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Research Article

Formulation And Evaluation Of Capsule Of Nifedipine By Liquisolid Compact

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ABSTRACT

The most suitable and helpful measurement structure is a container. the ability to conceal awful preferences and scents. They might work on the dynamic fixings' bioavailability and promptly break down in the gastrointestinal system's gastric juices. The calcium-channel blocker nifedipine is much of the time used to treat fundamental hypertension and angina pectoris. Nifedipine has a somewhat short half-existence of two hours and is totally solvent in water. Subsequently, it is by and large recognized that the best type of Nifedipine for routine hypertension treatment is in container structure. The essential objective of the exploration was to make and evaluate a hard gelatin case measurement type of nifedipine, which is utilized to treat hypertension. To work on the dissolvability of the prescription, polymers like Transcutol and Stake 400 were utilized.

INTRODUCTION

The improvement of the oral medication conveyance framework primarily relies upon drug solvency, in this manner its oral bioavailability.[1] More than 90 % of dynamic drug fixings a work in progress and 50 % of as of now marketeddosage structures have dissolvability issues. Nifedipine is one of the most intense cal-cium-channel blockers. It is broadly utilized in the treatment of vascular illnesses, for example, hypertension, angina pectoris and Raynaud's peculiarity. it is a profoundly non-polar com-pound, which ingested totally from the gastrointestinal plot. However, has an exceptionally low bioavailability essentially due to presystemic digestion. On account of the restricted aque-ous solvency, it shows unfortunate disintegration attributes and its oral assimilation is dis-arrangement rate limited.The new 'liquisolid" method might be applied to figure out fluid meds (i.e., slick fluid medications and arrangements, sus-annuities or emulsions of water-insoluble strong medications conveyed in nonvolatile fluid vehicles) into powder. liquisolid smaller method is a promising and novel procedure to upgrade inadequately water-dissolvable medications' dissolvability and disintegration rate.[2] In this

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strategy, the fluid type of a medication in a non-unpredictable dissolvable is changed over into dry-looking, non-follower, and openly streaming powder by usingcarrier and covering materials.[2, 3] The essential system behind liquisolid definitions is expanded wettability and surface region accessible for drug discharge. Thus, utilizing the liquisolid strategy, we can accomplish better bioavailability of ineffectively dissolvable medications.

Need :

The rationale behind the research is used for poor solubility of nifidipine in water.

Objective of liquisolid system :

- Improve the bioavailability of water insoluble drug which are given by oral route.
- Absorption can be enhanced.
- Improve release of drug.

Application of Liquisolid Technique :

- Solubility And Dissolution improvement
- Flowability
- Bioavailability improvement.

Liquid loading factors (Lf)

It is defned as the weight ratio of the liquid formulation (W) and the carrier material (Q) in the system:

$$Lf = W/Q \quad (1)$$

(W is the weight of the liquid medication (the drug + non-volatile liquid vehicle) and Q is the weight of the carrier.)

Represents the ratio between the weights of the carrier (Q) and the coating (q) material present in the formulation:

Then optimum weight of the coating material (q) could also be obtained (Equation 2).

$$R=Q/q \quad (2)$$

The liquid load factor that ensures acceptable fowability (Lf) can be determined by:

$$Lf=\Phi+ \varphi. (1/R) \quad (3)$$

By calculating Lf and W, we can calculate the amount of Q and q required for the liquisolid system.

Theoretical Aspects of liquisolid system :

To accomplish ideal stream conduct and compressibility of liquisolid frameworks, a numerical model created by Spireas et al. was utilized as the detailing configuration model for the liquisolid tables. Requirements for this incorporate a reasonable medication competitor, a proper non-unstable dissolvable, transporter materials, and covering materials. The fluid stacking factors (Lf) and the flowable fluid maintenance possible qualities (X-esteem) are utilized to compute the measures of excipients (transporter and covering materials) utilized in the readiness of liquidsolid pieces.

MATERIALS & METHODS :

Materials

Nifedipine was obtained from J B chemicals & pharmaceutical Ltd , Transcutol was obtained from Gattefossé India Pvt. Ltd , Crospovidone was obtained from Cipla Ltd, Polyethylene glycol (PEG) , Glycerol , Glycerine , Span 80 , Microcrystalline cellulose (MCC), Silicon dioxide , Starch were obtained from Loba Chemie Pvt Ltd.

Methods

A. Micromeretics study:

The drug and excipient powder mix was subjected to following micromeretics study parameters.

1. Angle of repose
2. Bulk density
3. Tapped density
4. Compressibility index

1. Angle of Repose:

The point of rest is the most extreme point that structures between the outer layer of the powder heap and the even surface. The point of rest values for most of drug powders fall somewhere in the range of 25 and 45°; lower values signify better stream qualities [4]. The fix channel strategy was used for deciding point of rest. In the decent pipe technique, diagram paper is laid on a level even surface and a channel is situated with its tip at a foreordained level, H. Till the highest point of the

conelike heap simply arrives at the channel's tip, powder or granulation is delicately poured through the pipe. Then, the point of rest is determined utilizing the distance across of the tapered heap's base [5].It is determined using the given formula,

$$\tan\emptyset = h / r \quad (1)$$

where, h is height of pile, r is radius of pile

Table 1: Angle of repose [6]

Sr. No.	Angle of Repose	Flowability
1	25-30	Excellent
2	31-35	Good
3	36-45	Fair possible
4	46-55	Poor
5	56-65	Very poor
6	>66	Very, very poor

2. Bulk Density:

The volume of a known mass of powder that went through the screen is used for determining the bulk density [4]. It is calculated by using the given formula,

$$\text{Bulk Density} = M / Vb \quad (2)$$

Where,

M= Mass of sample,

Vb= Volume of sample [5].

3. Tapped density:

It is obtained by tapping the measuring cylinder containing known mass of powder and then measuring the volume of powder [7]. It was performed using the Electrolab's tapped density apparatus.

4. Compressibility index:

Carr's Compressibility index and Hausner ratio gives the indication about the ease with which a powder material can flow using following equations,

Carr's Compressibility index (CI)

$$CI = \frac{\text{(tapped density} - \text{bulk density)}}{\text{Tapped density}} \times 100 \quad (3)$$

tapped density

Hausner's ratio (HR):

$$HR = \frac{\text{Tapped density}}{\text{Bulk density}} \quad (4)$$

Table 2: Scale of flowability for CI and HR [5]

Sr. No.	Carr's Index	Hausner's Ratio	Flowability
1	5-15	1.05-1.18	Excellent
2	12-16	1.14-1.20	Good
3	18-21	1.20-1.26	Fair passable
4	23-35	1.30-1.54	Poor
5	33-38	1.50-1.61	Very poor
6	>40	>1.67	Very very poor

B. Determination of solubility

Nifedipine's solubility was tested in a variety of solvents, including water, PEG 400, propylene glycol, and Tween 20. Excess medication was added to the vehicles to create saturated solutions, which were then shaken continuously for 48 hours at 25 ± 0.5°C. Following this time, the solutions

were diluted, filtered, and UV-spectrophotometer-analyzed at 238 nm.[8]

Table 3 : Determination of solubility

Solvent	Solubility
Transcutol	310 mg/ml
PEG	119 mg/ml
Glycerol	13 mg/ml
Glycerin	4 mg/ml
Span 80	85 mg/ml

C. Carrier and coating material ratio

Carrier material

For a liquid vehicle, the carrier material should have strong absorption qualities and be porous in nature.[9] A restricted amount of liquid should be held by both the coating and the carrier materials while maintaining flowability and compressibility. Example : microcrystalline cellulose (MCC).

Coating Material

Typically, coating materials are made of coarsely ground particles that cover wet particles by absorbing excess liquid and producing a free-flowing, dry powder.[10] Example : Silicon Dioxide.

Table 4: Carrier and coating material ratio

R	Transcutol	Carrier (MCC)	Coating material (silicon dioxide)
5	0.5 = Good flow 0.5 = Better 0.5 = Bad (1.5 ml)	2.5	0.5
10	0.5 = poor 0.5 = Bad (1 ml)	2.7	0.27
15	0.5 = Bad (0.5 ml)	2.812	0.187
20	0.5 = Bad (0.5ml)	2.85	0.142

D. Formulation design of liquisolid capsule:

Table 5: Formulation design of liquisolid capsule of Nifedipine

Ingredients (Mg)	Ls1	Ls2	Ls3	Ls4
R	5	10	15	20
Drug(Nifedipine)	10	10	10	10
Transcutol	50.76	50.76	50.76	50.76
Loading factor	0.6	0.4	0.28	0.20
Carrier(MCC)	101.26	151.9	217	303.8
Coating material(silicon dioxide)	20.25	15.19	14.46	15.15
Glidant(starch)	1.89	2.36	3.03	3.94
Disintegrant (Starch)	7.2908	9.114	11.68	15.94
Total Wt.	184.16	239.324	306.93	398.83

Preparation of Capsule of Nifedipine : [11]

- Placing Capsules in the Manual Capsule Filler.
- Put empty capsules in the loading tray and place it onto the machine.
- Pull locking handle forward, push down the long lever to lift the caps of the capsule bodies.
- Put the tray with caps aside.
- Push the locking handle back and capsule bodies will come to the filling surface.
- Filling Powder in the Capsules.
- Put powder tray to avoid spilling of the powder.
- Pour the right quantity of powder and spread it. Bring down the tamper and lock it.
- Turn the handle given above to compress the powder.
- Bring up the tamper. Pour & spread the extra powder.
- Covering the Capsules.
- Put the tray with caps to filler and bring down the locking plate.
- Lock the plate and turn the front knob to the right.
- Push the long lever down to push capsule bodies into caps.
- Open the locking plate lock, lift the locking plate and turn the front knob to the left.
- Pull down the long lever and lift the tray with filled capsules.
- Turn the tray to get filled capsules out of the tray.

C) Evaluation of Capsules:

1. Drug–polymer compatibility studies :

Due to their close proximity during the manufacture of the capsule formulation, the medicine and polymer may interact and cause the drug to become unstable. Therefore, choosing the right polymers requires careful consideration of preformulation studies pertaining to the drug-polymer interaction. The compatibility of nifedipine with the chosen polymers was determined using FT-IR spectroscopy[12].

3. Capsule evaluation :

1. To measure the diameter and thickness of capsule shell and body by using Vernier caliper.
2. To measure the height and length of whole capsule.

4. Weight Variation Test :

Capsules meet the requirements of the following test with respect to variation in weight of contents. Weigh 20 intact capsules individually, and determine the average weight. [13]The requirements are met if each of the individual weights is within the limits of 90% and 110% of the average weight.

5.Disintegration test :

Disintegration test was performed using the Disintegration test apparatus. One capsule introduced into each tube and added a disc to each tube. The assembly was suspended in the water in a 1000 ml beaker . [14]The volume of water such that wire mesh at its highest point is at least 25 mm below the surface of the water ,and its lower point was at least 25 mm above the bottom of the beaker . The apparatus was operated and maintained the temperature at 37+_ 2 degree celcius.[15]

Procedure of Disintegration : [16]

- Preparation of 0.1 N HCL . Measure Accurately 8.62 ml HCL add in 1000 ml distilled water.
- Clean the apparatus carefully and take 900 ml 0.1 N HCL in a beaker then maintain the temperature upto 37+/-0.2 degree celcius then add the capsule in basket of 10 mesh sieve, Start the motor.
- Switch and record the capsule release time.

6.Dissolution test :

Dissolution is the process in which a substance forms a solution. Dissolution testing measures the extent and rate of solution formation from a dosage form, such as tablet, capsule, ointment, etc. The

dissolution of a drug is important for its bioavailability and therapeutic effectiveness.[17]

RESULT AND DISCUSSIONS:

1. Micromeritics study :

The result of micromeretics properties of all the batches from Ls1 to Ls4 of capsule of nifedipine by liquisolid technique are shown in table 5. These batches were evaluated for parameters like bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose. [18]

Table 6: Result of Micromeritics study on powder blend

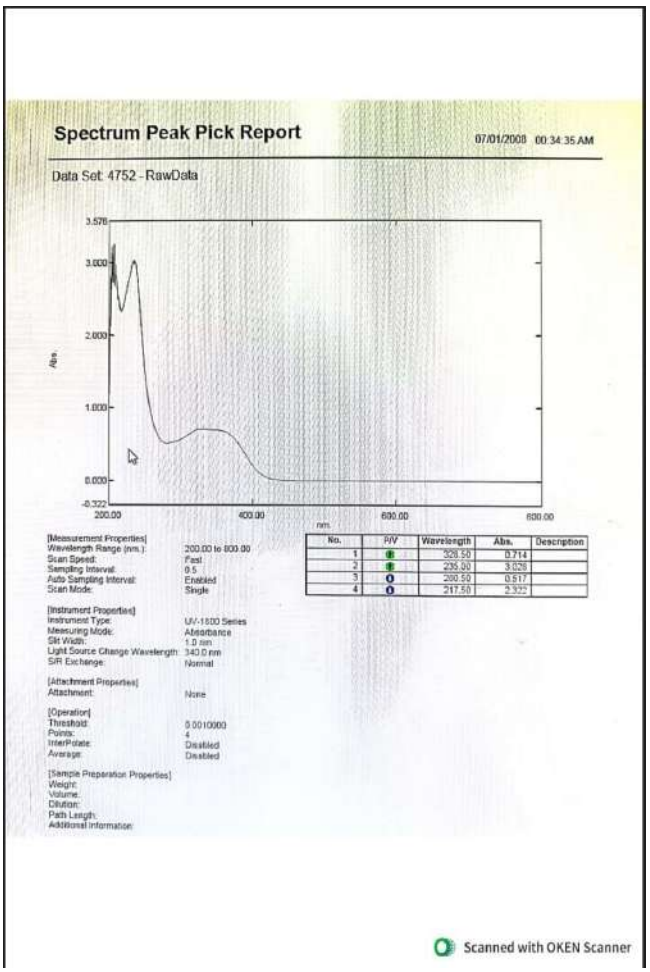
Batch	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Angle of repose	Carr's Index	Hausner's Ratio
Ls1	0.75	0.93	29.72	19.354	1.25
Ls2	0. 75	0.95	32.61	21.05	1.26
Ls3	0.69	0.98	28.81	29.59	1.420
Ls4	0.78	0.97	34.21	19.58	1.24

2. Drug–polymer compatibility studies :

Solubility studies were performed to select the solvent for liquisolid system. Table 3 explains the results of solubility studies.[18] Nifedipine showed maximum solubility in Transcutol, hence the same was selected as non-volatile solvent.

IR of Nifedipine :

Capsules were evaluated for Infrared Spectroscopy [19] , the Ls1 batch was showing the highest wavelength. The result for the test is given in image.



Capsule evaluation :

Table 7 : Capsule evaluation

Capsule Evaluation	Dimensions
Cap length	1 cm
Body length	1.9 cm
Body Diameter	0.6 cm
Cap Diameter	0.7 cm

Weight Variation Test :

Capsules were evaluated for weight variation test, the Ls1 batch was within the acceptable limits as per the IP, BP and USP[20]. The result for the test is given in table 8.

Table 8 : Weight Variation Test

Sr. No.	Capsule shell wt.in (mg)	Net content wt. (mg)	Whole capsule wt. (mg)
1	75	252	328
2	75	252	327
3	76	246	322
4	74	250	324
5	77	249	326
6	75	256	331
7	76	251	327

8	77	261	338
9	75	265	331
10	76	250	326
11	75	255	327
12	76	251	327
13	77	247	323
14	75	249	324
15	76	251	327
16	77	251	328
17	74	250	324
18	76	250	327
19	77	255	328
20	74	252	324
		Average wt.= 251.65 mg	Average wt.= 327.2 mg

Formula : Average weight- Individual weight = NMT 7.5

251.65-253= 2

5.Disintegration test :

Capsules were evaluated for Disintegration test, the Ls1 batch was within the acceptable limits as per the IP, BP and USP[21]. The result for the test is 2.17 min .

6.Dissolution test :

The capsules belonging to all the 4 formulation were evaluated, all showed control release pattern for drug release for upto 40 min as given in table.[22] The test result showed that as the concentration of polymer was increases the amount of drug release was retarded. The formulation batch Ls1 showed the drug release about 94%.

Table 9: Concentration vs Absorbance

Sr No.	Concentration	Absorbance
1	2	0.14
2	4	0.287
3	6	0.395
4	8	0.566
5	10	0.671

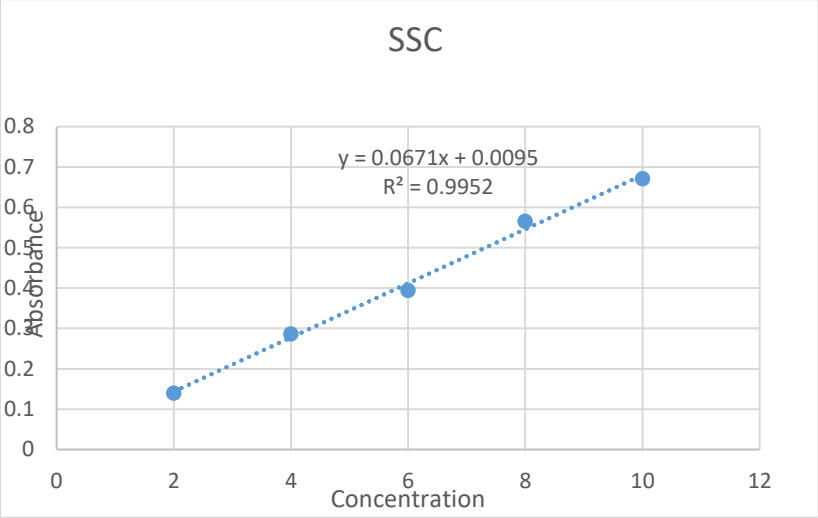
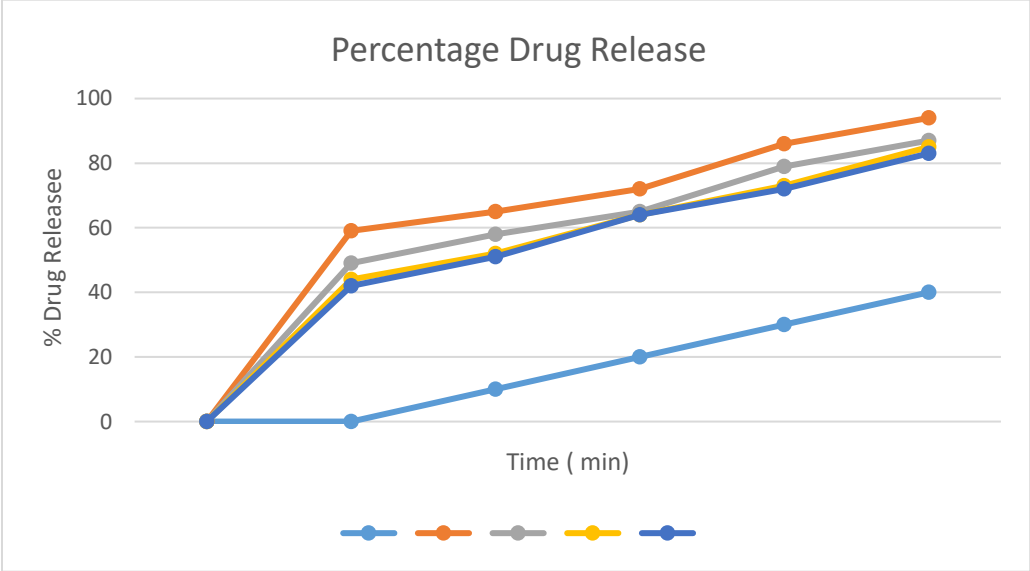


Table 10:Time and % drug release

Time (min)	F1	F2	F3	F4
0	59	49	44	42
10	65	58	52	51
20	72	65	64	64
30	86	79	73	72
40	94	87	85	83



CONCLUSION

In the present work, Nifedipine capsule prepared by liquisolid compact technique using polymer such as Tanscutol. The flow property of the powder has shows satisfactory result for various physico-chemical evaluation of capsule .The in – vitro dissolution study of nifedipine capsule is tested in 0.1 N HCL. From the in-vitro dissolution study it is observed that the increases in dissolution and bioavailability. As the solubility increases bioavalibility and rate of drug release increases. From the overall study concluded that Nifedipine drug capsule shows good release with good absorption .

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