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DEVELOPMENT AND EVALUATION OF NIMODIPINE FAST DISSOLVING TABLETS PREPARED WITH A COMPLEX BY DIRECT COMPRESSION METHOD

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ABSTRACT

Nimodipine is an antihypertensive, calcium channel blocker, vasodilator agent and used in the treatment of various cardiovascular disorders such as angina pectoris, cardiac arrhythmia and hypertension. Oral bioavailability of Nimodipine is around 13% and having half life 9 hrs. In present research work an attempt has been made to prepare fast dissolving tablets of Nimodipine by direct compression technique with β-cyclodextrin complexes using various superdisintegrants. The powder blends were subjected for pre-compressional parameters. The prepared tablets were evaluated for post-compressional parameters. The prepared tablets were characterized by DSC and FTIR Studies. No chemical interaction between drug and excipients was confirmed by DSC and IR studies. The values of pre-compression parameters evaluated were within prescribed limits and indicated good free flowing property. All the post-compressional parameter are evaluated were prescribed limits and results were within IP acceptable limits. The tablets were evaluated for the in-vitro disintegration time and it was observed that the time for all the formulations varied from 19.24 to 48.29 sec. The promising formulations CCP_4, CCC_4 and CSS_1 shows the 90 % of drug released within 5-8 min. Among all the formulation CCP_4 (15 % crospovidone) were found to be best and showed a disintegration time of 19.24 sec, 50 % of drug released in 0.96 min, and 90 % of drug released in 4.78 min. The stability study was conducted as per the ICH guidelines and the formulations were found to be stable, with insignificant changes in hardness, drug content and disintegration time. These results revealed that fast dissolving tablets of the poorly soluble drug, Nimodipine, showing enhanced dissolution and, hence, better patient compliance.

Key words: Fast dissolving tablets, Nimodipine, sodium starch glycolate, croscarmellose sodium, crospovidone, β-cyclodextrin.

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INTRODUCTION

Nimodipine is chemically described as 3-(2-methoxyethel)5-propane-2-yl2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate, used in the treatment of various cardio vascular disorders such as angina pectoris, cardiac arrhythmia and hypertension. Nimodipine is rapidly absorb from GIT following oral administration, but undergoes extensive first-pass metabolism in the liver. The oral bioavailability is reported to be about 9 hrs, Nimodipine is practically insoluble in water but highly permeable drug. The rate-limiting step in its absorption is its dissolution rate in gastro intestinal fluids[1, 2]. The rate of dissolution can be increased by increasing the surface area of available drug by various methods (micronization, complexation and solid dispersion)[3]. The dissolution of a drug also influenced by disintegration time of tablets. Faster the disintegration of tablets delivers a fine suspension of drug particle resulting in the higher surface area and faster dissolution.

Of all the orally administered dosage forms, tablet is most preferred because of ease of administration, compactness and flexibility in manufacturing. Because of changes in various physiological functions associated with aging including difficulty in swallowing, administration of intact tablet may lead to poor patient compliance and ineffective therapy. The paediatric and geriatrics patients are of particular concern. To overcome this, dispersible tablets[4] and fast-disintegrating tablets[5] have been developed. Most commonly used methods to prepare these tablets are; freeze-drying/Lyophilization[6], tablet molding[7] and direct-compression methods[8]. Lyophilized tablets show a very porous structure, which causes quick penetration of saliva into the pores when placed in oral cavity [6, 9]. 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 drug[4]. Moulded tablets dissolve completely and rapidly. However, lack of strength and taste masking are of great concern[7, 10]. Main advantages of direct compression are low manufacturing cost and high mechanical integrity of the tablets[8, 11]. 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, crospovidone and sodium starch glycolate. The effect of functionality differences of the superdisintegrants on tablet disintegration has been studied[12]. Main advantages of direct compression are low manufacturing cost and high mechanical integrity of the tablets. Therefore, direct compression appears to be a better option for manufacturing of tablets. The fast

disintegrating tablets are prepared by direct compression method, in general based on the action established by super disintegrants such as croscarmellose sodium, crospovidone and sodium starch glycolate. The effect of functionality differences of the superdisintegrants on tablet disintegration has been studied [13, 14].

Hence, in the present work, Nimodipine fast dissolving tablets were prepared by Nimodipine with a β-cyclodextrin complex using different superdisintegrants like Sodium starch glycolate (SSG), croscarmellose sodium (CCS) and crospovidone (CP). A total number of 12 formulations were prepared with the complex by the direct compression technique**.** Effects of superdisintegrants on wetting time, disintegrating time, drug content, *in-vitro* release, and stability studies parameters have been studied.

MATERIALS AND METHODS

Nimodipine was procured from Aarti Scientific Company Old Puna Naka, Murarji Peth, Solapur (MS). CCS, SSG and CP were procured as a gift sample from Maruti Chem., Ahmedabad. Mannitol, MCC, aspartame, talc and magnesium stearate purchased from S.D. Fine chem., Mumbai. All other materials were of analytical reagent grade.

Preparation of complex of Nimodipine with β-cyclodextrin[15]: A mixture of Nimodipine and β-cyclodextrin was ground in a glass container and minimum amount of solvent (methanol: water = 1:1 molar ratio) was added. The mixture was reacted for 90 sec at 60 °C in the oven. After the reaction was completed an adequate amount of solvent was added to remove the residual Nimodipine and β-cyclodextrin and then the precipitate was filtered. After drying in a oven at 60 °C A white powder product was obtained, which was the inclusion complex of Nimodipine and β-cyclodextrin.

Preparation of fast dissolving tablets containing complex of Nimodipine and β-cyclodextrin: The amount of complex equivalent to 30mg of drug were taken and then mixed with directly compressible diluents and superdisintegrants in a plastic container. Mg. stearate and talc were passed through sieve No.60, mixed and blended with the initial mixture in the plastic container followed by compression of the blend. Compression was performed on a 10 station Rimek tablet compression machine (M/s Karnawati Engg. Ltd., Ahmedabad, India) using 8 mm punches. The compositions of the different formulations are given in the Table 1.

Table 1: Formulation of Nimodipine fast dissolving tablets prepared by complexation method

Ingredient (mg)	Formulation code											
	CCP_1	**CCP_2**	**CCP_3**	**CCP_4**	**CCC_1**	**CCC_2**	**CCC_3**	**CCC_4**	**CSS_1**	**CSS_2**	**CSS_3**	**CSS_4**
Amount of complex equivalent to 30 mg of Nimodipine	111.37	111.37	111.37	111.37	111.37	111.37	111.37	111.37	111.37	111.37	111.37	111.37
CP	10	15	20	30	--	--	--	--	--	--	--	--
CCS	--	--	--	--	10	15	20	30	--	--	--	--
SSG	--	--	--	--	--	--	--	--	10	15	20	30
MCC	34	34	34	34	34	34	34	34	34	34	34	34
DC-Mannitol	36.63	31.63	26.63	16.63	36.63	31.63	26.63	16.63	36.63	31.63	26.63	16.63
Aspartame	4	4	4	4	4	4	4	4	4	4	4	4
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Mg stearate	2	2	2	2	2	2	2	2	2	2	2	2
Total	200	200	200	200	200	200	200	200	200	200	200	200

Compatibility studies:

IR Studies: IR spectra for pure drug and CCP_4, CCC_4 and CSS_1 powdered tablets were recorded in Infrared spectrophotometer with KBr pellets.

DSC Studies: DSC studies were carried out pure drug Nimodipine and best formulations like, CCP_4, CCC_4 and CSS_1, DSC scan of about 10 mg, using an automatic thermal analyzer system performed accurately weighed Nimodipine and formulation (Mettler Toledo, USA). Sealed and perforated aluminum pans were used in the experiments for all the samples, temperature calibrations were performed using indium as standard. All empty pans sealed in the same way as the sample was used as a reference. The entire samples were run at a scanning rate of 10^{o} C / min from 50 - 300^{o} C.

Evaluation of Nimodipine tablets:

Pre-compression Parameters: The tablet blends were evaluated for their bulk density, tapped density, Carr's index and flow properties.

Post-compression Parameters: The prepared tablets were evaluated for weight variation, hardness, friability, disintegration time, wetting time, water absorption ratio, drug content studies. In weight variation test twenty tablets were selected at a random and average weight was calculated. Then individual tablets were weighed and the weight was compared with an average weight. The Pfizer hardness tester was used for the determination of hardness of tablets. A tablet was placed in contact between the plungers, and the handle was pressed, the force of fracture was recorded. The friability of the tablets was determined using Roche's friabilator (Cambel Electronics, Mumbai, India).

In the Disintegration time[16] study six tablets were tested from each formulation, in the disintegration time study tablets was put into 100 ml of distilled water at 37 ± 2^{o} C, time required for complete dispersion of a tablet was measured with the help of digital tablets disintegration test apparatus and in wetting time[17] study a piece of tissue paper folded twice was placed in a small Petridish (internal diameter = 6.5 cm) containing 5 ml of distilled water. A tablet was placed on the paper and the time for complete wetting of tablet was measured in second. For the determination of drug content total 10 tablets were weighed and powdered, powder equivalent to 100 mg of Nimodipine was weighed and dissolve in methanol and filtered the solution through Whatman filter paper. The filtrates was collected and diluted to a sufficient amount with methanol till the concentration of drug lies within the standard plot range. The diluted solution

was analyzed for the Nimodipine content by UV -spectrophotometer (UV-1700 Shimadzu Japan) at 317 nm using methanol as a blank.

In-vitro Release Studies[18, 19] was carried out in the USP dissolution test apparatus (Electrolab TDT - 08 L Dissolution testers USP) type 2 (paddle). 900 ml of dissolution medium (4.5 acetate buffer) [20] was taken in covered vessel and the temperature was maintained at 37± 0.5^{o} C. The speed of the paddle was set at 75 rpm. Sampling was done every one min interval. For each sample 5 ml of the dissolution medium was withdrawn and the same amount of dissolution medium at 37^{o} C was replenished to the dissolution medium. The sample withdrawn was diluted with 4.5 acetate buffer solution and analyzed in UV -Spectrophotometer (UV-1700 Shimadzu Japan) at 317 nm. All the results were performed in triplicate. The stability study of the tablets was carried out according to International conference on Harmonization guidelines for zone III and IV. The formulations were stored at 40 ± 2^{o} / 75 ± 5 % RH for three months by storing the samples in stability chamber (Thermo Lab, Mumbai).

RESULTS AND DISSCUSION

IR spectra of Nimodipine and formulations CCP_4, CCC_4 and CSS_1 are shown in (**Figure 1**). The pure drug Nimodipine contains 2 carboxylic functions of a ring substitution exhibiting two intense peaks at 3529 cm^{-1} and 3409 cm^{-1}. The pyridine N-H group shows an absorption peak at 3313cm^{-1}. The C-H peaks are seen at 3027 cm^{-1} due to the presence of aromatic ring system. The absorption peak of C-H are seen at 2950 cm^{-1} to 2915 cm^{-1}, C=O give a distinct peak at 1751 cm^{-1} and 1673cm^{-1}.

The IR spectra of CCP_4 shows that due to presence of number of hydroxyl group exhibited peaks at 3621.66 cm^{-1} to 3413.39 cm^{-1} the pyridine N-H which is substituted by ortho methyl groups shows a absorption peak at 3320.82 cm^{-1}, suggesting that all the characteristic peaks of drug and β-cyclodextrin. The IR spectra of CCC_4 revealed that in this case also all the characteristic absorption peaks of drug and β-cyclodextrin have remained un affected suggesting that drug is present in un reacted form or free form. The IR spectra of CSS_1 shows that due to the presence of number of hydroxyl groups exhibited peaks at 3687.23 cm^{-1} to 3585.95 cm^{-1}, the absorption peaks also seen at 1762.62 cm^{-1} to 1673.91 cm^{-1} suggesting that during the formulation of complex with β-cyclodextrin. The FT-IR studies revealed that Nimodipine is compatible with the excipients used in the formulation.

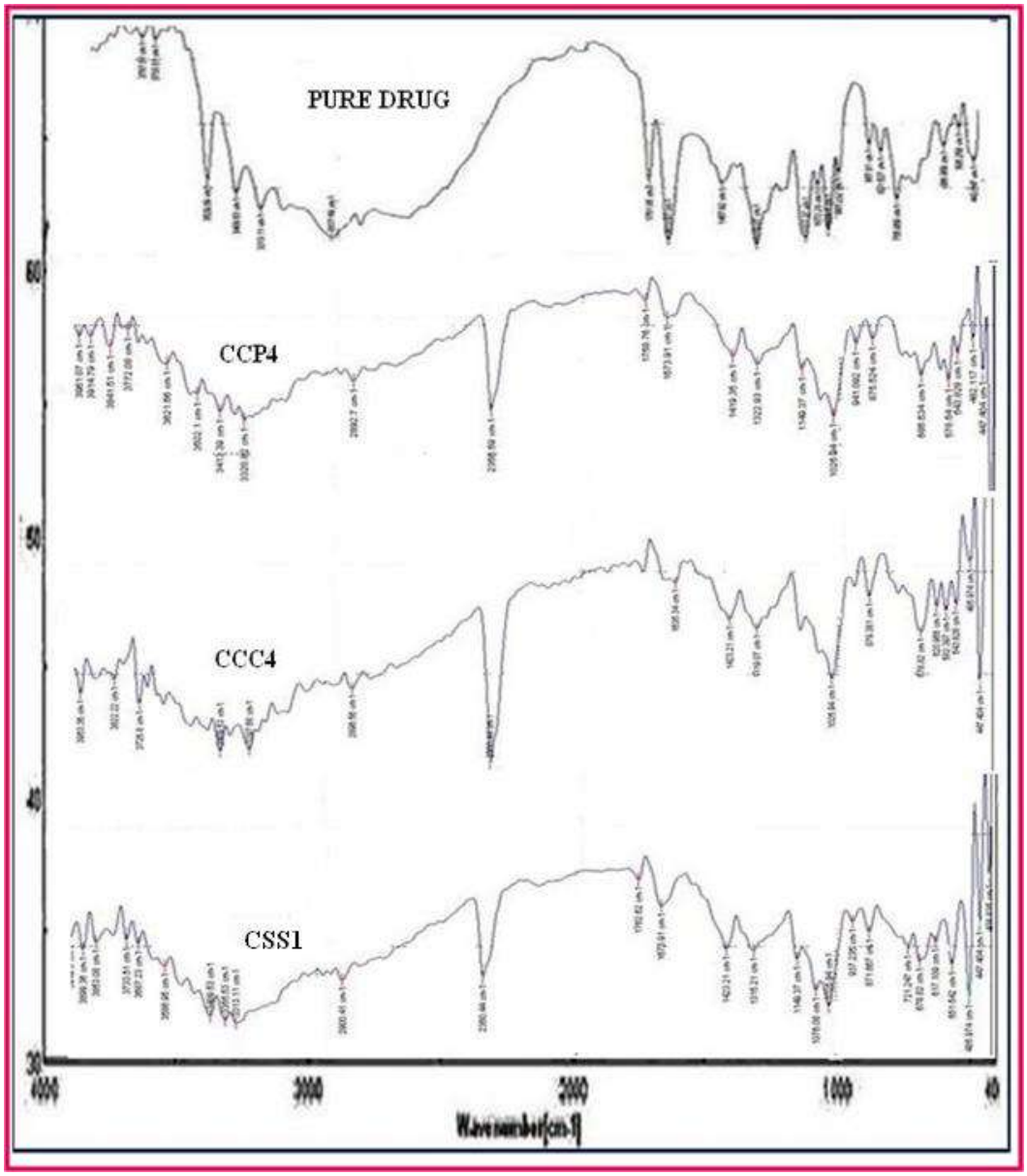

Figure 1: IR spectrum of pure drug Nimodipine, IR spectrum of Formulation CCP_4, CCC_4 and CSS_1

Thermograms of pure drug Nimodipine and the formulations CCP_4, CCC_4 and CSS_1 (**Figure 2**). The Nimodipine is subjected to DSC which has shown a sharp melting at 193.83°C.

The DSC of CCP_4 also shows the wide melting range as well as three step decomposition of excipients in first stage melting start at 78.83°C and complete at 104.07°C and another step start at 157.65°C and complete at 170.35°C, in the third stage melting start at 190.21°C and complete at 222.47°C. The DSC of CCC_4 shows first stage melting start at 72.51°C and complete at 95.10°C and in another stage start at 157.07°C and complete at 168.89°C in the third stage

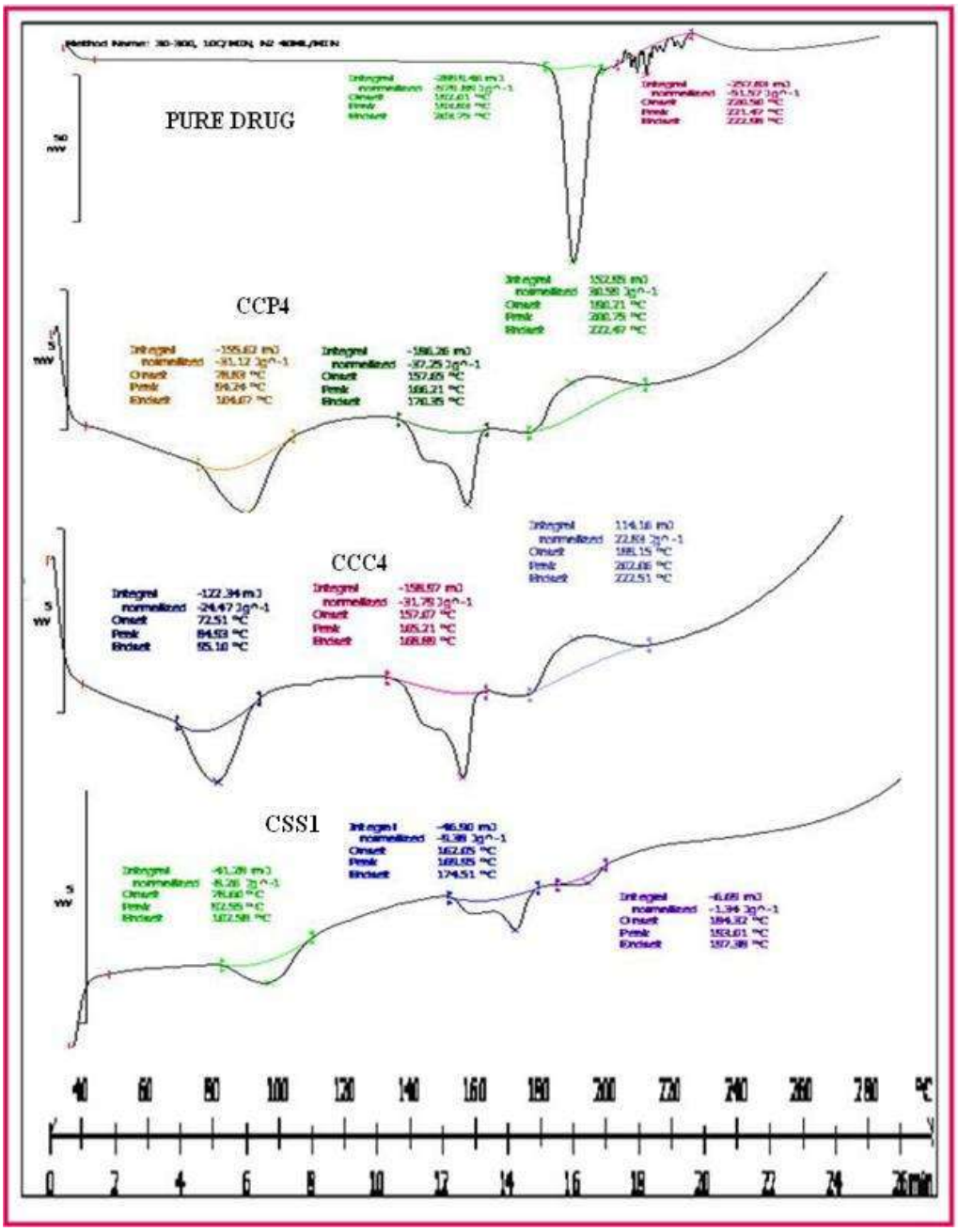

Figure 2: DSC Thermograms of pure drug Nimodipine, DSC Thermograms of Formulations CCP_4, CCC_4 and CSS_1.

melting start at 189.15°C and complete at 222.51°C. The DSC of CSS_1 reveals that in one case melting start at 78.60°C and complete at 102.58°C in another case start at 162.05°C and completed at 174.51°C and in third stage melting start at 184.32°C and complete at 197.38°C suggesting that is a mixture and also excipients in this case under goes decomposition because of its bulkier molecularity, hence this formulation is also a mixture, where in constituents are present in the free form not in the form of reactant product. Looking at the data observe in all the

case one can conclude that during the formulation process with various excipients no chemical reaction takes place between drug and excipients.

Table 2: Pre-compression parameters of powder blend of complexation method.

FC	Bulk density (g/cc) ± SD, n=3	Tapped Density (g/cc) ± SD, n=3	Angle of repose (degree) ± SD, n=3	Carr's index (%) ± SD, n=3	Hausner's Ratio ± SD, n=3
CCP_1	0.55 ± 0.007	0.66 ± 0.03	21.34 ± 0.09	16.66 ± 0.11	1.20 ± 0.08
CCP_2	0.54 ± 0.006	0.64 ± 0.02	20.26 ± 0.11	15.62 ± 0.16	1.18 ± 0.09
CCP_3	0.56 ± 0.005	0.65 ± 0.05	19.21 ± 0.12	13.84 ± 0.15	1.16 ± 0.11
CCP_4	0.54 ± 0.046	0.64 ± 0.04	19.04 ± 0.14	13.42 ± 0.12	1.14 ± 0.06
CCC_1	0.51 ± 0.003	0.61 ± 0.03	23.19 ± 0.16	16.39 ± 0.12	1.19 ± 0.10
CCC_2	0.51 ± 0.002	0.62 ± 0.04	21.32 ± 0.15	17.74 ± 0.14	1.21 ± 0.05
CCC_3	0.52 ± 0.001	0.63 ± 0.02	21.24 ± 0.18	17.46 ± 0.16	1.20 ± 0.03
CCC_4	0.52 ± 0.004	0.62 ± 0.05	21.06 ± 0.12	17.12 ± 0.12	1.18 ± 0.04
CSS_1	0.53 ± 0.009	0.63 ± 0.03	24.30 ± 0.16	15.87 ± 0.12	1.18 ± 0.06
CSS_2	0.50 ± 0.007	0.62 ± 0.04	25.29 ± 0.12	19.35 ± 0.15	1.24 ± 0.08
CSS_3	0.52 ± 0.009	0.62 ± 0.04	22.14 ± 0.15	16.12 ± 0.20	1.19 ± 0.12
CSS_4	0.50 ± 0.006	0.62 ± 0.06	21.84 ± 0.12	15.64 ± 0.14	1.16 ± 0.14

* Average of three determinations.
FC=Formulation code

Table 3: Post-compression parameters for complexation method

FC	Hardness * (Kg/cm^2) ± SD	Friability (%)	Thickness* (mm) ± SD	Weight variation* (mg) ± SD
CCP_1	3.33 ± 0.16	0.61 ± 0.07	4.67 ± 0.13	199.5 ± 1.6
CCP_2	3.24 ± 0.14	0.64 ± 0.09	4.80 ± 0.14	198.75 ± 0.9
CCP_3	3.39 ± 0.19	0.65 ± 0.10	4.73 ± 0.10	200.08 ± 1.4
CCP_4	3.28 ± 0.12	0.63 ± 0.08	4.78 ± 0.12	199.75 ± 0.8
CCC_1	3.25 ± 0.11	0.59 ± 0.03	4.59 ± 0.17	199.63 ± 1.7
CCC_2	3.23 ± 0.13	0.64 ± 0.12	4.71 ± 0.16	197.18 ± 1.0
CCC_3	3.36 ± 0.15	0.60 ± 0.11	4.75 ± 0.8	200.37 ± 0.6
CCC_4	3.26 ± 0.12	0.63 ± 0.14	4.73 ± 0.12	199.18 ± 1.0
CSS_1	3.41 ± 0.12	0.61 ± 0.13	4.67 ± 0.21	200.22 ± 0.9
CSS_2	3.31 ± 0.17	0.69 ± 0.10	4.78 ± 0.12	199.59 ± 1.3
CSS_3	3.26 ± 0.15	0.66 ± 0.13	4.60 ± 0.21	199.56 ± 1.4
CSS_4	3.34 ± 0.14	0.65 ± 0.12	4.64 ± 0.14	198.59 ± 1.2

* Average of three determinations
FC=Formulation code

The values of pre-compression parameters evaluated were within prescribed limits and indicated good free flowing property **(Table 2).** All the post-compressional parameter are evaluated were prescribed limits and results were within IP acceptable limits. Results were shown in **Table 3.** In all the formulations, hardness test indicated good mechanical strength ranges from 3.24 to 3.41

kg/cm^2. The friability is less than 1% indicated that tablet had good mechanical resistance ranges from 0.59 to 0.69 %.

The thickness was almost uniform in all the formulations and values ranged from 4.59 to 4.80 mm. The standard deviation values indicated that all the formulations were within the range. The weight variation was found in all designed formulations in the range 198.59 to 200.37 mg. All the tablets passed weight variation test as the average percentage weight variation was within 7.5% i.e. in the pharmacopoeia limits.

The disintegration time were rapid within several minutes was observed in all the formulations. The *in-vitro* disintegration data is tabulated in the **Table 4.** The *in-vitro* disintegration time of fast dissolving tablets were found to be in the range of 19.24 to 48.29 sec fulfilling the official requirements. By the addition of super disintegrants along with complex the disintegration time increased significantly ($P<0.05$) tablets prepared.

The tablets were subjected for evaluation of the *in-vitro* disintegration time (**Figure 3).** The tablets were evaluated for the in vitro disintegration time and it was observed that the time for all the formulations varied from 19.24 to 48.29 sec. It was observed that when CP was used as disintegrant, the tablet disintegrated rapidly within a short time due to the easy swelling ability of CP when compared with other tablets prepared using CCS and SSG. It is observed that the disintegration time of the tablets decreased with an increase in the level of CCS, CP. However, the disintegration time increased with an increase in the level of SSG in the tablets. It indicates

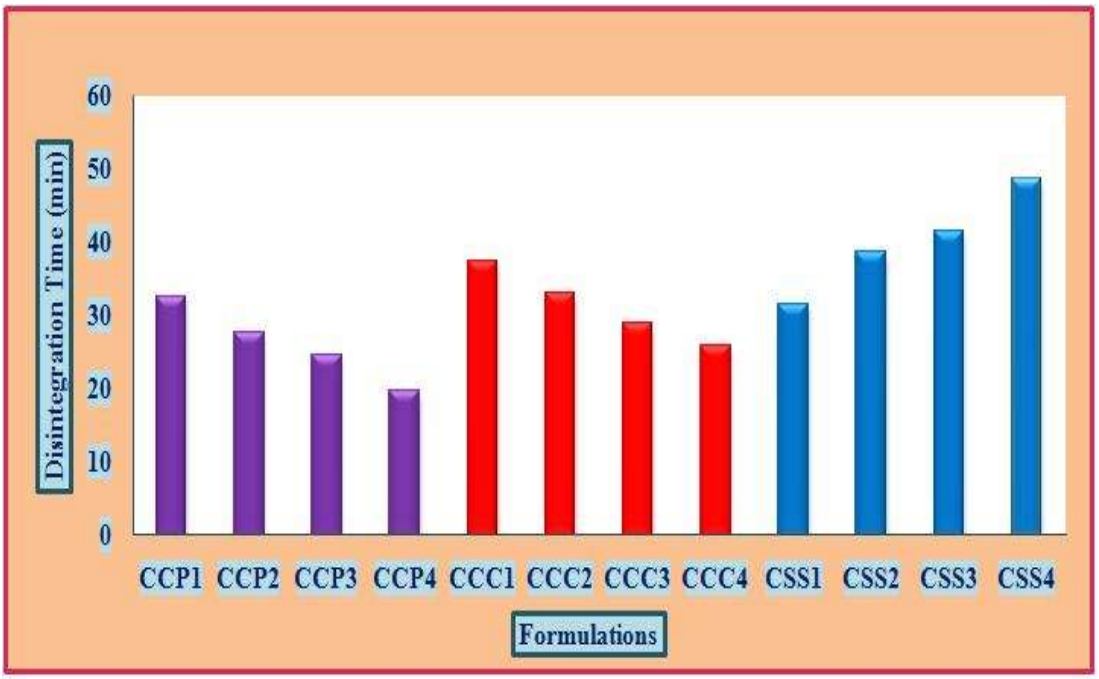

Figure 3: Disintegration time Vs Formulations (All 12)

Table 4: Post-compression parameters for complexation method

FC	Disintegration time* (sec)± SD	Wetting time* (sec) ± SD	Water absorption ratio* ± SD	Drug Content* (%) ± SD
CCP_1	32.26 ± 1.5	53.98 ± 1.6	84.41 ± 1.2	99.29 ± 2.2
CCP_2	27.30 ± 1.2	44.48 ± 1.2	82.98 ± 1.6	99.31 ± 0.6
CCP_3	24.32 ± 1.3	36.33 ± 1.0	80.43 ± 1.9	99.64 ± 1.7
CCP_4	19.24 ± 1.4	26.42 ± 1.2	78.36 ± 1.4	99.84 ± 1.2
CCC_1	36.99 ± 1.7	63.31 ± 1.3	78.32 ± 1.0	100.46 ± 0.6
CCC_2	32.63 ± 1.6	58.40 ± 1.5	81.32 ± 1.1	99.55 ± 0.8
CCC_3	28.53 ± 1.1	53.36 ± 0.9	82.87 ± 1.7	99.47 ± 0.9
CCC_4	25.43 ± 1.2	49.46 ± 0.8	83.64 ± 1.4	99.76 ± 0.6
CSS_1	35.23 ± 1.2	76.46 ± 1.4	75.50 ± 1.8	99.47 ± 2.0
CSS_2	38.23 ± 1.0	80.69 ± 1.8	73.44 ± 1.5	100.34 ± 0.6
CSS_3	41.20 ± 0.9	83.15 ± 1.7	77.53 ± 1.4	99.64 ± 1.2
CSS_4	48.29 ± 1.2	92.34 ± 1.4	79.53 ± 1.2	99.84 ± 1.4

* Average of three determinations

FC=Formulation code

that the increase in the level of SSG had a negative effect on the disintegration of the tablets. At higher levels, formation of a viscous gel layer by SSG[21] might have formed a thick barrier to the further penetration of the disintegration medium and hindered the disintegration or leakage of the tablet contents. Thus, tablet disintegration is retarded to some extent with tablets containing SSG when compared with the disintegration time of the tablets containing CP[22]. These results suggest that using wicking type of disintegrants like CP can decrease the disintegration time. The results were compiled in **Table 4**.

Because the dissolution process of a tablet depends on the wetting followed by disintegration of the tablet, the measurement of wetting time may be used as another confirmative test for evaluation of the fast dissolving tablets. In the wetting time study, the wetting time was rapid in CP followed by CCS and SSG. It was observed that as the concentrations of CCS, CP increased, the time taken for wetting was reduced. However, in case of SSG, as the concentration increased, time taken for wetting time also increased. The water absorption ratio in the range 75.50 to 84.41%. It was observed that as concentrations of superdisintegrants increases water absorption ratio increases. The percentage drugs content of the tablets were found to be between 99.29 to 100.46 % of Nimodipine. The results were within the range and that indicated uniformity of mixing. The wetting time, water absorption ratios and drug content results were tabulated in the **Table 4.**

In-vitro dissolution studies on the promising formulations CCP_4, CCC_4 and CSS_1 formulations were carried out in 4.5 acetate buffer solution, and the various dissolution

parameter values viz., percent drug dissolved in 2 min, 4 min, 6 min, 8 min and 10 min (D_2, D_4, D_6, D_8,and D_{10}), $t_{50\%}$, and $t_{90\%}$ are shown in **Table 5**. This data reveals that overall, the formulation CCP_4, CCC_4 and CSS_1 shows nearly faster drug release. The formulations CCP_4, CCC_4 and CSS_1 50 % of drug released in 0.96 min, 1.07 min, and 1.85 min respectively, and 90 % of drug released in 4.78 min, 6.30 min, and 7.70 min respectively when compared to other tablet formulation. *In-vitro* dissolution studies of all the formulations were shown in Figures 4-6.

Table 5: In-vitro release profile of promising Nimodipine fast dissolving tablets

Formulation	Parameters						
Code	D_2	D_4	D_6	D_8	D_{10}	$T_{50\%}$	$T_{90\%}$
CCP4	62.51	84.43	99.90	--	--	0.96 min	4.78 min
CCS4	54.27	72.09	85.73	99.77	--	1.07 min	6.30 min
CSS1	54.14	67.10	80.46	93.56	99.90	1.85 min	7.70 min

CCP_4 most promising fast dissolving tablet containing 15 % CP as super disintegrating agent, CCS_4 promising fast dissolving tablet containing 15 % CCS as super disintegrating agent, CSS_1 promising fast dissolving tablet containing 5 % SSG as super disintegrating agent. D_2 is percent drug released in 2 min, D_4 is percent drug release in 4 min, D_6 is percent drug release in 6 min, D_8 is percent drug release 8 min, D_{10} is percent drug release 10 min, and $t_{50\%}$ is time for 50 % drug dissolution, $t_{90\%}$ is time for 90% drug dissolution.

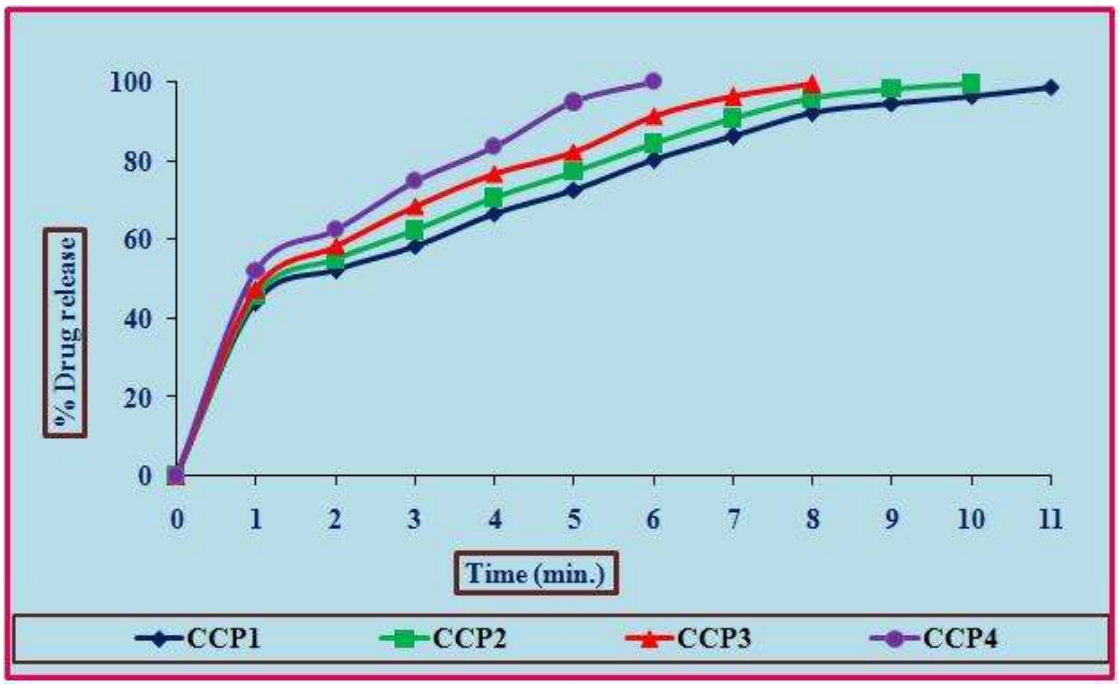

Figure 4: Release profile of formulations containing drug and CP complex (CCP_1-CCP_4)

The $t_{50\%}$ and $t_{90\%}$ values decreased with increase in the concentration of CCS and CP. However, $t_{50\%}$ and $t_{90\%}$ values decreased with increase in concentration of SSG. The rapid increase in dissolution of Nimodipine with the increase in CCS may be due to rapid swelling and disintegrating tablets rapidly into apparently primary particles[23, 24]. While tablets formulated with

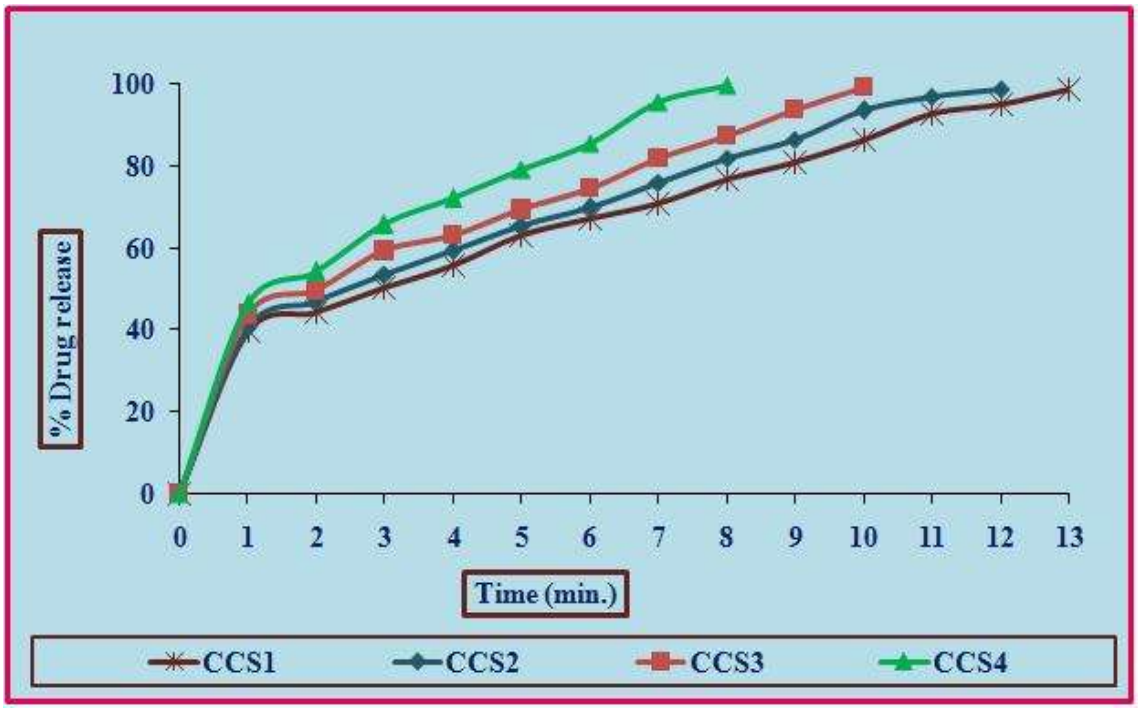

Figure 5: Release profile of formulations containing drug and CCS complex (CCS_1-CCS_4)

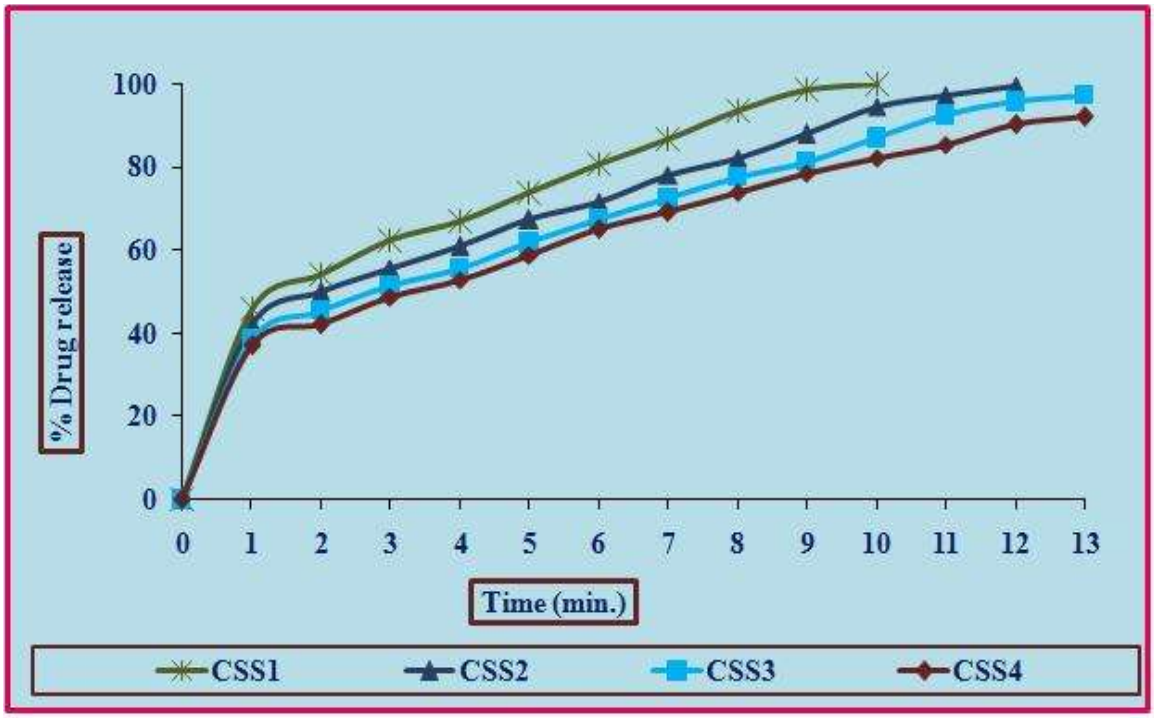

Figure 6: Release profile of formulations containing drug and SSG complex (CSS_1-CSS_4)

SSG, disintegrate by rapid uptake of water, followed by rapid and enormous swelling[24] into primary particle but more slowly[25] due to the formation of a viscous gel layer by sodium starch glycolate[26]. CP and CCS containing tablets rapidly exhibits high capillary activity and pronounced hydration with a little tendency to gel formation[24] and disintegrates the tablets

rapidly but into larger masses of aggregated particles[23]. Thus difference in the size distribution generated with different superdisintegrants might have contributed to difference in the $t_{50\%}$ and $t_{90\%}$ values with the same amount of superdisintegrants in the tablets. Among all the formulation CCP_4 (15 % crospovidone) were found to be promising and showed a disintegration time of 19.24 sec, 50 % of drug released in 0.96 min, and 90 % of drug released in 4.78 min.

The **Table 6-7** shows the parameters of the tablets after stability study. The promising formulations were subjected to short term stability study by storing the formulations at 25°C/65% and 40°C/75% RH up to three month. The formulations CCP_4, CCC_4 and CSS_1 were selected. After three month the tablets were again analyzed for the hardness, friability, drug content uniformity and disintegration time. The increase in the disintegration time was observed in case of tablets prepared with direct compression method and complexation method. This may be due to increase in the hardness of the tablets during storage [26].

Table 6: Result for 25°C/60% RH) for 3 months

Sl. No.	Formulation code	Month	Hardness Kg/cm²	% Friability	Disintegration time (sec)
1	**CCP_4**	1st	3.2	0.63	19.24
		2nd	3.3	0.61	20.71
		3rd	3.3	0.62	21.12
2	**CCC_4**	1st	3.2	0.63	25.43
		2nd	3.3	0.62	26.27
		3rd	3.4	0.63	27.14
3	**CSS_1**	1st	3.3	0.65	35.23
		2nd	3.2	0.67	36.76
		3rd	3.3	0.68	37.00

Table 7: Result for 40°C/75% RH) for 3 months

Sl. No.	Formulation code	Month	Hardness Kg/cm²	% Friability	Disintegration time (sec)
1	**CCP_4**	1st	3.2	0.63	19.24
		2nd	3.3	0.62	19.68
		3rd	3.4	0.61	20.04
2	**CCC_4**	1st	3.2	0.63	25.43
		2nd	3.3	0.64	25.84
		3rd	3.2	0.63	26.16
3	**CSS_1**	1st	3.3	0.65	35.23
		2nd	3.3	0.66	33.02
		3rd	3.4	0.67	33.42

ONCLUSION

The major problem of Nimodipine is that it is erratically absorbed from the gastrointestinal tract and its limited aqueous solubility, which may hinder dissolution. Results

reveled that it is possible to enhance the dissolution rate and the bioavailability by a with β-cyclodextrin complexes using various superdisintegrants. The overall results indicate that formulation CCP_4, which contains 15% CP, was better and that it satisfies all the criteria as a fast dissolving tablet.

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