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FORMULATION AND EVALUATION OF NICARDIPINE LIQUISOLID COMPACT TABLETS

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ABSTRACT

Main objective of the present study was to enhance the dissolution rate of nicardipine by liquisolid compact method. Nicardipine is practically insoluble in water. Solubility of nicardipine was estimated in different non volatile solvents. Then different formulations were prepared at the drug concentration of 10%, 15% and 20% with excipient ratios (R) 5:1, 7:1, 9:1. Liquisolid compact powder was subjected to angle of repose, Carr's compressibility index, and hausner's ratio to determine flow property. Hardness, friability, disintegration time, drug content, dissolution rate are determined. Fourier transforms infrared analysis, x-ray diffraction studies also performed. All the formulations showed acceptable flow property and better drug release. Fourier transform infrared spectroscopy conformed that drug does not interact with excipients which are added in the formulation. X-ray diffraction study proved that nicardipine (crystalline form) converted into amorphous form. From this study it was concluded that liquisolid compact technique improves dissolution rate of nicardipine.

KEY WORDS: **Loading factor, carrier material, coating material, liquid medication**

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INTRODUCTION

When drug is given by oral route Solubility and permeability are rate determining steps in absorption process. For poorly soluble, highly permeable (class II) drugs the rate of oral absorption is often controlled by the solubility in the gastro intestinal tract[1]. So many methods are developed to enhance the solubility of this drug. These include (1) micronization (2) solid dispersion (3) complexation (4) polymorphism (5) co-precipitation and recent technique is liquid solid compact technique. Several studies have shown that the liquid solid compact technique is a promising method for enhancing dissolution rate of poor water soluble drugs[2-8]. Liquid solid systems are generally considered as acceptably flowing and compressible powdered forms of liquid medication. (that implies water insoluble solid drug dissolved in suitable water missible non volatile solvent) such liquid medication may be converted into a dry looking, non-adherent, free-flowing, readily compressible powders by a simple admixture with selected powder excipients referred to as carrier and coating material [9]. The aim of this study was to increase dissolution rate of Nicardipine using liquid solid compact technique. Nicardipine is poorly water soluble, calcium channel blocking agent, which is widely used in the management of mild to moderate hypertension, angina pectoris and cerebrovascular diseases [10-11].

MATERIALS AND METHODS

Nicardipine was gifted by Natco laboratories Hyderabad, tween80, avicel pH 102 and aerosil were purchased from E.Mecrk (India), cross povidone was purchased from SD fine chemicals (India).

Solubility study

The solubility of Nicardipine was determined in different solvents by preparation of saturated solution in 0.1 N Hcl, 6.8 phosphate buffer and in tween-80. Excess amount of Nicardipine was added to above solvents and shaking on shaker for 48 hrs at 25 ^{o}C. Then solutions were filtered and diluted with water and analyzed with uv-visible double beam spectrophotometer at 230 nm. (Elico SL 210)

Table 1
Solubility of nicardipine in different solvents

Solvent	Solubility (mg/ml)
0.1 N Hcl	0.288
6.8 phosphate buffer	0.117
Tween-80	80

Calculation Of Liquid Load Factor (L_f) Required Quantities Of Carrier (Q) And Coating (q) Materials

The formulation design was done by using mathematical model described by spires et al
In this study tween 80, avicel, aerosil were used as vehicle, carrier, coating material. The concentration of the drug solution were taken as 10%, 15%, 20% w/w, and carrier coating ratios were taken as 5:1, 7:1, 9:1.
Ratio of carrier and coating material was calculated by
R = Q/q
Where Q is amount of carrier, q is amount of coating material.
Loading factor was determined by adding carrier material to drug solution until it produce good flow property and compressibility.
Lf= W/Q
Where W is weight of liquid medication, Q is weight of carrier material.
Loading factor was also calculated by using Φ-values of carrier, coating material and by using R value.
Lf = Φ + *Φ* (1/R)
Once, liquid loading factor was obtained, the appropriate quantities of carrier (Q) and coating (q) material required were calculated using following equations,
Q = W/Lf
q = Q/R

Drug excipient compatibility studies

X-Ray Powder diffraction (XRD) studies

X-ray powder diffraction studies were conducted to pure nicardipine, liquid solid compact physical mixture. These samples were exposed to Cu-K_α radiation at a scan rate of 1.5^{0}/ min over the 2θ range of 4-40^{0}C.

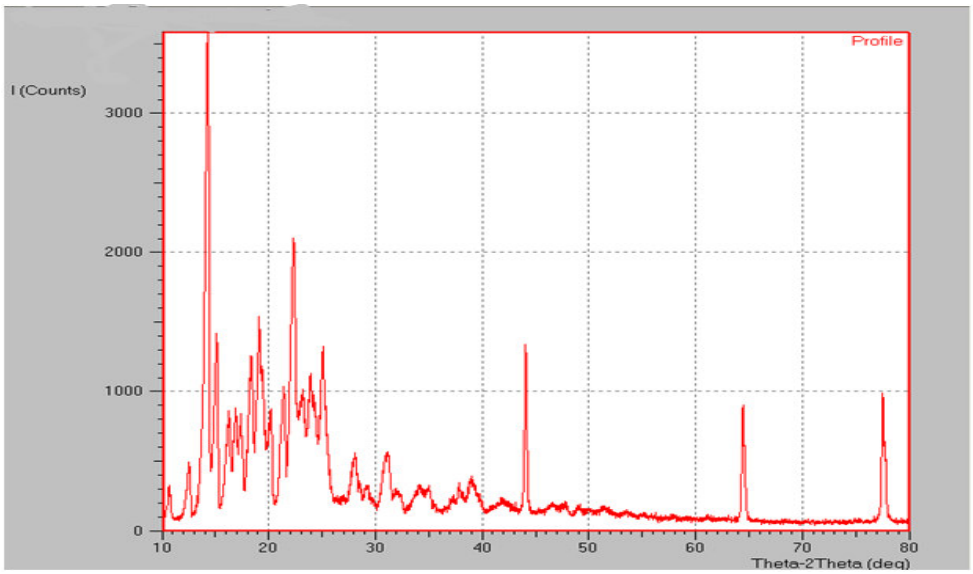

Figure 1
X-ray diffraction of pure nicardipine

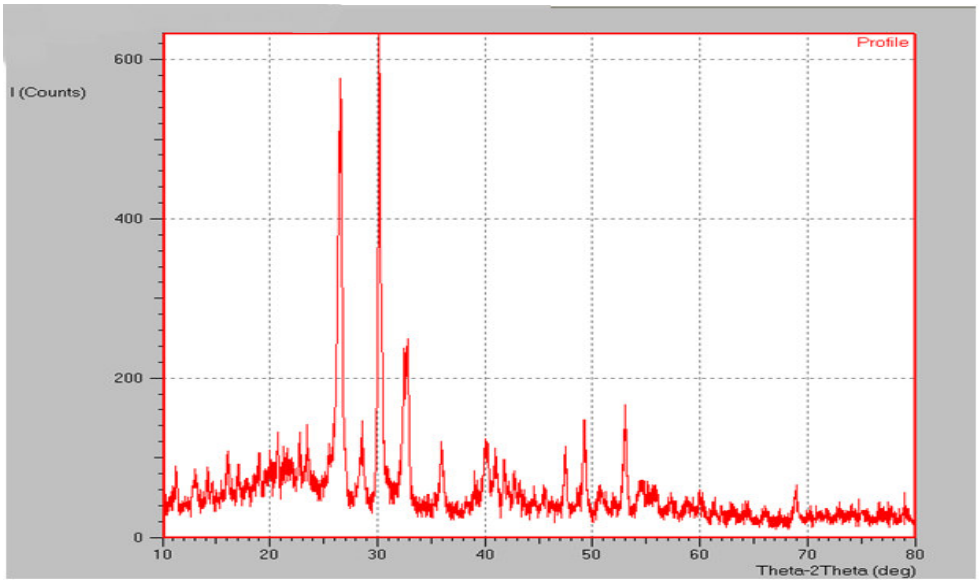

Figure 2
x-ray diffraction of liquisolid compact

Infra red spectra analysis

The infra red spectra of pure drug and liquid solid formulation physical mixture were recorded by the KBr pellet technique. A base line correction was taken by using dried potassium bromide and then the spectrum of the pure nicardipine, liquid solid system was obtained.

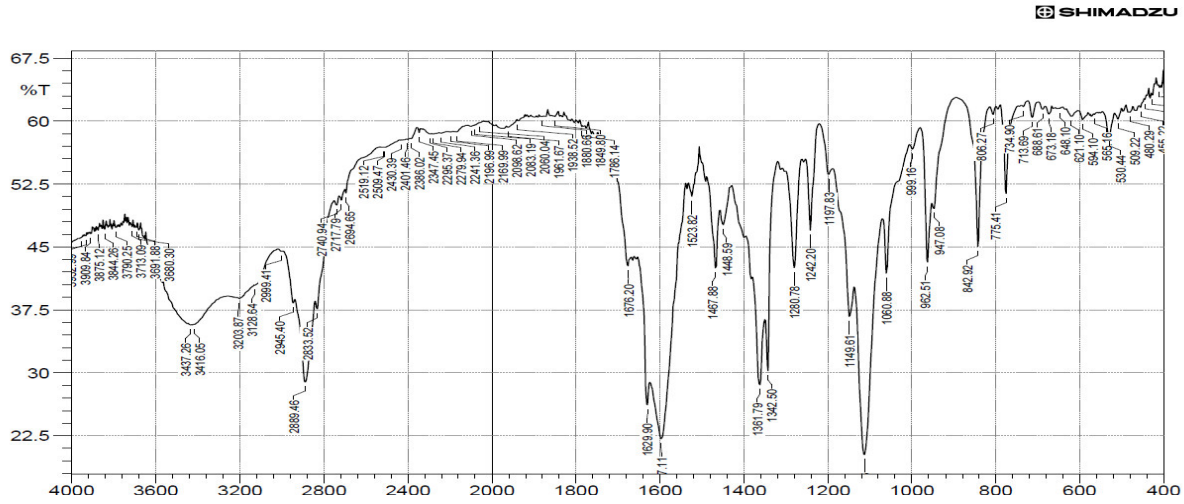

Figure 3
FTIR spectra of pure nicardipine

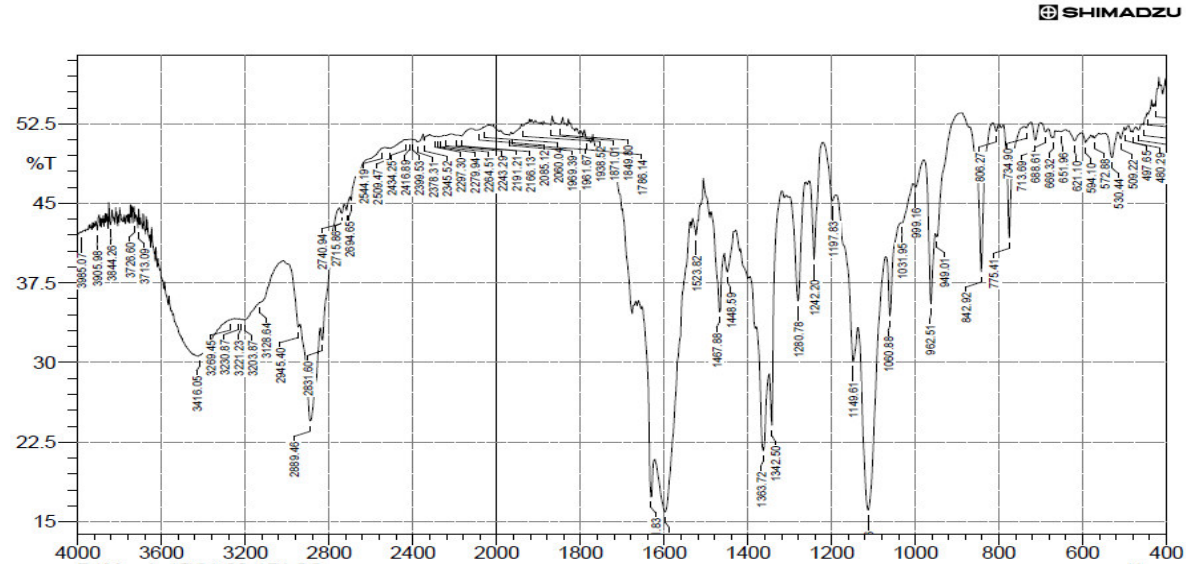

Figure 4
FTIR spectrum of liquisolid powder

Formulation of liquisolid powders and compaction into tablets

Accurate amount of drug was suspended in the liquid vehicle in a mortar using pestle, then the calculated amount of the carrier material (table-2) was added with continuous mixing till homogenous wet mix is obtained. The coating material was then added to the wet mix with gentle mixing. Finally, each liquisolid formulation was blended with disintegrating agent, glidant and lubricant. The blended bulk was finally compacted using flat faced punches using rotary tablet compression machine[12].

Table 2
Composition of nicardipine liquisolid compacts (All formulations contain 20 mg nicardipine)

Liquisolid system	Drug conc. in liquid medication (%W/W)	Carrier: coating ratio (R)	Liquid loading factor (Lf)	Liquid vehicle (mg) TWEEN-80	Carrier Q (mg) avicel pH102	Coating Q (mg) aerosil	Cross povidone	Unit dose (mg)
F1	10	5	0.79	200	278	55	...	553
F2	10	7	0.56	200	393	56	...	669
F3	10	9	0.43	200	512	57	...	789
F4	15	5	0.79	140	202	40	...	402
F5	15	7	0.56	140	286	41	...	487
F6	15	9	0.43	140	372	41	...	573
F7	20	5	0.79	100	152	30	...	302
F8	20	7	0.56	100	214	31	...	365
F9	20	9	0.43	100	279	31	...	430
F10	10	9	0.43	200	512	57	16	805
F11	10	9	0.43	200	512	57	32	821
F12	10	9	0.43	200	512	57	48	837
F13	10	9	0.43	200	512	57	64	853

Evaluation of blend
Angle of repose
The angle of repose was determined by fixed funnel method. Angle of repose was calculated by the following equation[13].
$\tan\theta = h/r$
Where, θ is the angle of repose
h is the height in cms
r is the radius in cms

Bulk Density
The bulk density and tapped density were determined by using bulk density apparatus. The bulk density was calculated using the formula
$D_b = M/V_b$
where, M is the mass of powder
V_b is bulk volume of powder

Tapped Density
The tapped density was calculated using the formula
$D_t = M/V_t$
where, M is the mass of powder
V_t is tapped volume of powder

Carr's Index (%)
Carr's index (CI) is calculated as follows:
CI (%) = [(Tapped density – Bulkdensity) / Tapped density] x100

Hausner's Ratio
Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula.
Hausner's Ratio=Tapped density / Bulk density

Table 3
Flow property of nicardipine liquisolid compact powder

Liquisolid system	Angle of repose (θ)	Carr's index	Hausner's ratio
F1	31.70 ± 1.53	12.24 ± 1.39	1.14±0.02
F2	31.70± 2.89	12.60 ±1.32	1.14±0.02
F3	32.30± 2.52	12.37 ±4.41	1.14±0.02
F4	30.70± 1.15	13.14±1.59	1.15±0.02
F5	31.70± 1.53	14.95±2.81	1.18±0.04
F6	35.10± 2.10	14.39±2.75	1.17±0.04
F7	33.70 ± 1.15	15.17±0.75	1.18±0.01
F8	31.30 ± 1.15	14.10±2.01	1.16±0.03
F9	36.30 ± 1.15	17.65±0.46	1.21±0.01
F10	35.70 ± 1.15	15.13±1.51	1.18±0.02
F11	36.30 ± 1.15	15.81±0.76	1.19±0.01
F12	31.30 ±1.15	16.95±1.12	1.20±0.02
F13	30.70 ± 1.15	18.24±0.11	1.22±0.10

Evaluation of tablets

Hardness

Hardness of the table was determined by Monsanto hardness tester.

Friability

Friability of the tablets was determined by roche friabilator. Ten tablets were randomly selected and weighed then placed them in friabilator. After 100 revolution tablets were de dusted and re weighed. Then calculate friability by the given equation.

F= (1-Wo/W) 100

Wo = weight of the tablet before the test

W = weight of the tablet after the test

Disintegration time:

The *in-vitro* disintegration time was determined by using disintegrating apparatus. A tablet was placed in to each of the six tubes of the apparatus and one disk was added to each tube. The time was recorded after completion of the disintegration of the tablets.

Table 4
Evaluation of liquisolid compact tablets

Formulation	Hardness (kg/cm²)	Friability (%)	Disintegration time (sec)	Assay (%)
F1	4.13 ±0.12	0.18	80	97.47 ±0.64
F2	4.33 ±0.29	0.21	70	97.90 ±0.71
F3	5.07 ±0.12	0.16	60	99.97 ±0.68
F4	4.23 ±0.16	0.32	90	96.41 ±0.11
F5	4.63 ±0.15	0.12	85	96.62 ±0.22
F6	4.83 ±0.21	0.31	75	97.12 ±0.34
F7	4.23 ±0.16	0.46	108	95.37 ±0.25
F8	4.53 ±0.21	0.66	86	95.83 ±0.25
F9	4.77 ±0.26	0.23	80	96.33 ±0.21
F10	4.31 ±0.17	0.42	51	99.07 ±0.12
F11	4.13 ±0.06	0.24	45	99.23 ±0.16
F12	4.17 ±0.12	0.48	40	99.47 ±0.23
F13	4.11 ±0.16	0.31	35	99.5 1±0.31

Dissolution

The *in-vitro* dissolution study was carried out in USP dissolution test apparatus Type 2 (paddle) with a dissolution medium of 900 ml of 0.1N HCL at 50 rpm (37±0.5 ^{0} C). 5 ml sample was withdrawn at the specific time intervals and same amount of fresh dissolution medium is replaced in dissolution apparatus after withdrawn. The samples were analyzed by UV visible double beam spectrophotometer. The dissolution of the drug was expressed as percentage drug dissolved.

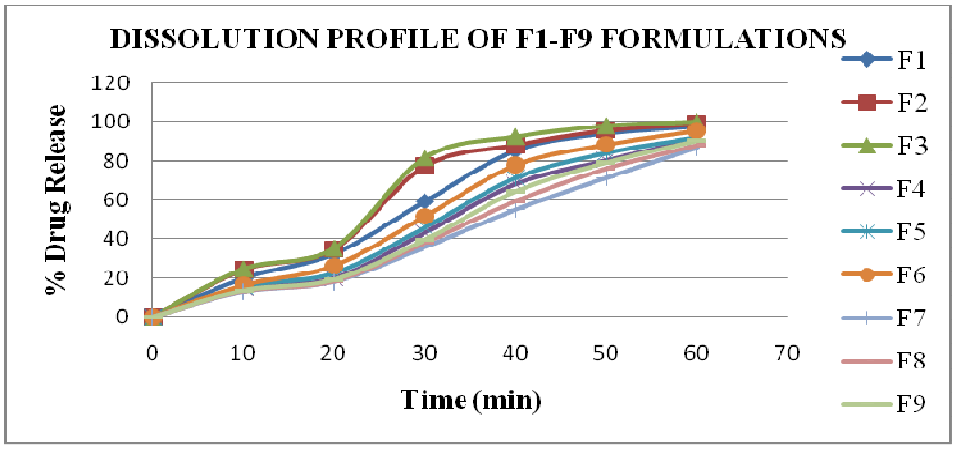

Figure 5
Drug release profile of liquisolid compact formulations F1-F9

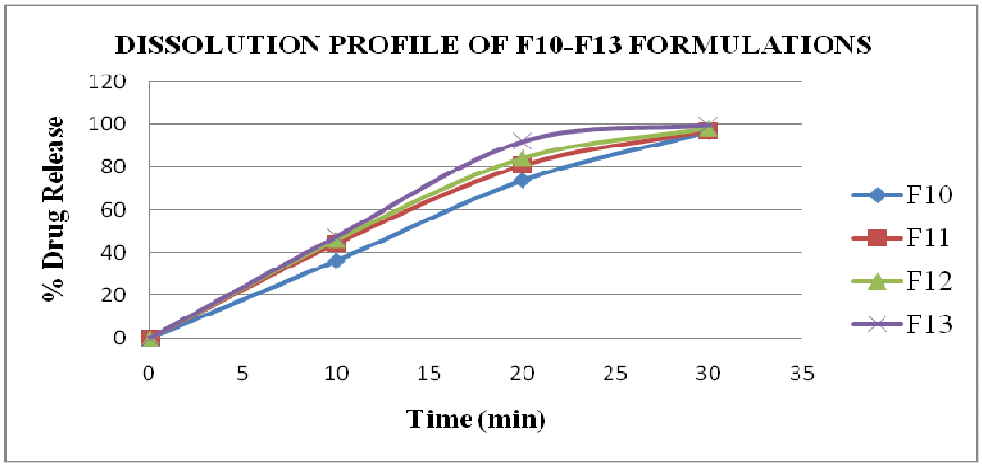

Figure 6
Drug release profile of liquisolid compact formulations F10-F13

DISCUSSION

The FTIR spectrum of pure nicardipine (figure 3) showed the distinct peak at 1361cm^{-1} of NO_2 stretching, 2889 cm^{-1} of CH stretching of aromatic ring, 621 cm^{-1} of CH-out of plane vibrations of mono substituted phenyl ring, 1629 cm^{-1} of C=C stretching, 3416 cm^{-1} of N-H stretching, 1676 cm^{-1} of stretching of ester. All these peaks present in FTIR spectrum of liquisolid compact physical mixture (Figure 4), so it is concluded that drug is not interact with excipient which are used in liquisolid compact preparation. X-ray diffraction of pure nicardipine (Figure 1) shown several sharp peaks at different angles (2θ) 14, 15, 19, 22, 25 it indicates drug exist in crystalline form. Liquisolid physical mixture (Figure 2) does not contain this distinct peak in x ray diffraction pattern this is due to completely solubilization of nicardipine in non volatile solvent. It indicates nicardipine converted into amorphous form. Solubility of nicardipine was performed in different solvents and the amount of drug solubilized was estimated by UV method. Results were given in the table 1. Solubility of nicardipine in 0.1N Hcl was 0.288mg/ml, in 6.8 phosphate buffer 0.117 mg/ml and 80mg/ml in tween-80.Maximum solubility shown by nicardipine in tween-80 so it was selected for further work. Angle of repose, Carr's index and hausner's ratio were determined. The results were given in the table 3. Angle of repose found between the ranges of 30.7-36.3, it indicates all the formulations shown passable flow property. Carr's index of all formulations were 12.24- 18.24, so the all the formulations shown passable flow property. Hausner's ratio for all formulations was found less than 1.25 it means showing good flow property. Tablet evaluation was given in the table 4. Hardness of the tablets ranges from 4.1±0.1 to 5.1±0.1. Generally the ideal hardness is preparing the tablet with less compression force by this less disintegration time and fast dissolution rate is achieved at the same time. It was observed in all the formulation that hardness of the tablet was increased by addition of increased amount of avicel, hardness of the tablet was decreased by decreasing R value because of less amount of avicel and low compressibility of aerosil [14]. All the formulations shown friability less than 1%, it indicates all formulations passed friability. Content uniformity of all the formulations shown in the ranges of

95.37-99.97, are within the pharmacopeal requirement. All the formulations disintegration time was less than 2min. formulation F10-F13 shown better disintegration time than F1-F9 due to presence of superdisintegrants. Among F10- F13 formulation F13 showed better disintegration time because it contains higher concentration of disintegrant. From dissolution profile of F1-F9 (figure 5) formulations F3 batch shown better drug release than remaining formulations. From the results it is observed that formulation which contains 10% drug solution shows better drug release than15%, the later shown better drug release than 20% drug solution. This is due to the complete wettability is achieved in less concentrate liquid medicament formulations (F1-F3), and larger surface area is exposed to dissolution medium. Tween 80 wet the drug particle by reducing the interfacial tension between tablet surface and dissolution medium. The carrier coating ratio (R) also plays an important role in drug release rate, the formulation which has a higher R value shown increase drug release than others. Formulation which has R value 9 shown faster drug release than the formulation has R value 7, later shown better drug release than formulation has R value 5. Concentration of super disintegrants also affect on drug release. Relationship between concentration of disintegrants and drug release is directly proportional, formulation which has more super disintegrant shown faster drug release than others. From the results (Figure 5, 6) it is concluded that F13 formulation was best liquisolid formula and shown better drug release than other formulations.

CONCLUSION

The solubility, dissolution of nicardipine was significantly enhanced by using the liquisolid compact technique. In this study tween-80 is used as non volatile solvent, it improves wetting property and increase solubility of nicardipine in solvent. Infra red analytical study conforming that there is no chemical interaction between nicardipine and other ingredients. XRD study confirmed that nicardipine completely converted in to amorphous form.

REFERENCES

1. Lobenberg R, Amidon GL. Modern bioavailability, bioequivalence and biopharmaceutics classification system; new scientific approaches to international regulatory standards. Eur. J. Pharm. Biopharm. 2000, july; 50(1): 3-12.
2. Spireas S, Wang T, Grover R. Effect of powder substrate on the dissolution properties of methchrothiazide liquisolid compacts. Drug Dev. Ind. Pharm.1999; Jan; 25(2): 163–168.
3. Spireas S, Bolton M. Liquisolid Systems and Methods of Preparing Same. U.S. Patent5. 1999; 968-550.
4. Javadzadeh Y, Siahi MR Jalali B., M.Nokhodchi A. Enhancement of dissolution rate of piroxicam using liquisolid compacts. IL Farmaco. 2005; Apr; 60(4): 361–365.
5. Nokhodchi, A., Javadzadeh Y, Siahi M.R., Barzegar-Jalali, M. The effect of type and concentration of vehicles on the dissolution rate of a poorly soluble drug (indomethacin) from liquisolid compacts. J. Pharm. Pharmaceut. Sci. 2005; Jan;8(1): 18–25.
6. Javadzadeh, Y., Siahi, M.R, Asnaashari S, Nokhodchi A. Liquidsolid technique as a tool for enhancement of poorly water-soluble drugs and evaluation of their physiochemical properties. Acta Pharm. 2007; Mar; 57(1): 99–109.
7. Tiong N, Elkordy AA. Effects of liquisolid formulations on dissolution of naproxen. Eur J Pharm Biopharm. 2009; Nov 73(3): 373–384.
8. Javadzadeh Y, Jafari, Navimipour B, Nokhodchi A. Liquisolid technique for dissolution rate enhancement of a high dose water-insoluble drug (carbamazepine). Int J Pharm. 2007; Aug; 341(1-2): 26–34.
9. Spireas S, Sadu S. Enhancement of prednisolone dissolution properties using liquisolid compacts. Int JPharm. 1998; may; 166(2): 177–188.
10. Harvey R, Camphe PC. Anti hypertensive. In: Richard finker, Luigi X, editors. Lippincotts Illustrated Review Pharmacology.4th ed, New Delhi: wolters kluwer; 2009. p. 215-28.
11. Satoshkar RS, Bhandarkar. Vasoldialator drugs and pharmacotherapy of angina pectoris. In: RR Satoshkar, editor. Pharmacology and pharmacotherapeutics.17th ed. Mumbai: ramdas bhatkal for popular prakashan pvt. Ltd; 2001. P.390-404.
12. Mays a. al-sarraf, Ahmed a. hussein, Ahmed S. Abdul J. Dissolution enhancement of telmisartan by liquisolid compacts; Int J Pharm Pharm Sci,2014; 6(2), 743-749
13. Manpreet kaur, rajni bala, sandeep arora. Formulation and evaluation of amlodipine besylate; irjp, 2013; 4(1); 156-160.
14. Sandip V. Enhancement of dissolution rate of poorly water soluble diclofenac sodium by liquisolid technique. IJPCS. 2012; 1(3):989-1000.