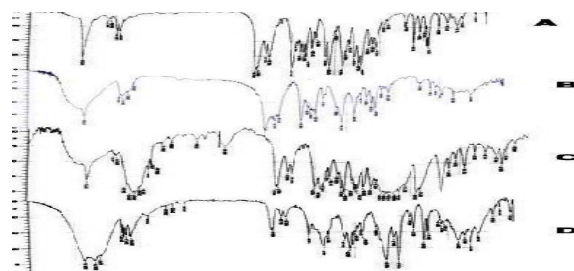


Fig 6: FTIR spectrum of pure drug felodipine (A), spectrum of formulation P3 (B), spectrum of formulation E3 (C), FTIR spectrum of formulation M4 (D).

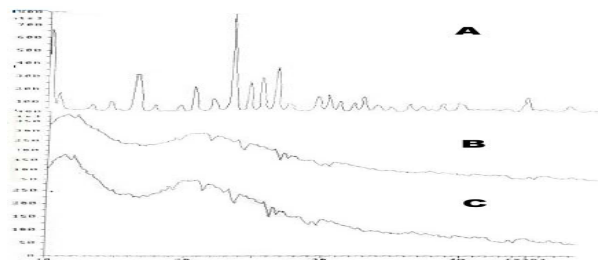


Fig 7: XRD patterns of pure felodipine (A), pure PVP (B), XRD of felodipine SD with PVP (C).

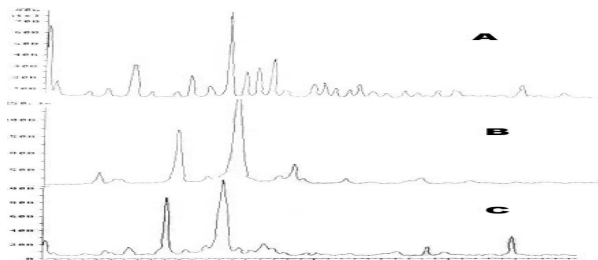


Fig 8: XRD patterns of pure felodipine (A), XRD of pure PEG (B), XRD of felodipine SD with PEG (C).

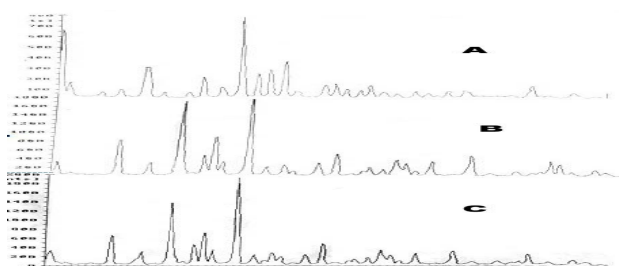


Fig 9: XRD patterns of pure felodipine (A), XRD of pure mannitol (B), XRD of felodipine SD with mannitol (C).

CONCLUSION

Felodipine is a dihydropyridine calcium channel blocker. It's widely used in the management of hypertension and angina pectoris. Felodipine is practically insoluble in water. Here felodipine is used as a model drug in formulating the fast dissolving tablets. From this study, it can be concluded that dissolution rate of felodipine could be enhanced by tablets containing SD and sublimation technique. Tablets containing SD with PVP of ratio 1:4 (P3), with PEG of ratio 1:4 (E3) and with mannitol of ratio 1:9 (M4) yielded best results in terms of dissolution rate. Tablets prepared by sublimation method containing 40% camphor (C5) yielded best result in terms of dissolution rate.

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