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FORMULATION AND IN-VITRO EVALUATION OF LACIDIPINE ORAL DISINTEGRATING TABLETS: ENHANCEMENT OF SOLUBILITY AND DISSOLUTION RATE

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ABSTRACT

The aim of present study was to develop the Lacidipine oral disintegrating tablets (LCDP ODTs), thereby enhancing the solubility and dissolution rate. Solubility was enhanced by solid dispersion technology using hydrophilic carriers like Hydroxy Propyl Methyl Cellulose Acetate Succinate (HPMCAS), β-Cyclodextrin (BCD), Polyethylene Glycol 6000 (PEG 6000) and it was confirmed by phase solubility studies. LCDP ODTs were prepared by using super disintegrants like Croscarmellose Sodium (CCS), Crospovidone (CP), Sodium Starch glycolate (SSG). Evaluation parameters were complied with the official limits. From the in-vitro dissolution studies, it was observed that the formulation F9 consists of CP showed maximum drug release within short period of time.

Key words: Lacidipine, Solid dispersions, Oral disintegrating tablets, Phase solubility studies, Solubility enhancement.

INTRODUCTION

The oral route of drug administration is the most common and preferred method of delivery due to convenience and ease of ingestion (Venkateswarlu K *et al*, 2016). From patient's perspective, swallowing a dosage form is a comfortable and a familiar means of taking medication (Venkateswarlu and Shanthi, 2012). LCDP belongs to the group of dihydro pyridines and acts by blocking the calcium channels. It is chemically, diethyl (E)-4-{2-[(*tert*- butoxyl carbonyl) vinyl] phenyl}-1, 4-dihydro-2, 6-dimethyl pyridine -3, 5-dicarboxylate. It is freely soluble in acetone but not in water. The solubility and dissolution rate of LCDP might be enhanced by SD technology. Numerous solid dispersion systems have been demonstrated in the pharmaceutical literature to improve the dissolution properties of poorly water-soluble drugs (Alfred and Louis, 2001). Other methods, such as salt formation, complexation, solubilisation of drugs in solvent(s) and particle size reduction have also been utilized to improve the dissolution properties of poorly water-soluble drugs; however, there are substantial limitations with each of these techniques. On the other hand, formulation of drugs as solid dispersions offers a variety of processing and the excipient options that allow for flexibility when formulating oral delivery systems for poorly water-soluble drugs (Hiton and Summers, 1986). In the present study, LCDP ODTs are developed and LCDP solubility and dissolution rates are enhanced by SD technology. Hydrophilic carriers used are PEG 6000, BCD, HPMCAS and superdisintegrants used are CP, CCS and SSG.

MATERIALS AND METHODS

Materials

Lacidipine (LCDP) obtained from Dr. Reddy's Laboratories, Hyderabad, India and PEG 6000, HPMCAS, CP, CCS, SSG, BCD, PEG 6000, Mannitol, MCC pH 102, SS, Talc, SSF were purchased from SD Fine Chem Ltd., Mumbai, India.

Phase Solubility Studies

Phase solubility studies were the preliminary requirements for evaluation of affinity between the ligand or carrier and drug. These were carried out according to the method reported by Higuchi and Connors (Higuchi and Connors, 1965). Phase diagram was constructed by plotting the molar concentration of dissolved LCDP solute on Y-axis against the concentration of complexing agent or carrier on X-axis. Two general types of phase solubility profiles were generated. Type A: Where soluble complexes were formed, Type B: Where complexes of limited solubility were formed. Depending on the nature of complexes formed in type- A diagrams, the diagram can be linear (A_L) or show curvature in a positive (A_P) or negative (A_N).

Phase solubility studies of LCDP with BCD, PEG 6000 and HPMCAS

Different concentrations of BCD, PEG6000 and HPMCAS solutions (5, 10, 15, 20, and 25% w/v) were prepared separately by using distilled water and an excess amount of LCDP was added to the above solutions of ligand or carrier. Then these solutions were kept for shaking on orbital shaker for 72 h followed by centrifuged and the supernatant was suitably diluted for estimating the LCDP concentration using UV-Visible spectrophotometer (Lab India 1700 UV-Visible spectrophotometer, India) at 240 nm.

Gibbs free energy

The values of Gibbs free energy of transfer (ΔG°_{tr}) of LCDP from plain distilled water to aqueous solution of the carriers were calculated according to the following relationship. ΔG°_{tr} = -2.303RT Log (S_o/S_s). Where, S_0/S_S is the ratio of molar solubility of the LCDP in aqueous solution of carrier to that of same medium without carrier.

Apparent stability constant

The values of apparent stability constant (K_s) between drug-carrier combinations were calculated from the phase solubility diagrams, using the following equation. K_s = slope/ intercept (1-Slope).

Drug excipients compatibility studies

The pure drug LCDP and its physical mixtures subjected to IR spectral studies using FTIR spectrophotometer (Model-IR Affinity-1, Shimadzu, Japan) in the wave length region between 4000cm^{-1} to 400cm^{-1}. The KBr pellet method was used and the spectra obtained for pure drug and the physical mixture were compared.

Preparation of Solid Dispersions (SDs)

SDs of LCDP with the carriers like PEG 6000, BCD, HPMCAS were prepared separately by employing the methods like fusion, complexation and solvent evaporation methods respectively in drug to carrier ratios of 1:1, 1:2, 1:3 (Table 1) (Ladan AN *et al*, 2012).

Preparation of LCDP SDs with PEG 6000 by Fusion method

LCDP with water soluble carrier PEG 6000 SDs of different ratios (1:1, 1:2, 1:3) were prepared by fusion method. The fixed amount of PEG 6000 was weighed accurately, melted in a china dish and added fixed amount of LCDP with thorough mixing for atleast 1-2 min followed by cooling. The dried product was then made to undergo pulverization by passing through the sieve no.60 and stored in a desiccator for further studies.

Preparation of LCDP SDs with BCD by Complexation method

LCDP and BCD in various ratios of 1:1, 1:2 and 1:3 were mixed using mortar and pestle. The mixture was passed through the sieve no. 60 and stored in a desiccator for further studies.

Preparation of LCDP SDs with HPMCAS by Solvent evaporation method

LCDP SDs were prepared by dissolving LCDP and HPMCAS in various ratios (1:1, 1:2 and 1:3) in methanol. After complete dissolution of drug and HPMCAS in methanol, the solution was evaporated at room temperature. Subsequently, the solid mass was ground and passed through sieve no.60 and kept in desiccator for further use.

Table 1
Composition of LCDP SDs

SDs Composition	Method	Drug-Polymer ratio	Formulation code
LCDP : PEG 6000	Fusion method	1:1	SDF
		1:2	SDF
		1:3	SDF
LCDP : BCD	Complexation method	1:1	SDC
		1:2	SDC
		1:3	SDC
LCDP : HPMCAS	Solvent Evaporation method	1:1	SDE
		1:2	SDE
		1:3	SDE

Preparation of LCDP Orodispersible tablets (ODTs) by direct compression method

ODTs of LCDP were prepared by direct compression method. SDs of LCDP:HPMCAS (1:2) ratio equivalent to 6 mg of LCDP was taken and various superdisintegrants like CP, CCS, SSG were taken in specified amount. All the excipients were blended with SDs containing LCDP in a dried mortar and pestle for suitable time period. Prior to the compression, the SSF was added and mixed gently for 2-3 min. The tablets were punched with BB tooling using RIMEK rotary tablet punching machine of 5 mm diameter (Table 2).

Table 2
Composition of LCDP ODTs with HPMCAS (1:2)

Ingredients	Formulations (Quantity in mg/ 1 tablet)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
LCDP:HPMCAS (1:2)	18	18	18	18	18	18	18	18	18
MCC PH 102	50	48	46	50	48	46	50	48	46
Mannitol	20	20	20	20	20	20	20	20	20
SSG	2	4	6	-	-	-	-	-	-
CCS	-	-	-	2	4	6	-	-	-
CP	-	-	-	-	-	-	2	4	6
SS	5	5	5	5	5	5	5	5	5
SSF	3	3	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2	2	2
Total weight (mg)	100	100	100	100	100	100	100	100	100

Determination of drug content of LCDP SDs

SDs of LCDP (equivalent to 6 mg of LCDP) containing BCD, PEG 6000 and HPMCAS were taken in a conical flask containing 25 ml of methanol and kept on a rotary shaker for 1 h. Then the resulting samples were centrifuged for 15 min and supernatant was filtered, suitably diluted and analysed by UV-Visible spectrophotometer at 240 nm (Thirumalesh SB *et al*, 2016a).

In-vitro dissolution study

The dissolution was carried out for pure drug LCDP and experimental formulations. Freshly prepared pH 6.8 phosphate buffer of 900 ml was placed in each dissolution vessel of dissolution test apparatus (USP, II paddle method). The temperature of the dissolution medium was maintained at 37±0.5^{o}C and the paddle was rotated at 50 rpm. At the specific intervals (0, 10, 20, 30, 40, 50, 60 min), 5 ml of sample was withdrawn and the same volume was replaced by fresh media. The withdrawn samples were filtered, diluted and estimated spectrophotometrically at 240 nm, thereby the cumulative percent drug release at each interval was calculated.

Precompression studies
The precompression parameters like bulk and tapped density, angle of repose, Hausner's ratio and Carr's index were carried out for powder mixture according to the standard procedures (Thirumalesh SB *et al*, 2016b).

Post compression studies
Post-compression parameters like friability, hardness, thickness, weight variation, content uniformity, disintegration tests were evaluated for the prepared tablets according to the standard procedures (Thirumalesh *et al*, 2016c).

Wetting time
Five circular tissue papers were placed in a petridish with a 10 cm diameter and this petridish contains 10 ml of water soluble dye i.e. eosin which helps to know the complete wetting of tablet surface. A tablet was carefully placed on the surface of tissue paper at room temperature and the time required for water to reach the upper surface as well as complete wetting of tablet was noted as the wetting time using stop watch (Tejvir K *et al*, 2011).

In-vitro dissolution test
The dissolution was carried out for pure drug, SDs and different experimental formulations. Freshly prepared pH 6.8 phosphate buffer of 900 ml was placed in each dissolution vessels of Electro Lab TDT-06N USP dissolution apparatus type-II (paddle method). The tablets were placed in the dissolution medium. The temperature of the dissolution medium was maintained at 37 ± 0.5^0C and the paddle was rotated at 50 rpm. 5 ml samples were withdrawn and the sample volume was immediately replaced with the same volume of fresh media as when a sample was taken. The samples withdrawn were filtered, diluted and estimated spectrophotometrically at 240 nm.

Stability studies
The optimized formulation was subjected to stability studies at 40°C ± 2°C/75%±5% RH in humidity chamber for 3 months. At the end of 3 months, all preparations were analyzed for any physical changes such as drug content and percentage drug release and the results were analyzed (Venkateswarlu K *et al*, 2013).

RESULTS AND DISCUSSION

In the present study, LCDP ODTs were prepared by using polymers (carriers) like PEG 6000, BCD, HPMCAS, superdisintegrants like CP, CCS, SSG, diluents like Mannitol, MCC PH 102, sweetener SS, glidant Talc and lubricant SSF.

Compatability study
On comparison of FTIR spectra of pure drug with spectra of its physical mixtures confirmed that there was no appearance of new peaks and shifting of already existed peaks and it indicates the absence of drug excipients incompatibility (Table 3-5).

Table 3
Interpretation of IR spectra of Lacidipine API

Drug	Wave number, cm^{-1}		Functional group
	Range	Observed	
	3700-3500	3728	O-H (stretch)
	3500-3300	3391	-N-H 2^0 amide (stretch)
LCDP	3500-3300	3349	-N-H 2^0 amide (stretch)
	3550-3200	3278	O-H (stretch)
	2775-2720	2551	-C-H (stretch) aldehydes

Table 4
Interpretation of IR spectra of best solid dispersion (SDE 1:2)

Sample	Wave number, cm^{-1}		Functional group
	Range	Observed	
Solid dispersion (1:2)	3700-3500	3728	O-H alcohols or phenols (stretch)
	3650-3580	3584	O-H(stretch)
	3500-3200	3477	O-H (stretch)
	~3300	3337	-C =C-H (stretch)
	2960-2850	2889	-C-H alkanes (stretch)

Table 5
Interpretation of IR spectra of best formulation (F9)

Sample	Wave number, cm^{-1}		Functional group
	Range	Observed	
Formulation (F9)	~3300	3386	-C =C-H (stretch)
	2960-2850	2830	-C-H (stretch)
	~1788	1782	-C=O cyclobutanone (stretch)
	1610-1550	1550	-C=O carboxylate anion (stretch)
	1550-1510	1543	-N-H 2^0 amide

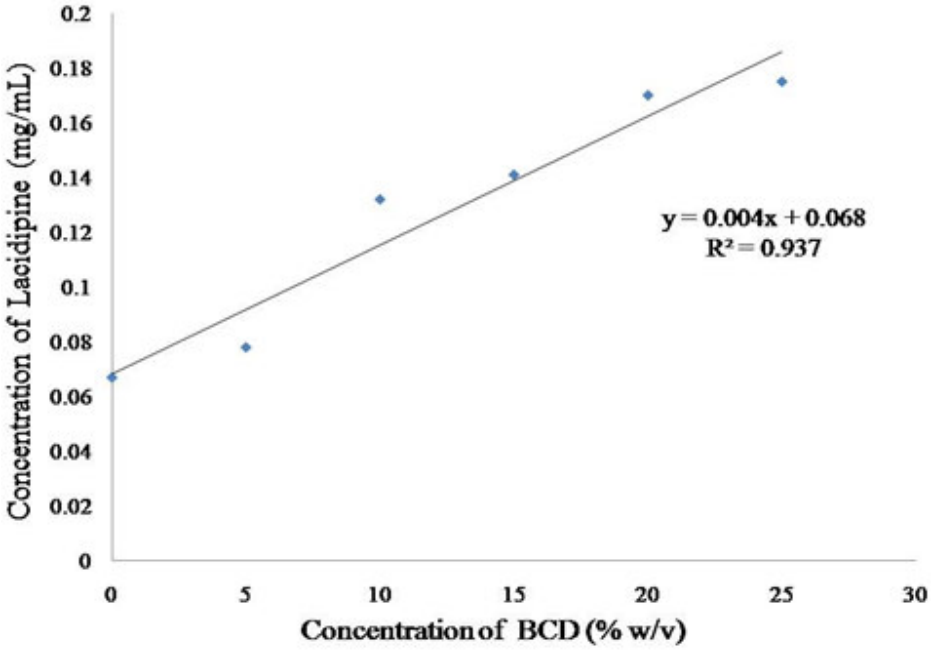
Phase solubility study of LCDP with BCD

The phase solubility of LCDP with BCD was carried out by taking varied concentrations of BCD. The solubility of LCDP was increased with increase in the concentration of BCD. The Gibbs free energy for the resulting solution decreases as the concentration of the carrier increases and it indicates increase in the solubility of the drug. The stability constant was calculated as to indicate the stability of the complex formed between the drug and carrier. The stability constant 67.45 value indicates the weak complexation of drug and carrier. The phase solubility curve indicates the linear an increase in solubility of LCDP (Table 6 & Figure1).

Table 6
Phase solubility study of LCDP with different concentrations of BCD

Concentration of BCD (% w/v)	Concentration of LCDP (mg/mL)	ΔG°tr (J/mole)
0	0.067	-
5	0.078	-0.44
10	0.132	-1.67
15	0.141	-1.64
20	0.170	-1.79
25	0.175	-2.36
Stability Constant (ml/g)	67.45	-
R^2	0.937	-
Slope	0.004	-
Type of curve	A_L	

Figure 1
Phase solubility study of LCDP using BCD



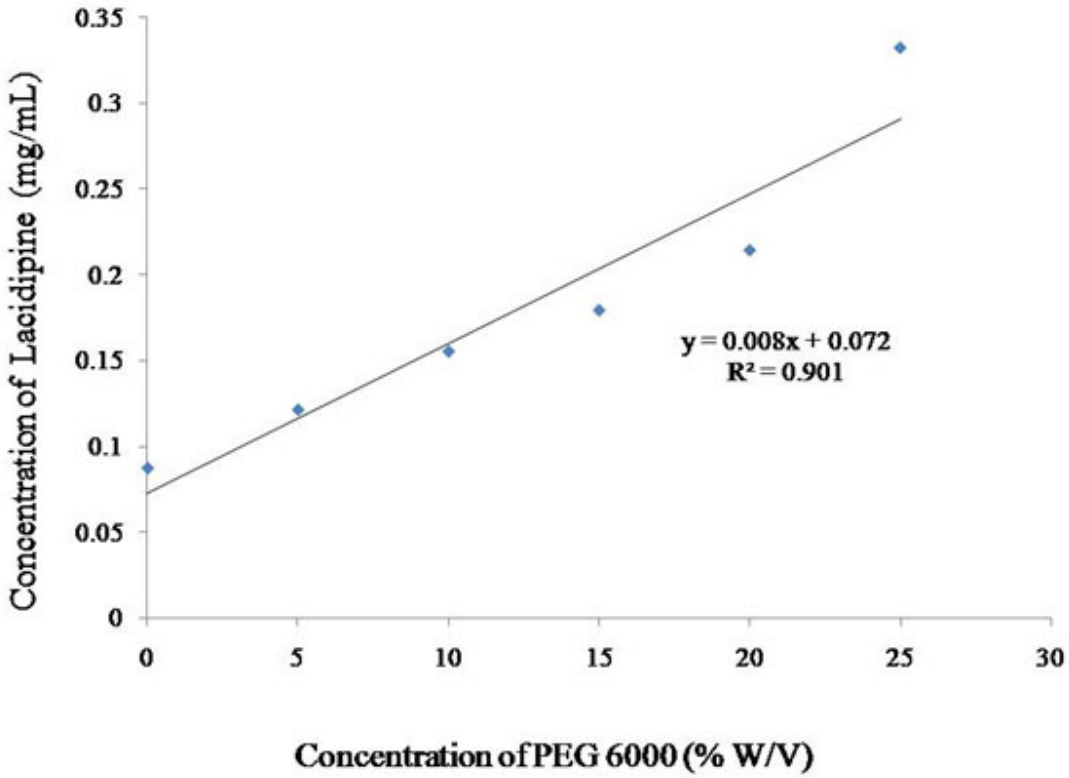
Phase solubility study of LCDP with PEG6000

The phase solubility of LCDP with PEG6000 was carried out by taking varied concentrations of PEG6000. The solubility of LCDP was increased with increase in the concentrations of PEG6000. The Gibbs free energy for the resulting solution decreases as the concentration of carrier increases. The decrease in Gibbs free energy indicates increase in the solubility of the drug. The stability constant 115.8 (optimum stability constant) value indicates the stable complexation of drug and carrier (Table 7 & Figure 2).

Table 7
Phase solubility study of LCDP using different concentrations of PEG6000

Concentration of PEG 6000 (% w/v)	Concentration of LCDP (mg/mL)	ΔG°tr (J/mole)
0	0.087	-
5	0.121	-0.84
10	0.155	-1.53
15	0.179	-2.08
20	0.214	-2.54
25	0.332	-3.59
Stability Constant (ml/g)	115.800	-
R^2	0.901	-
Slope	0.008	-
Type of curve	A_L	

Figure 2
Phase solubility curve of LCDP with PEG6000



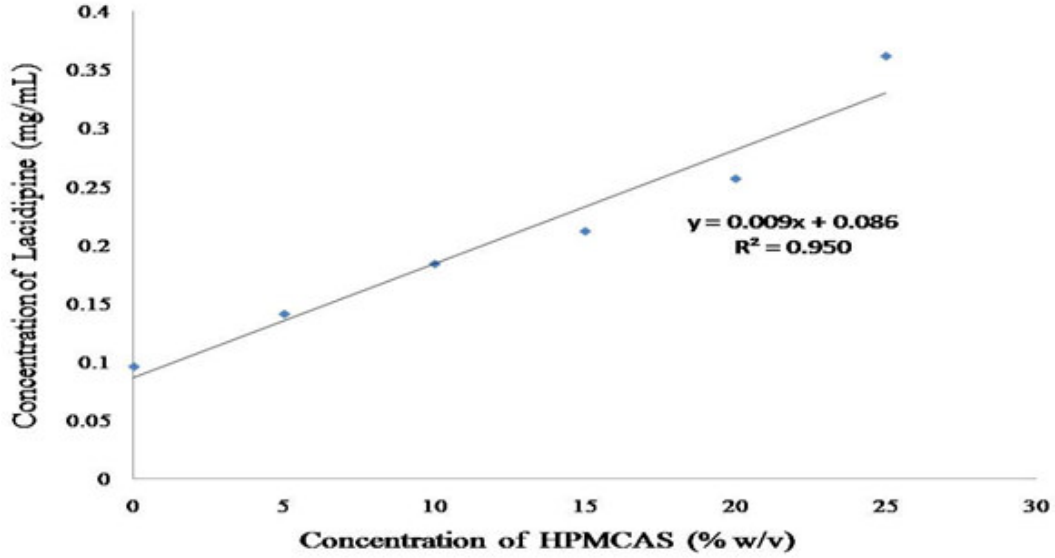
Phase solubility study of LCDP with HPMCAS

The phase solubility of LCDP with HPMCAS was carried out by taking varied concentrations of HPMCAS. The solubility of LCDP was increased with increase in the concentrations of HPMCAS. The Gibbs free energy for the resulting solution decreases as the concentration of carrier increases. The decrease in Gibbs free energy indicates increase in the solubility of the drug. The stability constant 144.36 (optimum stability constant) value indicates the stable complexation of drug and carrier (Table 8 & Figure 3).

Table 8
Phase solubility study of LCDP using different concentrations of HPMCAS

Concentration of HPMCAS (% w/v)	Concentration of LCDP (mg/ml)	ΔG°tr (J/mole)
0	0.096	-
5	0.141	-0.91
10	0.184	-1.60
15	0.212	-2.15
20	0.257	-2.61
25	0.362	-3.74
Stability Constant (ml/g)	144.36	-
R^2	0.9506	-
Slope	0.0097	-
Type of curve	A_L	

Figure 3
Phase solubility curve of LCDP with HPMCAS



Drug content of LCDP SDs

Drug content from SDs of BCD were found to be 82.16±0.78 to 85.90±0.98%, PEG 6000 were found to be 84.26±0.18 to 90.23±0.51% and HPMCAS were found to be 93.52±0.63 to 98.34±0.16%. It was observed from the results that the LCDP SDs with HPMCAS had shown more % drug content of 98.34% (Table 9). From the results of % drug content and % drug release, the SDE 1:2 ratio was selected as an optimised solid dispersion for the formulation of Lacidipine ODTs.

Table 9
Drug content of LCDP SDs with BCD, PEG 6000 and HPMCAS

Formulations	Drug content (%) (mean ± SD, n=3)
SDC (1:1)	82.16±0.78
SDC (1:2)	83.16±0.71
SDC (1:3)	85.90±0.98
SDF (1:1)	84.26±0.18
SDF (1:2)	90.23±0.51
SDF (1:3)	87.47±0.86
SDE (1:1)	93.52±0.63
SDE (1:2)	98.34±0.16
SDE (1:3)	97.21±0.18

***In-vitro* drug release of LCDP SDs**

The dissolution study was carried out for the prepared LCDP SDs and the results were compared with pure drug (LCDP) (Table 10). At the end of 60 min time interval, pure drug showed a maximum drug release of 34.1% whereas SDC of 1:1, 1:2, 1:3 showed 63.2%, 73.7% and 84.6% respectively. In the case of SDF of 1:1, 1:2, 1:3 showed 71.0±0.28%, 82.6±0.64% and 88.7±0.36% respectively and SDE of 1:1, 1:2, 1:3 showed 83.7±0.59, 92.6±0.08 and 90.7±0.59% respectively, SDC of 1:1, 1:2, 1:3 showed 63.2±0.28%, 73.7±0.64% and 84.6±0.5% respectively. It was evident from the results that the solubility of LCDP in SDs showed more solubility when compared to the pure drug. From the results of % drug content and % drug release, the SDE in 1:2 ratio was selected as an optimised SD for the formulation of LCDP ODTs.

Table 10
In-vitro drug release data of SDC, SDF, SDE

Time (min)	% Drug Release (mean ± SD, n=3)									
	LCDP	**SDF (1:1)**	**SDF (1:2)**	**SDF (1:3)**	**SDC (1:1)**	**SDC (1:2)**	**SDC (1:3)**	**SDE (1:1)**	**SDE (1:2)**	**SDE (1:3)**
0	0	0	0	0	0	0	0	0	0	0
10	4.1± 0.96	12.4±0.26	16.7±0.1	19.3±0.9	9.3±0.46	14.8±0.06	17.4±0.9	16.9±0.41	20.9±0.83	18.6±0.99
20	13.9± 0.32	23.2±0.34	31.6±0.74	32.8±0.26	18.5±0.97	20.9±0.64	28.0±0.23	29.5±0.44	34.6±0.01	32.8±0.26
30	17.6±0.69	39.7±0.57	43.6±0.82	44.5±0.5	34.6±0.97	39.1±0.82	43.9±0.7	40.3±0.71	52.6±0.25	44.5±0.15
40	21.8±0.33	54.1±0.82	57.4±0.23	62.4±0.96	50.6±0.34	52.2±0.21	56.4±0.58	51.6±0.69	66.7±0.58	55.2±0.96
50	29.4±0.86	59.3±0.52	65.1±0.74	71.5±0.16	56.7±0.52	61.3±0.74	64.9±0.16	65.5±0.23	79.2±0.91	71.5±0.12
60	34.1±0.51	71.0±0.28	82.6±0.64	88.7±0.36	63.2±0.28	73.7±0.64	84.6±0.5	83.7±0.59	92.6±0.08	90.7±0.59

Precompression studies

Bulk density and tapped density were ranged from 0410 to .718 and 0.462 to 0.873 respectively. Hauser's ratio was found to be less than 1.31 indicates that the powder blend possess good flow properties for compression. Carr's index was found to be 11.62 to 16.62, the results were indicated that the LCDP blends had shown good to fair flow properties for compression. Angle of repose was carried out and it was found to be 31^0 to 35^0, indicates that the powder blends possess good flow ability (Table 11).

Table 11
Precompression studies

Formulation	Bulk density (gm/ml)	Tapped density (gm/ml)	Hauser's ratio	Carr's index (%)	Angle of repose (º)
F1	0.541±0.23	0.691±0.21	1.236±0.27	16.62±0.85	34±0.41
F2	0.484±0.28	0.615±0.36	1.247±0.87	14.30±0.52	33±0.27
F3	0.710±0.87	0.873±0.71	1.251±0.34	12.71±0.51	31±0.84
F4	0.712±0.41	0.870±0.24	1.206±0.81	15.12±0.24	32±0.67
F5	0.718±0.54	0.871±0.67	1.223±0.37	14.51±0.32	30±0.31
F6	0.410±0.47	0.483±0.24	1.178±0.34	15.13±0.84	32±0.26
F7	0.420±0.35	0.462±0.37	1.131±0.56	15.01±0.24	35±0.67
F8	0.541±0.80	0.691±0.62	1.276±0.24	11.62±0.1	34±0.69
F9	0.450±0.21	0.585±0.81	1.310±0.83	13.07±0.7	31±0.5

Results were expressed in mean±SD (n=3)

Post compression studies

All the prepared tablets of Lacidipine were evaluated for post compression parameters. The weight of all the tablets was found to be uniform with low values of standard deviation and within the prescribed IP limits of ±10%. The hardness of the tablet formulations was found to be in the range of 4 to 5 kg/cm^2. The friability values were found to be in the range of 0.50 to 0.72 %. All the formulations showed less than 1% friability ensuring that the tablets were mechanically stable. The low values of standard deviation indicate uniform drug content within the tablets. The percent drug content of all the tablets was found to be in the range of 97.3 to 101.1% (which was within the acceptable limits of ±5%). The results of *in-vitro* disintegration time of all the tablets were found to be within the prescribed limits and satisfy the criteria of oral dispersible tablets. Among all the formulations, crospovidone formulations showed the lower disintegration time. The results of wetting time of all the formulations were found to be satisfactory and those have to an ideally be less than 1 min. This rapid disintegration needed to assist in swallowing and enhancing the bioavailability in buccal cavity (Elkhodairy KA *et al*, 2014)

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Table 12
Post compression studies

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%)	Thickness	Drug Content (%)	Disintegration time (sec)	Wetting time (sec)
F1	96±0.15	4.4±0.24	0.72±0.36	2.6±0.84	99.28±0.32	73±0.46	63±0.64
F2	92±0.23	4.3±0.36	0.68±0.83	2.6±0.63	97.16±0.57	67±0.91	54±0.54
F3	93±0.31	4.8±0.56	0.69±0.61	2.7±0.33	101.1±0.46	62±0.72	48±0.35
F4	98±0.84	4.6±0.85	0.66±0.25	2.5±0.41	97.68±0.81	51±0.38	35±0.67
F5	94±0.64	4.7±0.22	0.68±0.51	2.6±0.3	99.41±0.34	42±0.63	28±0.61
F6	97±0.86	4.3±0.36	0.65±0.35	2.6±0.44	98.19±0.65	36±0.45	22±0.37
F7	96±0.44	4.0±0.38	0.73±0.41	2.6±0.7	102.6±0.47	25±0.24	19±0.68
F8	102±0.35	4.2±0.72	0.88±0.35	2.5±0.2	99.5±0.38	20±0.37	15±0.64
F9	98±0.82	4.5±0.91	0.70±0.66	2.5±0.7	97.3±0.25	18±0.81	11±0.45

***In-vitro* drug release studies**

All the prepared LCDP ODTs were subjected to *in-vitro* release studies using paddle dissolution apparatus in pH 6.8 phosphate buffer. Formulations were prepared with different superdisintegrants like SSG (F1-F3), CCS (F4-F6) and CP (F7-F9). Formulations with SSG showed the drug release ranged from 93.48% to 95.51%, formulations with CCS showed 96.01% to 97.35% and formulations with CP showed 97.37% to 98.56%. Amongst all the formulations prepared with different superdisintegrants, formulation with CP (F9) showed maximum drug release within short period of time (15 min), which might be due to the superdisintegrant and solubility enhancing property of CP (Raymond CR *et al*, 2009).

Table 13
In-vitro drug release data all formulations

Time (min)	% Drug Release (mean ± SD, n=3)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	36.35±0.74	40.23±0.54	48.21±0.47	38.04±0.87	40.21±0.81	46.84±0.25	45.24±0.54	49.25±0.75	53.21±0.81
10	68.25±0.31	73.24±0.24	76.56±0.21	72.65±0.54	78.56±0.62	83.57±0.74	62.47±0.24	78.14±0.65	86.65±0.46
15	79.58±0.25	81.42±0.68	85.54±0.22	76.32±0.36	87.21±0.95	89.44±0.23	91.55±0.45	94.34±0.47	98.56±0.73
20	85.32±0.24	87.42±0.94	89.24±0.36	89.45±0.65	91.56±0.67	93.98±0.74	94.67±0.68	97.58±0.24	
25	89.89±0.64	92.64±0.74	95.51±0.14	92.75±0.46	95.43±0.37	96.74±065	96.35±0.74		
30	93.48±0.78	94.21±0.54		96.01±0.27	96.67±0.71	97.35±0.98	97.37±0.77		

Stability studies

Parameters like % drug release and drug content at the condition of 40^0C/ 75% RH were determined for F9 and it was observed that there was no significant change occurs in above parameters.

Table 14
Results of stability studies of optimized formulation F9

Parameters	Initial	1 month	2 month	3 month
40^0C/75% RH (% Release)	98.56	98.52	97.79	96.56
40^0C/75% RH (Drug content)	97.3	96.87	95.71	95.14

CONCLUSION

From all the above results, it was observed that the SDs of LCDP:HPMCAS (1:2) ratio prepared by solvent evaporation method was found to be optimum in terms of solubility and dissolution rate. Hence, we concluded that solubility of LCDP can be enhanced using this carrier ratio. Hence, the optimized solid dispersion further formulated as ODTs. The formulation F9 containing 6% of crospovidone tablets disintegrate within seconds; there by enhance absorption leading to increased bioavailability. Thus the present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and increased patient compliance.

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