A Novel Technique to Enhance Dissolution Rate of Cilnidipine Using Liquisolid Compact & Wet Granulation

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ABSTRACT
The main objective of the work was to improve the dissolution rate of the drug, Cilnidipine (CLD) by using the liquisolid compact technique and wet granulation. Cilnidipine drug is poorly soluble in water and it's highly soluble in higher pH. In this study drug is solubilize in tween 80 and sodium hydroxide and meglumine solution. And then drug solution binding on Pearlitol SD 200. PVP K30 used as a binder and crospovidone used as a disintegrant. Sodium hydroxide and meglumine used as a buffering agent for basic media preparation. The drug release rates of tablets which prepared by liquisolid compact have higher solubility and dissolution than conventional tablets.

Keywords: Liquisolid compact, Cilnidipine, Tween 80, Pearlitol SD 200, Liquid load factor.

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INTRODUCTION

The design of liquid solid compact with wet granulation requires physical and chemical compatibility with the excipients and API. Solubility and dissolution directly link to the bioavailability of API. Various approaches use to increase dissolution and bioavailability of the API. Liquisolid compact is a promising approach to enhance solubility and dissolution rate.

In the present study solubility and dissolution of the API was increases by wetting the API with nonvolatile solvent. And wet granulation with the API + solvent media on the carrier and coating material which is simple wet granulation process. Meglumine and NaOH used as a buffering agent to dissolve an API in a nonvolatile solvent.

The liquisolid technique was given by Spireas, in which liquid convert into a free flowing, powder by simple blending with carrier and coating material. Liquid portion is liquid drug or a liquid concentrate is added in to carrier material which is a diluent solvent mainly a PG, PEG and glycerin. [1] As a addition of liquid

absorb on surface of carrier material, and liquid layer formation occur on particle surface. Liquisolid compact are a powder form which is prepared by a liquid and diluent.

Liquid medication means liquid drug or a insoluble drug mixed in a solvent. By liquisolid compact drug with solvent converted into a dry, non- sticking, compressible powder by using a diluent and a lubricant. [2] The main objectives of research to enhance a dissolution rate and solubility by developing liquisolid compact by wet granulation.

In the liquisolid compact, the drug is liquid form or a solid form which is convert in to a solubilize form. [3] As a liquid add into a drug is solubilize in it and addition of carrier material absorption occur on a drug layer and as addition of carrier material adsorption occur. The purpose of the study is to optimization of the concentration of NaOH and meglumine to dissolve a drug on response dissolution. ANOVA design used to construct a polynomial equation and counter plots prepared and depending on optimizes design space optimization of formula done and optimize tablets and marketed tablets are compared.

MATERIALS AND METHODS
Materials
Cilnidipine was obtained from J. B. Chemicals, Ankleshawar. Tween 80 (Merck), Crospovidone (Dow), Microcrystalline cellulose (Avicel PH102, PH 101, PH 200, PH 112), cross carmellose sodium (FMC biopolymer), Miglyol 810, Miglyol 812, Miglyol 840, Capmul MCM, Capmul MCM PG8, Capmul GMO, Labrafec PG, Captex 355 Labrafil 1944 CS, Starcap 1500 (colorcone ltd, Goa), Captex 200, Captex 200 P, from (gattefose) Fujacalin (Canberra chemicals, Mumbai). All materials were of analytical grade.

Spectrophotometer Analysis
The UV-Spectrophotometric analysis of Cilnidipine was performed in methanol at 240 nm using a UV-visible spectrophotometer. A standard curve prepare in range of 2-10μg/mL using methanol as a diluent for calculation of drug content. And for measure drug release standard curve perform in 0.1 N HCL at 243 nm in the range of 8-40μg/mL. [10-12]

Selection of solvent
Solubility study used to select the solvent. Solubility study of drug was performed in different solvents like (Propylene glycol, PEG-200, Paraffin Oleic acid, Tributyrin, Captex 200 P, Labrafac CC PEG-400, PEG-600, Glycerin, Labrafil M 1944 CS, Cremophore® EL, Tween 20, Tween 80, Span 80, Span 20, Liq., Captex 355 EP/NF, Migloyl 829, Maisine 35-1) to select suitable non-volatile solvent. More amount of API adds in vail of selected solvent. [13]

Then all vials containing solvent vortex on Vortexer and shake on rotary shaker for 72 hr at room temp. After 72 hours solution centrifuge and supernants were diluted with methanol and concentration measure. [14]

Angle of slide measurement
Lab model was used in this study. Model contains wooden blocks joined. Upper wooden block is polished. [15-16] 10 grams of carrier and coating material take and add optimize solvent add till powder started to slide. Angle at 33° called as ideal. [17]

Flowable liquid retention potential determination
Take 10 grams of each material and addition of optimized solvent and mixed it. Phi value calculates from equation. [18]

$$Phi - value = \frac{Weight\ of\ liquid(g)}{Weight\ of\ solid(g)}$$

Phi-value plotted in graph to the angle of slide Φ). The phi-value 33° called as flowable liquid retention potential of coating and carrier material. [19]

Calculation for the amount of carrier and coating material
The carrier and coating material liquid load factor calculated as per the Phi-value. [20-21]

$$L_f = \varphi_{CQ}(1/R) + \Phi_{CA}$$
$$Q = W/L_f$$
$$q = Q/R$$

Where,
L_f=Liquid load factor
Φ_{CA}= Phi value for carrier material
φ_{CQ}= Phi value for coating material
R=Excipient ratio (Q/q)
W=Amount of liquid
Q=Amount of carrier material
q= Amount of coating material

Preparation of Liquisolid Compacts
Several liquisolid systems of CLD (denoted as TF-1 to TF-30) were prepared which is given in Table 1. For improve flow property of liquisolid compact we combine the two mechanism [22-24]

1. Liquisolid compact technique
2. Wet granulation

Manufacturing process
Sifting
Sift through 40 # s.s. sieve. Pearlitol SD 200, Sodium Lauryl sulphate, Croscarmellose sodium, Aerosil 200, Magnesium Stearate.

Binding (Binder preparation)
Mix 50.0 gram water plus NaOH cool solution 1 hour. Add meglumine in 6.66 grams of water till dissolve add Cilnidipine and mix continue. Add PVPK30 in 3.34 grams of water and add to main solution. Add tween 80 and mix it till dissolve and keep it over night.

Granulation
Mix sifted Pearlitol SD 200, Croscarmellose sodium, 10 minutes. Add binder solution to above dry mix at slow speed to prepare medium hard granules.

Drying
The drying of granule performed at 50 to 60°C. Target LOD 2.2% Pass dry granule through 24 # sieve.

Blending & Lubrication
Add Crospovidone, Sodium Lauryl sulphate, Pearlitol SD 200 Mix for 10 min. Add magnesium stearate mix for 5 min. compress the tablet.

Table 1: Selection of solvent

S. No	Solvents	Solubility (mg/mL)*
1.	Propylene glycol	1.25 ± 0.041
2.	PEG-200	7.15 ± 0.12
3.	PEG-400	2.52 ± 0.38
4.	PEG-600	7.56 ± 0.26
5.	Glycerin	4.756 ± 0.316
6.	Labrafil M 1944 CS	6.14 ± 0.46
7.	Cremophore® EL	3.55 ± 0.29
8.	Tween 20	18.10 ± 0.348
9.	Tween 80	20.00 ± 0.19
10.	Span 80	1.74 ± 0.37
11.	Span 20	12.20 ± 0.083
12.	Liq. Paraffin	0.46 ± 0.041
13.	Oleic acid	1.42 ± 2.00
14.	Tributyrin	1.26 ± 1.26
15.	Captex 200 P	15.03 ± 0.55
16.	Labrafac CC	2.18 ± 0.34
17.	Captex 355 EP/NF	6.40 ± 1.36
18.	Migloyl 829	2.45 ± 0.21
19.	Maisine 35-1	3.19 ± 0.03
20.	Peceol	1.59 ± 0.07

*All the values are in mean ± SD (n=3)

Experimental Design

In experiment design, change in one or more variable to saw the effect of variable on result. The design of experiment is good procedure for doing experiments so that data obtained is analyze and find a conclusion from that

Design of experiment started with a choosing an objective of the practical and selecting the processing factor for the study. Good design maximizes the good results. Design of experiment used in preparation and development of liquisolid compact preparation. Different design used in experimental design. [25-26]

The weight of NAOH and weight of Meglumine play a crucial role in the preparation of Cilnidipine liquisolid compact. Center composite design (CCD) was employed for systemic study of joint influence of the effect of Independent variables [weight of NAOH (X_1) and weight of Meglumine (w) (X_2)] on responses such as 100% dissolution at min.

The selections of dependent variables were done on the basis of the aim of the present investigation (enhanced solubility and dissolution rate of Cilnidipine). In this design, two factors with five levels were probed to investigate the main effects and interaction of the two factors on five levels A design consists of thirteen runs. A second- order quadratic model incorporating interactive and polynomial terms was used to evaluate the responses.

$$Y_1 = Bo + b_1X_1 + b_2X_2 + b_3 X_1X_2 + b_4X_1^2 + b_5 X_2^2$$

Where, Y_1 was the dependent variables, b_0 was arithmetic mean response of the 13 runs and b_1 was the estimated coefficient for factor X_1. The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value. The interaction terms (X_1X_2) show how the responses changes when two factors simultaneously changed.

Data analyzed by Microsoft Excel® 2010 version. Analysis of variance (ANOVA) was implemented to check that was no difference between the models. The

Response surface and contour plots were plotted using DOE® 7.1.5 (Stat- Ease, Inc. Minneapolis, USA). [28]

Evaluation of powder blend

To measure good flow of powder blend following parameter measure, Angle of repose, Determination of bulk density, Determination of tapped density, Carr's compressibility index, "Hausner" s ratio.

Evaluation of Liquisolid tablets
Evaluation of powder material

Powder material is used to determine flow of the powder and compressibility of the powder by Carr's compressibility index and Hausner' s ratio, angle of repose, bulk density, tapped density.

Evaluation of Liquisolid tablets
Hardness

Monsanto Hardness tester used measure hardness expressed in Kg/cm².

Friability

6.50 grams of tablets taken from the batch and tablets were initially weighed ($W_{initial}$) and add in to Roche's friabilator. And friabilator operate at 25 rpm for 4 minutes. Then tablets were weighed again (W_{final}).

Weight variation

20 Tablets are selected weight variations of individual tablets were determined with respect to average weight and % weight variation.

Disintegration

Disintegration test was performed in 900ml distilled water at 37±0.5°C temperature and at the rate of 30±2 cycles/min.

Drug Content Uniformity

The CLD content was determined in 20 tablets Each tablet was then crushed and a quantity of powder equivalent to 10 mg of CLD was dissolved in 100 mL methanol and 1 mL of this solution was diluted to 10 mL with methanol and measured spectrophotometrically at λmax of 240 nm. The CLD content in different liquisolid tablet formulations was determined by accurately weighing 20 tablets of each formula individually. Each tablet was then crushed and a quantity of powder equivalent to 10 mg of CLD was dissolved in 100 mL methanol and 1 mL of this solution was diluted to 10 mL with methanol and measured spectrophotometrically at λmax of 240 nm. [29-31]

In vitro Drug Release

Dissolution studies were performed using USP Dissolution apparatus type II (paddle type) with 900 mL 0.1 N HCl as dissolution medium. All studies were carried out at 37± 0.5°C, 50 RPM speed for 30 min at a fixed time intervals 5 mL aliquots were withdrawn, filtered with whatman filter paper fresh dissolution medium were added to maintain constant volume throughout the test period sample was determined by UV-Visible spectrophotometer at 237 nm.

RESULTS AND DISCUSSION
Selection of nonvolatile solvent

In the liquisolid compact non-volatile liquid solvent is optimized for the high drug solubility in solvent. The

Int. J. Pharm. Sci. Drug Res. July-August, 2017, Vol 9, Issue 4 (160-168)

162

solubility in various non-volatile solvents is shown in Table 1. The table shows that solubility of drug in Tween 80 is higher. For this reason, Tween 80 was selected to be the suitable solvent for preparing liquisolid compact.

Angle of slide measurement and flowable liquid retention potential determination

Angle of slide for carrier and coating materials was used to calculate flowable liquid retention potentials, which are needed for calculation of the liquid load factor (Lf).

Table 2: Trial Formulation

Formula	Weight of solvent (mg)	Drug conc. (%) w/w	R=Q/q	L_f=W/Q 0.51+1.78 (1/R)	Pearlitol SD 200 Q=W/L_f (mg)	Aerosil 200 q= Q/R(mg)	CCS 5% (mg)	Total Weight (mg)
TF$_1$			5	0.866	57.73	11.54	5.96	129
TF$_2$			10	0.688	72.67	7.26	6.49	141
TF$_3$	50	20%	15	0.628	79.61	5.30	6.74	145
TF$_4$			20	0.599	83.47	4.17	6.88	149
TF$_5$			25	0.581	86.05	3.44	6.97	150
TF$_6$			5	0.866	69.28	13.85	7.15	155
TF$_7$			10	0.688	87.20	8.72	7.79	169
TF$_8$	60	16.6%	15	0.628	95.54	6.36	8.1	175
TF$_9$			20	0.599	100.16	5.00	8.25	179
TF$_{10}$			25	0.581	103.27	4.13	8.37	181
TF$_{11}$			5	0.866	80.83	16.16	8.35	180
TF$_{12}$			10	0.688	101.74	10.17	9.09	197
TF$_{13}$	70	14.28%	15	0.628	111.46	7.43	9.44	205
TF$_{14}$			20	0.599	116.86	5.84	9.63	209
TF$_{15}$			25	0.581	120.48	4.81	9.76	211
TF$_{16}$			5	0.866	92.37	18.47	9.54	206
TF$_{17}$			10	0.688	116.27	11.62	10.39	225
TF$_{18}$	80	12.5%	15	0.628	127.38	8.49	10.79	234
TF$_{19}$			20	0.599	133.55	6.67	11.01	239
TF$_{20}$			25	0.581	137.69	5.50	11.15	242
TF$_{21}$			5	0.866	103.92	20.78	10.74	233
TF$_{22}$			10	0.688	130.81	13.08	11.69	253
TF$_{23}$	90	11.11%	15	0.628	143.31	9.55	12.14	263
TF$_{24}$			20	0.599	150.25	7.51	12.38	268
TF$_{25}$			25	0.581	154.90	6.19	12.55	272
TF$_{26}$			5	0.866	115.47	23.09	11.92	257.99
TF$_{27}$			10	0.688	145.34	14.53	12.99	280.00
TF$_{28}$	100	10%	15	0.628	159.23	10.61	13.49	292
TF$_{29}$			20	0.599	166.94	8.34	13.76	298
TF$_{30}$			25	0.581	172.11	6.88	13.94	301

Table 3: Factors and their different levels for Central composite design for preparation liquisolid tablets

Independent Variables	Levels				
	Lowest (-α)	Low (-1)	Medium (0)	High (+1)	Highest (+α)
X$_1$ weight of NAOH	2.59	3	4	5	5.41
X$_2$ (weight of Meglumine)	10.59	11	12	13	13.41
Transformed values	-1.414	-1	0	+1	+1.414
Dependent Variables	Y$_1$ (100% dissolution at min)				

Table 4: Experimental matrix and results

RUN	Independent Variables		Responses
	X$_1$	X$_2$	Y$_1$ (100% dissolution at min)
LS$_1$	3.00	13.00	20
LS$_2$	3.00	11.00	30
LS$_3$	5.41	12.00	16
LS$_4$	4.00	12.00	14
LS$_5$	2.59	12.00	25
LS$_6$	5.00	11.00	22
LS$_7$	4.00	12.00	14
LS$_8$	4.00	13.41	20
LS$_9$	4.00	12.00	14
LS$_{10}$	4.00	10.59	22
LS$_{11}$	4.00	12.00	14
LS$_{12}$	4.00	12.00	14
LS$_{13}$	5.00	12.00	25

Table 5: Regression analysis of central composite design batches

Model	Coefficient	Y$_1$ (100% dissolution at time min)
	β0	+15.20
	β1 (X$_1$)	-12.02
	β2 (X$_2$)	-10.61
	β12 (X$_1$X$_2$)	+3.25
	β3 (X$_1$²)	+6.46
	β4 (X$_2$²)	+7.46
	B5 (X$_1$²X$_2$)	+ 8.86
	B6 (X$_1$X$_2$²)	+11.27
	r²	0.8850
Cubic	Adjusted r²	0.7241
	PRESS	318.81

Table 6: Analysis of variance for dependent variables from CCD

Source	D.F.	Sum Square	Mean Square	F Value	p value
Y$_1$ (100% dissolution at time Min)					
Model	7	1685.38	240.77	5.50	0.0394
X$_1$	1	578.00	578.00	13.20	0.0150
X$_2$	1	450.00	450.00	10.28	0.0238
X$_1$X$_2$	1	42.25	42.25	0.96	0.3711
X$_1$²	1	290.53	290.53	6.64	0.0497
X$_2$²	1	387.40	387.40	8.85	0.0310
X$_1$² X$_2$	1	156.88	156.88	3.58	0.1169
X$_1$ X$_2$²	1	254.06	254.06	5.80	0.0610

For the carrier material 5 grams of the powder was used for determine angle of slide. But in case of the coating material i.e Aerosil 200 having low density; it

Int. J. Pharm. Sci. Drug Res. July-August, 2017, Vol 9, Issue 4 (160-168)

163

was not convenient to take 10 grams of material for measurement. Figure 2, 3 shows the relation between angle of slide and the corresponding Phi-value. It is show that Phi-value corresponding to an angle of slide of 33⁰ was higher for Pearlitol SD 200 and Aerosil 200 as carrier and coating material respectively.

From the graph flowable liquid retention potential of Pearlitol SD 200 is found to 0.51 and flowable liquid retention potential of Aerosil 200 is found to be 1.78.

$$L_f = \Phi_{CA} + \varphi_{CO} \, (1/R)$$
$$L_f = 0.51 + 1.78 \, (1/R)$$

Experimental Design

From the trial batch depending on different weight of solvent and different R ratio trial batches taken. The drug concentration range from 10% to 20% was taken. Above 20% of drug concentration not used because the tablet weight goes below 80 mg so can't compression of that weight done. If drug concentration below 10% is taken than weight of solvent is increased so difficulty occurs in compression. So from that design is applied. Design batches mentioned in Table 2, 3, 4. *All the batches contain 2% magnesium stearate, 10 mg CLD and 1% talc.

As we increases the weight of solvent total weight of tablet increases and also weight of carrier material increases and coating material decreases. As excipient ratio increases weight of carrier increases and coating material decreases.

From trail batch TF_1 to TF_{10} forming a liquisolid compact the flow of material is not good and cant compress the tablet because that formulation having a low quantity of excipients as carrier and coating material. In formulation of TF_{11} to TF_{15} tablet form but having not good hardness and friability of tablets is too high.

In formulation TF_{21} to TF_{30} tablet observe with good quality and further analysis of batches are carried out. But dissolution of tablet not found satisfactory. From the dissolution of all batches found that the dissolution of drug after 60-70 min not observed. So from above data we have to reformulate a liquisolid compact to improve the dissolution and also a flow property.

And in trial batches formula tween 80 only not able to bind the granule so we have added a PVP K30 as a binder in formulation and also from literature search found that Cilnidipine drug only dissolve PH above 7. So in new formula we have to add a NaOH and Meglumine to increases the PH. SLS added to solubilize the drug.

Contour plots and response surface analysis

Influence of formulation composition factor on 100% dissolution at time (Min)

For Dependent variable Y_1 (100% dissolution at time) For the Y_1 response, the interaction illustrated in Figure 4By keeping X_2 constant X_1 increased from -α to +α the 100% dissolution at time decreases from 50 to 16 Min. A lowest dissolution time of 14 min was observed with weight of NaOH (4 mg) and weight of Meglumine (12 mg).

Optimization of formula and Validation of CCD

The desirable ranges of these responses were described in Table and Figure. Therefore, to verify the evolved models, the optimum formulation was prepared according the above values of the factors and subjected to the analysis of responses. As shown in Table and Figure 5. It was demonstrating that the observed value of a new batch was quite closer to predicted value.

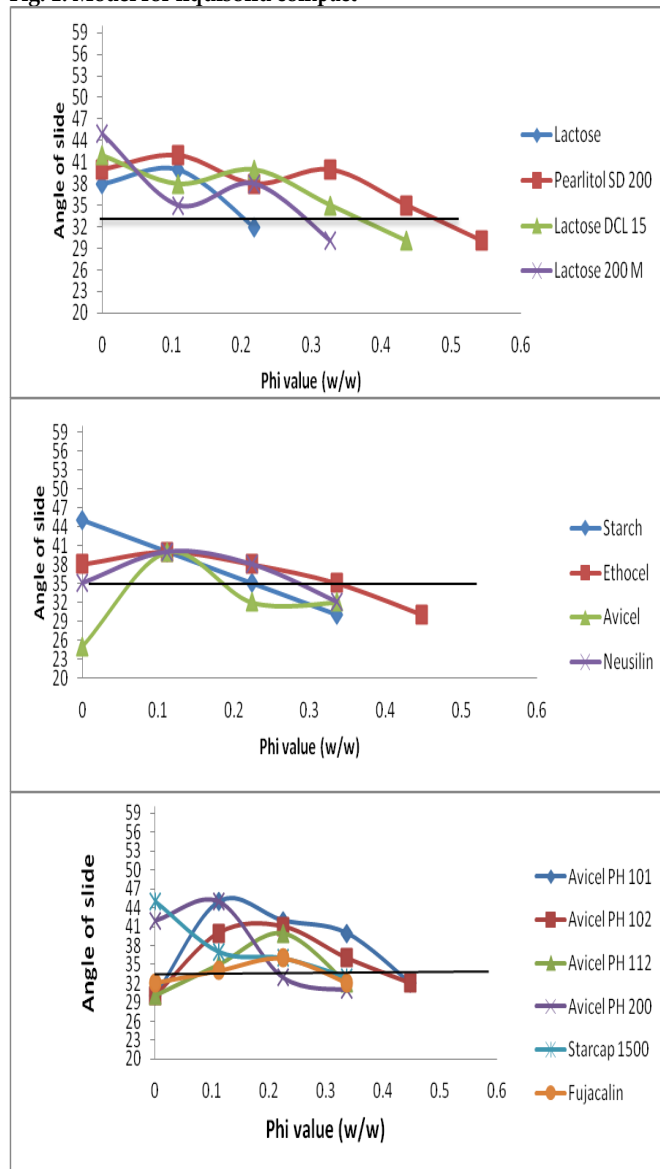**Fig. 1: Model for liquisolid compact**

Fig. 2: Determination of angle of slide for selection of carrier materials
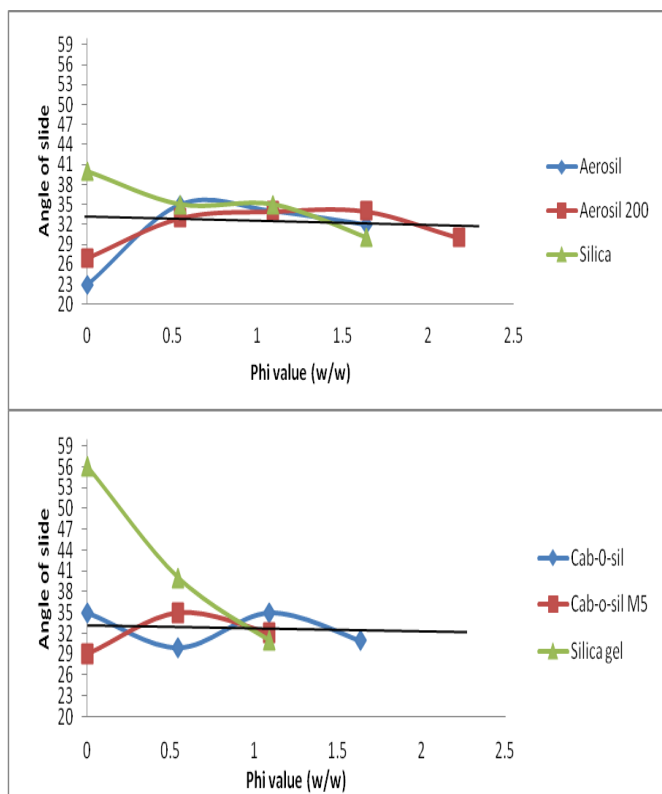
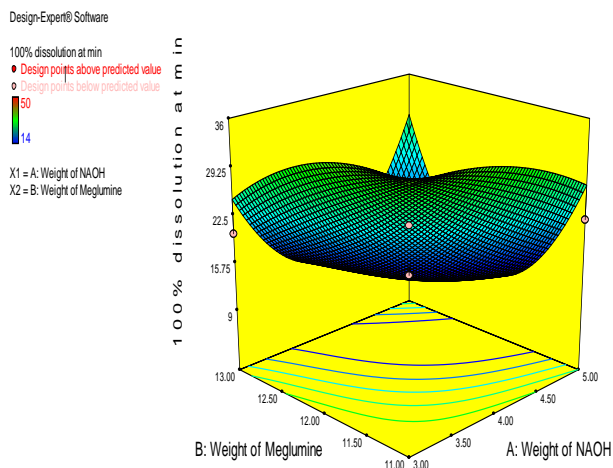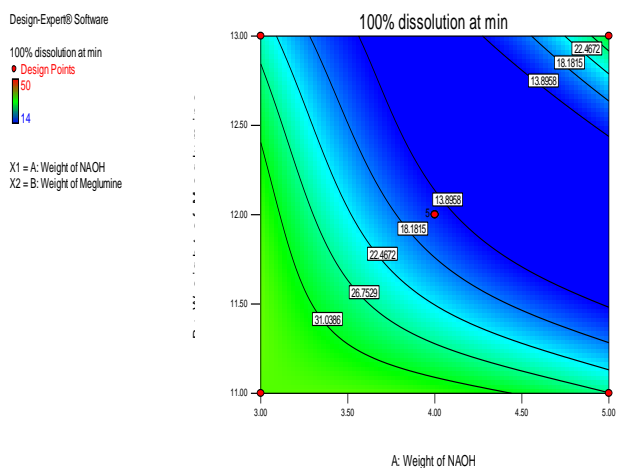**Fig 3: Determination of angle of slide for selection of coating material**

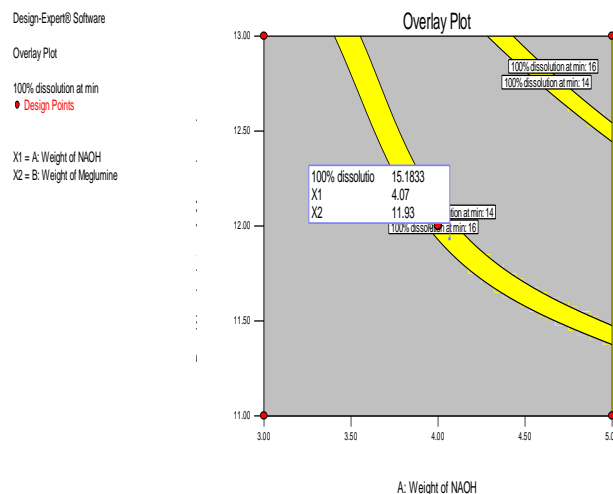**Fig. 4: Influence of formulation composition factor on 100% dissolution at time (Min)**
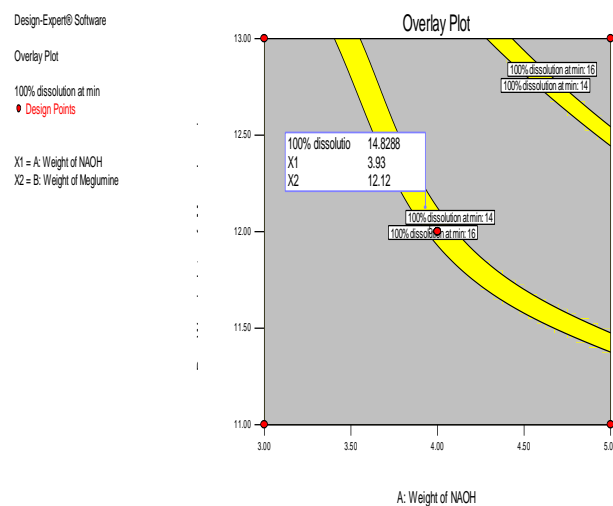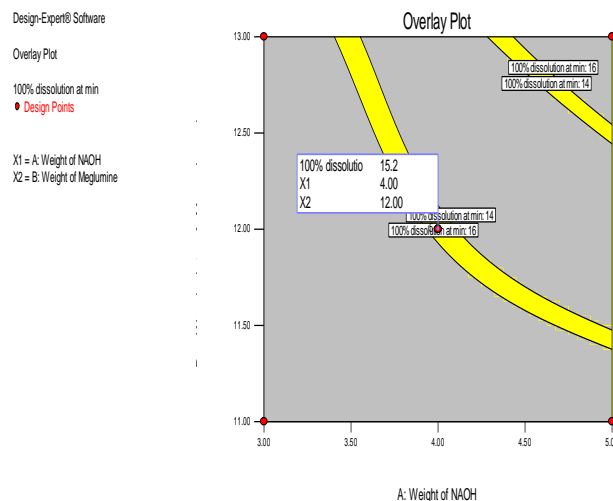

Fig. 5: Overlay plot showing combined effects of factors X_1 and X_2 on Y_1

Validation of central composite design

Validation by using Design Expert® 7.0 (Stat-Ease, Inc. Minneapolis, USA) software, an overlay plot was generated to select optimized/ check point batch with desired responses. For each of the responses of the optimized batch % error was calculated using following equation.

Relative Error (%) = $\dfrac{\text{(Predicted value} - \text{Experimental value)}}{\text{Predicted value}} \times 100$

The overlay plot of optimized batch is given in Table 8 Figure 5. The predicted batch shows significant reproducibility within the percentage deviation. From the result shows that the predictive value close to the experimental value so design is significant.

Evaluation of powder parameters

Powder flow property is crucial in handling and processing of powder material. Angle of repose, Carr's index, Hausner's ratio is parameter included in check powder flow material. The Hausner's ratio values lower than 1.2 has good flow and more than 1.2 have poor flow. Angle of repose 25° having good flow and more than 40° have poor flow.

In the case of angle of repose greater than 40° have not good flow properties, whereas minimum angle close to 25° corresponded to very good flow properties.

Table 7: Formulation of check point batches (CPB)

Batch code	Weight of NaOH (mg) [X_1]	Weight of Meglumine (mg) [X_2]
CPB$_1$	4.00	12.00
CPB$_2$	3.93	12.12
CPB$_3$	4.07	11.95

Table 8: Results of optimized batches

S. No	Responses	Experimental Values	Predicted Values	%Relative Error
CPB$_1$	100%	15	15.2	0.1
CPB$_2$	dissolution at	14	14	0.00
CPB$_3$	min	15	15	0.0

Table 9: Pre compression parameters of liquisolid compact

Batch code	Angle of repose*	Carr's index*	Hausner's ratio*
LS$_1$	29.0 ± 0.4054	10.240 ± 1.142	1.086 ± 0.221
LS$_2$	28.5 ± 0.1025	11.486 ± 1.247	1.120 ± 0.0040
LS$_3$	29.2 ± 0.025	11.452 ± 0.252	1.240 ± 0.045
LS$_4$	29.0 ± 0.012	10.051 ± 0.125	1.054 ± 0.02
LS$_5$	27.5 ± 0.01	11.251 ± 0.225	1.15 ± 0.04
LS$_6$	29.0 ± 0.02	11.045 ± 0.201	1.15 ± 0.05
LS$_7$	28.5 ± 0.02	10.012 ± 0.351	1.18 ± 0.210
LS$_8$	27.4 ± 0.02	11.451 ± 0.201	1.12 ± 0.04
LS$_9$	29.1 ± 0.03	11.351 ± 0.745	1.24 ± 0.02
LS$_{10}$	29.2 ± 0.4054	10.240 ± 0.651	1.14 ± 0.11
LS$_{11}$	28.8 ± 0.112	11.351 ± 1.104	1.12 ± 0.04
LS$_{12}$	29.0 ± 0.125	11.401 ± 0.254	1.18 ± 0.02
LS$_{13}$	29.1 ± 0.23	11.405 ± 0.02	1.16 ± 0.03

Table 10: Post compression parameters of liquisolid compact- I

Batch code	Hardness* (kg/cm²)	Friability*(%)	Thickness*(mm)
LS$_1$	4.60 ± 0.005	0.16 ± 0.07	2.50 ± 0.02
LS$_2$	4.70 ± 0.105	0.12 ± 0.01	2.51 ± 0.05
LS$_3$	4.65 ± 0.180	0.05 ± 0.12	2.52 ± 0.01
LS$_4$	4.20 ± 0.01	0.01 ± 0.04	2.53 ± 0.01
LS$_5$	4.15 ± 0.02	0.14 ± 0.01	2.51 ± 0.02
LS$_6$	4.20 ± 0.015	0.05 ± 0.02	2.50 ± 0.03
LS$_7$	4.00 ± 0.001	0.04 ± 0.45	2.51 ± 0.01
LS$_8$	4.14 ± 0.05	0.13 ± 0.12	2.51 ± 0.05
LS$_9$	4.02 ± 0.01	0.11 ± 0.01	2.50 ± 0.02
LS$_{10}$	4.08 ± 0.04	0.12 ± 0.08	2.50 ± 0.05
LS$_{11}$	4.14 ± 0.05	0.01 ± 0.08	2.51 ± 0.06
LS$_{12}$	4.02 ± 0.01	0.12 ± 0.01	2.52 ± 0.01
LS$_{13}$	4.02 ± 0.07	0.11 ± 0.04	2.52 ± 0.01

Table 9 shows that all the tested batches of liquisolid compact had a good flow property. The range was from 27.4 to 29.2 for liquisolid compact. From these entire batches LS 1 to LS 13 shows good angle of repose.

Hausner's ratio and Carr's index were calculated from the density value. In case of Carr's index below 20 giving good result. So in the all batches result shows good flow property, Hausner's ratio between 1.054 ± 0.02 to 1.24 ± 0.045 shows excellent flow ability of the powder blend.

Evaluation of Prepared Tablets

Thickness of tablets was between 2.50 to 2.53 mm. The hardness values shows in table 10 and it was in range from 4.0 to 4.5. There were no cracked, split or broken tables. Friability of tablets was found below 1% indicating a good. The disintegration time is below 15 minutes so it passes as per pharmacopoeial limit. Faster disintegration time indicate rapid release rates. Therefore, promote good content uniformity observed between liquisolid and conventional tablets in study. Uniform drug content was observed for all the formulation from 215 to 220 as described in Table 10.

Table 11: Post compression parameters of liquisolid compact- II

Batch code	Wt variation** (Average weight of 20 tablets)	Disintegration Time(Min.)*	Drug Content* (%)
LS$_1$	216 ± 0.02	2.10 ± 0.12	99.45 ± 0.56
LS$_2$	214 ± 0.01	1.45 ± 0.10	100.0 ± 0.12
LS$_3$	218 ± 0.20	1.45 ± 0.02	99.40 ± 0.45
LS$_4$	216 ± 0.01	1.10 ± 0.10	99.00 ± 0.01
LS$_5$	215 ± 0.2	1.12 ± 0.12	100.0 ± 0.13
LS$_6$	216 ± 0.20	2.10 ± 0.03	98.04 ± 0.04
LS$_7$	216 ± 0.01	1.10 ± 0.14	99.12 ± 0.05
LS$_8$	218 ± 0.02	1.30 ± 0.16	99.90 ± 0.01
LS$_9$	216 ± 0.01	1.10 ± 0.12	99.40 ± 0.12
LS$_{10}$	215 ± 0.01	2.20 ± 0.11	99.15 ± 0.05
LS$_{11}$	216 ± 0.02	1.10 ± 0.1	101.0 ± 0.11
LS$_{12}$	216 ± 0.05	1.10 ± 0.12	99.45 ± 0.04
LS$_{13}$	220 ± 0.01	1.60 ± 0.11	99.15 ± 0.12

*All the values are in mean ± SD (n=3) ** (n=20)

***In vitro* drug release**

Liquisolid tablet having higher dissolution rate than the simple conventional tablet due to solvent in this method used were ct as wetting agent for the tablet formulation. In this tablet Tween 80 used as a wetting agent.
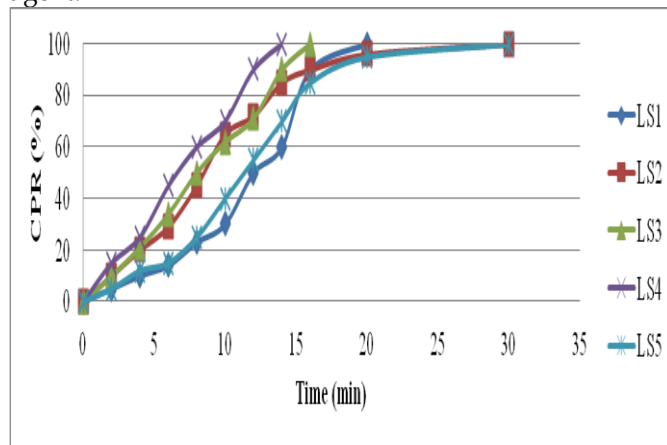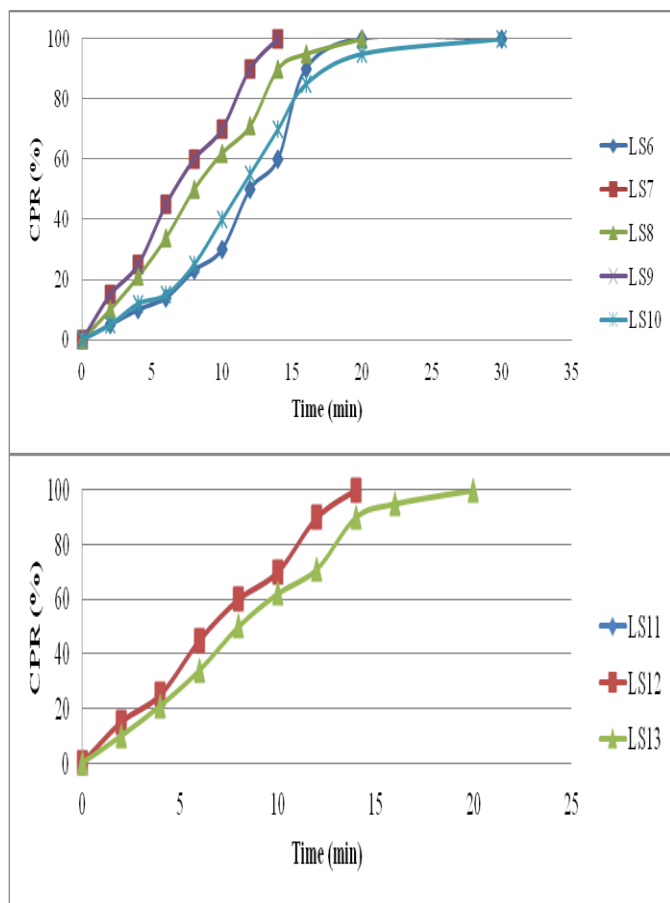
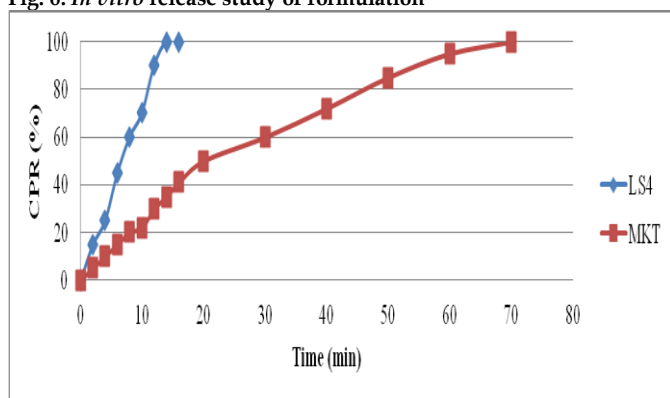**Fig. 6:** *In vitro* **release study of formulation**

Fig. 7: *In vitro* **release study of formulation**

From the above dissolution data LS 4 tablets dissolve with in 14 min as compare to LS2 dissolve with in 20 min and LS10 dissolve with in 16 min.

The dissolution profiles of the selected liquisolid tablet formulations together with the dissolution profile of conventional, directly compressed tablets (DCT) are presented in Fig. 6. It was apparent that formula LS 4 has the highest dissolution profile in both the rate and the extent of drug dissolved. The percentage of CLD dissolved from LS 1reached 100.11% after only 14 min, while the MKT had a maximum CLD content (100%) dissolved after 70 min.

The Liquisolid technique is a promising alternative for improvement of dissolution property of water-insoluble drugs, such as CLD. The higher dissolution rate showed by Liquisolid compacts may enhance oral bioavailability due to the increased wetting properties

and surface of drug available for dissolution. The Liquisolid compact of CLD made in Tween 80 showed better dissolution rate than marketed tablet based upon solubility.

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Int. J. Pharm. Sci. Drug Res. July-August, 2017, Vol 9, Issue 4 (160-168)

168