FORMULATION DESIGNING AND OPTIMISED CHARACTERISATION OF ORALLY DISINTEGRATING TABLETS OF CLINIDIPINE BY USING VARIOUS SUPER DISINTEGRANTS

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Abstract

Oral drug delivery is the easiest and most basic way to provide medication. Nevertheless, low and irregular bioavailability, which is mostly due to poor water solubility, is the fundamental issue with oral medication formulations. For medications that are not extremely water-soluble, dissolution is the phase of the absorption process that is rate-limited. Due to inconsistent or insufficient absorption from the GIT, bioavailability issues are common with very hydrophobic medicines (aqueous solubility of 0.1 mg/ml at 37°C). One of the most alluring and promising methods to enhance the inadequate aqueous solubility of pharmaceuticals is the solid dispersion spray drying technology combined with oral dispersible tablets.Cilnidipine is a marginally water-soluble antihypertensive drug (BCS II). Making the medicine more soluble was the aim of this experiment. The development of a cilnidipine fast-dissolving tablet was attempted. The study's designs aim to increase the drug's bioavailability and hasten the beginning of action.

Keywords: Oral drug delivery, Hydrophobic drugs, solid dispersions, spray drying technique, antihypertensive medication.

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1. Introduction

Oral drug delivery is the simplest and most direct way of drug administration. Nevertheless, the basic problem with oral pharmaceutical formulations is low and erratic bioavailability, which is primarily caused by inadequate water solubility. Hence, the most difficult component of the pharmaceutical industry is the formulation of poorly soluble chemicals for oral delivery. Hypertension, commonly referred to as elevated blood pressure, significantly increases the number of literature reviews that support the availability of standard dose forms for cilnidipine calcium channel blockers used in the heart, brain, kidney, and other organs. The prevalence of hypertension is estimated at 1.28 billion people between the ages of 30 and 79 worldwide. Adults with hypertension are approximately 46% less likely to be aware of their condition.Just 42% of adult instances of hypertension are diagnosed and treated. Of those with hypertension, 21% have it under control. One of the main causes of early mortality is hypertension. According to the literature assessment, the spray drying method for drug-loaded solid dispersions in combination with orally disintegrating tablets seems to have intriguing potential as cutting-edge oral administration delivery methods. So, the goal of this work is to enhance the model drug's solubility and release properties through the use of oral dispersible tablets and the solid dispersion technique. In order to improve the therapeutic efficacy and dosage frequency of the drug, it is advised that the current endeavour construct and evaluate clinidipine oral disintegrating tablets

Formulation Designing [1]

We employ three super-disintegrating agents. from a lower to a higher level of concentration. There were 12 formulations created. Concentrations of 2.5%, 5%, 7.5%, and 10% of sodium CMC, 2.5%, 5%, 7.5%, and 10% of chitosan, and 2.5%, 5%, 7.5%, and 10% of HPMC have all been employed. The diluent utilised was microcrystalline cellulose, which is also known as super disintegrant tannitol and MCC, which is a novel diluent employed at a 70:30 ratio. This design method was applied to improve the formulation with regard to in vitro dispersion time. Before eng, all of the materials were put through a 60 # screen. To ensure consistent mixing, all the ingredients were placed to a glass mortar and triturated. The tablet weight is of 200mg in which Clinidipine along with other ingredients such as sod.cmc, hpmc, chitosan, crosspovidone, kyron t314, ac-di-sol, mcc, mannitol, mg.stearae, talc, menthol. Total of 12 formulations F1-F12 has been made by fixing clinidipine has 10mg and all other ingredients in different ratios in the unit of mg and out of which F11 is taken as optimized formulation which shows expected activities. A single-punch tablet machine was used to compress the resulting powder combination into tablets.

Preformulation Studies[2-5]

The formulation study gives information needed to define the nature of the drug substance and provide a framework for the drug combination with pharmaceutical excipients in the dosage form. Hence, the following pre-formulation studies such as angle of repose,determination of bulk density and tapped density,Hausner's ratio, Carr's index were performed on the obtained sample of the formuations.

Preparation Of Cilnidipine Orodispersible Tablet

Phase-Solubility Studies

According to the procedure, a phase solubility investigation was carried out. A large dose (50 mg) of the medication was chosen for the investigation. Drug and carrier were precisely weighed and added to pure drug with 10 ml of water in screw-capped bottles in accordance with the prescribed drug-to-carrier ratio. At 37 and 24 degrees Celsius for 24 hours, all of the bottles were shaken in an incubator shaker. The medication and water container served as the control. The solutions were filtered using a 0.45-m filter after 24 hours, and the filtrates were then diluted. At 240 nm, the absorbance was measured in spectra. The drug's solubility was determined using absorbance.

Preparation of Spray dried dispersion

Spray drying was used to create solid dispersions of cilnidipine and different polymers at ratios of 1:0.5, 1:0.75, 1:1.25, and 1:5. A cilnidipine solution dissolved in ethanol was added after the polymers had been dissolved in methanol. Using a magnetic stirrer, this mixture was homogenised between 300 and 600 rpm. The solutions produced by this process were dried in a spray dryer designed for laboratories. All of the batches listed below were spray-dried using the predetermined settings.

Preparation of Orodispersible Tablets

Preliminary screening of super disintegrants

Using the direct compression technique, orodispersible tablets comprising a spray-dried dispersion of cilnidipine, PVP K30 (1:1) employing four super disintegrants (Croscarmellose sodium, Cross povidone, and Kyron T314) were created. Fast-dissolving pills quickly dissolve because disintegrants are added to them. The disintegrants primarily influence the rate of disintegration and, hence, the rate of dissolution in several direct compression-based fast-dissolving tablet technologies.

Direct Compression Technique

In this procedure, tablets are made by compressing a mixture of the medication and excipients without any prior processing. This is a pre-treatment since the mixture that will be compressed needs to have

appropriate flow properties and cohere under pressure. Prior treatment is necessary in order for the mixture that will be compressed to have the necessary flow properties and cohere under pressure. The mixture must have adequate flow properties and cohere under pressure; pre-treating it as wet granulation is not necessary. The type of disintegration and its severity are significant factors. Other factors to consider are tablet hardness, contact angle, pore size distribution, particle size distribution, and water absorption capacity.

Addition of Disintegrants

Fast-dissolving pills quickly dissolve because disintegrants are added to them. The disintegrants primarily influence the rate of disintegration and, hence, the rate of dissolution in several direct compression-based fast-dissolving tablet technologies.

Evaluation of Developed Oraldispersible Tablets of Cilnidipine

Weight variation[6]

Twenty tablets were randomly selected from the batch, and each one was weighed to check for weight variation.The table shows the weight variation specifications according to I.P. The outcomes are displayed in turn.

Thickness[7]

Tablet thickness was measured with a Vernier calliper. By measuring the thickness of 10 tablets, the average thickness was computed.

Hardness

A Monsanto tablet hardness tester was used to assess hardness, also known as tablet crushing strength (f.), or the amount of force needed to shatter a tablet in a diametric compression.

Friability (F)[8]

The Roche friabilator was used to assess the tablet's friability. This device subjects the tablet to the combined effects of abrasion and shock in a plastic container that rotates at a speed of 25 revolutions per minute and drops a tablet from a height of 6 inches with each revolution. A pre-weighed sample of pills was placed inside the friabilator, which was rotated 100 times. After being cleaned with a delicate muslin towel, the tablets were reweighed. The formula yields the friability (F).

$$F=(I_{nitial}-F_{inal}/I_{nitial})\times 100$$

Disintegration time (DT)[9]

To compute the DT of the generated ORD CLN, equipment was employed. Each tube was filled with six tablets, and the equipment was operated until all of the pills had broken up and were able to travel through the mesh of the tube. The IP 2018 acceptance criteria are taken into consideration. The table and figure show the results of all necessary parameters that were tracked.

Assay[10]

Ten pills of ORD-CLN were taken and ground into a powder. The average weight of a tablet's worth of powder was weighed and then transferred to a 100-ml volumetric flask. A volumetric flask containing 5 ml of methanol was filled to 100 ml with phosphate buffer solution at pH 6.8 after being agitated for 15 minutes. The supernatant from the 15-minute centrifugation of 10 ml of the solution was then filtered. At 240 nm, the amount of EHE in SD was measured spectrophotometrically. The table and figure listed the outcomes of all relevant parameters that were monitored.

Wetting time[11]

Wetting time is highly correlated with the internal makeup of the tablets and the excipient's hydrophilicity.Washburn E.W. (1921) proposed the following equation, which states that the water penetration rate into the powder bed is proportional to the pore radius and is affected by thehydrophilicity of the powders.

$$dl/dt = rY\cos 0/(4ml)$$

Where I is the length of penetration, r is the capillary radius, Y is the surface tension, n is the liquid viscosity, t is the time, and 0 is the contact angle.

In Vitro Dispersion time[12]

Three randomly chosen films from each formulation were dropped into a Petri dish containing 6 ml of water to assess the in vitro dispersion time.The relevant parameters were tracked, and the results are shown in the table and figure.

In vitro dissolution Studies[12]

Using a USP Dissolution Apparatus Type II (Paddle) and a citrophosphate buffer pH 6.8 with 0.1% Sodium Lauryl Sulphate as the dissolution medium (kept at 37oC 1), the in vitro dissolution investigation of the commercially available CLN 10mg and the created ORD CLN F11 was conducted. At 0, 2, 4, 6, 8, and 10 minutes, 5 ml of samples were removed and immediately replaced with the corresponding quantities of new dissolving medium. At 240 nm, samples were spectrophotometrically examined.

In Vivo Animal Studies

Bioavailability Studies [13,14]

Study Substances, System, and Sampling schedule design

Test substances

1. Cilnidipine solid dispersion loaded Orodispersible tablets F11.
2. Marketed Cilnidipine Tablet Formulations.

RP-HPLC analysis

To analyse the sample, C18 Merck C18 (250 x 4.6 mm) was pre-equilibrated with an acetonitrile/water (65%:35%) mixture at a flow rate of 1 ml/min. Without serum interference, peaks were eluted at 240 nm at that wavelength.

Calculation of cilnidipine's pharmacokinetic (PK) characteristics and statistical significance [16]

The PK parameters, including mean residence time (MRT), biological half-life (t12), peak serum concentration (Cmax), time for peak serum concentration (tmax), and AUCtotal, were examined and expressed as mean SD values. P 0.05 was regarded as statistically significant when comparing the data from eight research groups using a paired student t-test and the GraphPad Prism software (version 5.0, 2007).

DOCA Salt-Induced Hypertension Design Antihypertensive Study (Drugs and Groups) [17]

Drugs: optimal formulation (OF) of cilnidipine solid dispersion-loaded oral dispersible tablets, marketed formulation (MF), and pure drug.

The DOCA salt model of hypertension is used to determine antihypertensive activity.Six male Wistar rats (n = 5) were divided into five groups at random.The respectively provides information about the group. The usual meal was fed to the animals. On weeks 0, 1, 2, and 6, blood pressure was checked.

STABILITY STUDIES FOR MATRIX TABLET

The stability of the active ingredient must be a key factor in deciding whether or not dosage forms for medicines should be accepted. During a period of three months, this study conducted stability testing in accordance with ICH recommendations. For each type of stability research, the environment was kept at a constant 40°C ±2°C and 75% RH ± 5% RH.

2. Results And Discussion

Physical characterization and Drug Identification

Table. 1: Physical description / Organoleptic properties

Test	**Specification/limits**	**Observation**
Color	Yellow powder	Yellow powder
Taste	Tasteless	Tasteless
Odour	Almost odorless	Almost odorless

Solubility Studies

The solubility levels were determined, using the UV spectrometric method at 240 nm.

Table. 2: Solubility Studies of Cilnidipine

S. No	**Name of the Solvent**	**Solubility (mg/ml)***
1	Dimethyl Sulfoxide (DMSO)	0.788 mg/mL
2	Ethanol	0.822 mg/Ml
3	Methanol	0.878 mg/mL
4	Water	0.0059 mg/Ml
5	Citrophosphate buffer pH 6.8 with 0.1% Sodium Lauryl Sulphate	0.982 mg/Ml

The UV spectrometric technique at 240 nm was used to calculate the solubility levels. In citrophosphate buffer pH 6.8 with 0.1% Sodium Lauryl Sulphate, ethanol, methanol, Dimethyl Sulfoxide (DMSO), and very slightly in water, the cilnidipine was easily soluble.

UV-Visible Spectrophotometer

Table. 3: Standard Curve of Cilnidipine

Concentration (µg/ml)	**Absorbance λmax at 240 nm**
0	0
1	0.0896
2	0.167
3	0.252

4	0.343
5	0.412
6	0.517
7	0.593
8	0.656
9	0.767
10	0.799

Figure. 1: Standard Curve of Cilnidipine

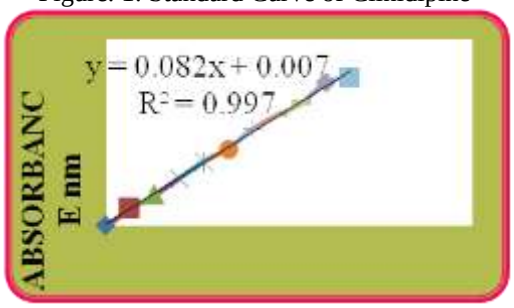


Table 4: Regression analysis

Parameters	**Value**
R ^{2}	0.9974
Slope	0.0821
Intercept	0.0074

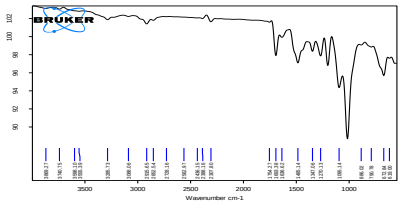
From the standard calibration curve of cilnidipine, it was observed that the drug obeys beer-lamberts law in the concentration range of i.e 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 ml µg/mL for citrophosphate buffer pH 6.8 with 0.1% Sodium Lauryl Sulphate in the media

Drug excipients compatibility study

Drug excipients name

Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes inthe chemical constitution of the drug after combining it with the excipients. The samples were taken for the FT-IR study.

Figure. 2: FTIR Spectrums of Cilnidipine + All Excipients



From the FTIR of the spectrum of pure drug and excipients, The characteristic peaks of cilnidipinein-developed formulations were present at almost the same positions, while the absence of shifts in the wave numbers of the FTIR peaks of pure drug of the developed solid dispersions in spray drying method that indicate the lack of significant interaction between the drug and the carrier in the solid dispersions. Thus, these results confirmed that there are no major shifting as well as any loss of functional peaks between the drug and excipients and confirmed that are no interaction between CLN and excipients (Figure: 2).

Pre-formulation study of Batch F1 to F12

Table 5: Evaluation of Cilnidipine Blend Formulations F1 – F12

Batch code	**Bulk density (gm/cm^3)***	**Tapped density (gm/cm^3)***	**The angle of Repose (θ)***	**% Compressibility ***	**Hausner ratio ***
F1-F12	0.42	0.50	23.58	16.00	1.19

*Mean ± SD, (n = 3)

These values, along with the fact that the powder blends had good compressibility, indicate that the powder blends can be compacted easily. The angle of repose for each of the dummy batches and the formulated batches,each of which included a different polymer and a different concentration of a separate super disintegrant. These values, which indicate that the powder blends had good flow ability and compressibility, were obtained.

The result of all necessary parameters monitored for blends was cited in Table

Post Compression Parameters optimized formulation F11

Table 6: Evaluation of Oral dispersible Cilnidipine Tablets in process Physical Parameter of optimized formulation F11

Batch code	**Weight Variation (mg±SD)***	**Thickness (mm± SD)***	**Hardness (kg/cm^2± SD)***	**Friability (%± SD)***
F11	200.8±0.86	3.01±0.4	2.4±0.2	0.31

Post Compression Parameters of optimized formulation F11

Table 7: Evaluation of Oral dispersible Cilnidipine Tablets in process Post compression Parameter of optimized formulation F11

Batch code	***In Vitro* Disintegrating Time (seconds)***	**Assay (%)***	**Wetting Time (seconds)***	***In Vitro* Dispersion Time (seconds)***
F11	14	100.24	23	19

In vitro drug release

The dissolving profiles for the two super disintegrants were found to be significantly different based on the data collected for the formulations' dissolution profiles. At the end of 10 minutes, formulations F1, F2, F3, and F4 release 93.3%, 96.76%, 97.55%, and 98.34% of the medicines, respectively. The proportion of medication release increased from 2.5 to 10% as the crospovidone concentration was raised. The quicker dissolving and finer dispersion of the post-disintegration particles may be the cause of the increased dissolution rates seen with crospovidone. At the conclusion of 10 minutes, formulations F5, F6, F7, and F8 release 96.36%, 97.68%, 98.36%, and 100.21%, respectively. As the concentration of Kyron T314 rose from 2.5 to 10%, the percentage of medication release also rose.

At the end of 10 minutes, formulations F9, F10, F11, and F12 release 97.85%, 100.44%, 100.66%, and 99.56%, respectively. With an increase in croscarmellose sodium (AC-DI-SOL) concentration from 2.5 to 10%, the percentage of medication release increased. With increasing concentration, the dissolving rate of croscarmellose sodium (AC-DI-SOL) increased steadily, reaching 7.5% w/w. Hence, the ideal concentration for croscarmellose sodium is 7.5% w/w (AC-DI-SOL). The highly porous structure of the super disintegrant may be the cause of the higher dissolution rates seen up to the optimum concentration [7.5% w/w], which allows for faster water uptake and, in turn, faster disintegration, easy particle breakdown, and quick drug absorption into the dissolution medium.

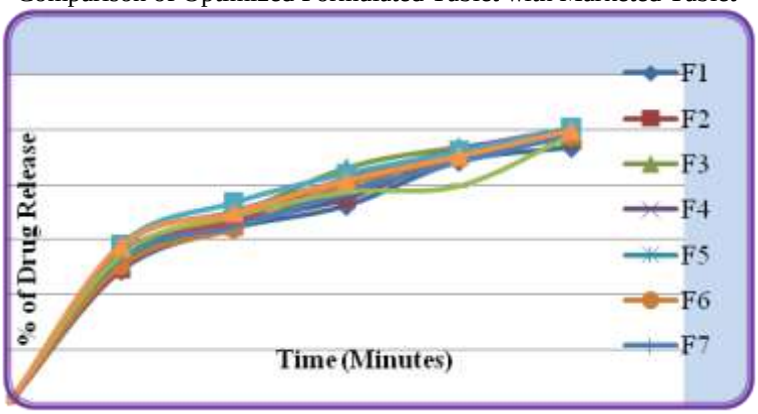
Table 8: Percentage release profile of prepared ORD of Clinidpine Batch F1 – F12

S.	**Time**	**% Drug Release**

No.	(Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	0	0	0	0	0	0	0	0	0	0	0	0	0
2	2	48.6	49.55	52.8	50.88	51.33	50.22	54	55.13	54.46	57.33	58.22	57.75
3	4	64	65.43	68	66.22	64.46	64	64.87	66.81	68.66	70.21	73.56	69.78
4	6	72.2	75.27	85.77	74.92	77.11	79.77	77.56	82.09	77.34	81.77	84.06	81.44
5	8	88.2	90.61	93..35	90.88	92.8	89.63	88.23	92.81	79.56	92.45	92.08	90.28
6	10	93.3	96.76	97.55	98.34	96.36	97.68	98.36	100.21	97.85	100.44	100.66	99.56

Figure 03: Percentage release profile of prepared ORD of Clinidpine Batch F1 – F12

Comparison of Optimized Formulated Tablet with Marketed Tablet

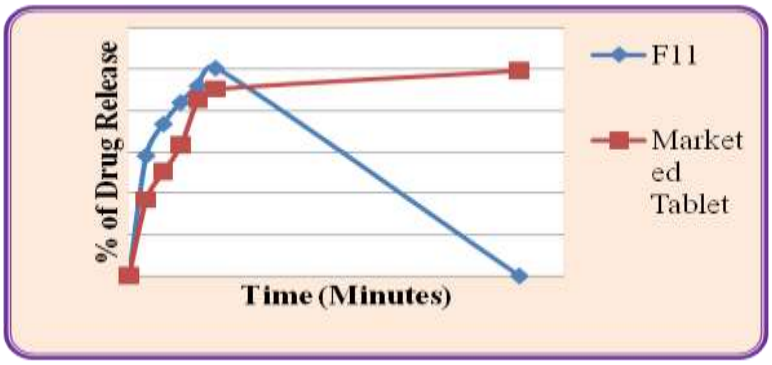


The optimized formulation ORD CLN F11 was compared with the marketed tablet *in vitro* dissolution study. The results were shown respectively.

Table 9: Percentage Drug Release Profile of Marketed Tablet and Optimized Formulation of F11

S. No.	Time (Minutes)	% Drug release		
		ORD CLN F11	Time (Minutes)	Marketed Tablet
1	0	0	0	0
2	2	58.22	5	36.71
3	4	73.56	10	50.23
4	6	84.06	15	63.27
5	8	92.08	20	75.09
6	10	100.66	30	90.18
7	---	---	45	99.16

Figure 04: Percentage Drug Release Profile of Marketed Tablet and Optimized Formulation of F11



In vivo studies

The pharmacokinetic parameters of Clinidpine in individual rats for marketed formulations and optimized cilnidipine solid dispersion loaded oro dispersible tablets F11 were calculated by non-compartmental estimations using Kinetica 2007 software. The pharmacokinetic parameters C_{max}, AUC_{tot}, T_{max}, MRT, and $t_{1/2}$ were calculated. The statistical comparison of data was done by a student's unpaired t-test at a significance level of p-value <0.01 using Graph pad prism (version 5.0, 2007).

From the results, it was found that optimized cilnidipine solid dispersion-loaded oro dispersible tablets F11 showed high C_{max} and AUC_{total} values of 14.6±4.2 µg/mL CLN &16.4±3.4 µg/mL. CLN F11, and AUC_{Total}37.0±17.9 µg.h/mL CLN & 38.7±19.7 µg.h/mL CLN F11 when marketed formulation, which showed lower $C_{max}$and AUC_{tot}values and there is a statistically significant difference between $C_{max}$and AUC_{tot} of the optimized CLN F11 with that of the marketed formulation.$t_{1/2}$ of optimized CLN F11 value 13.98±0.67h, showed a significant difference with that of marketed formulations CLN value 11.3±0.32h. MRT of optimized CLN F11 value 12.89±0.47h, showed a significant difference with that of marketed formulations CLN value 11.3±0.43h.T_{max} of optimized CLN F11 value 6.00h, and marketed formulations were as CLN value 4.00h respectively. The bioavailability of optimized ODT CLN F11 was found to be increased by percentage times for all drugs than that of tablet powder marketed formulation.

Table 10: In vivo standard graph of cilnidipineby RP-HPLC

Concentration	**Peak area***
0	0
0.25	0.078
0.5	0.49
1	0.961
2	2.06
3	3.58
4	4.58
6	7.21
8	9.27

Figure 05: *In vivo* calibration curve of cilnidipine in rat serum by RP-HPLCTable 20: Mean Serum Concentration of cilnidipine after oral administration of Optimized ORD CLN F11 and Marketed Formulation in rats

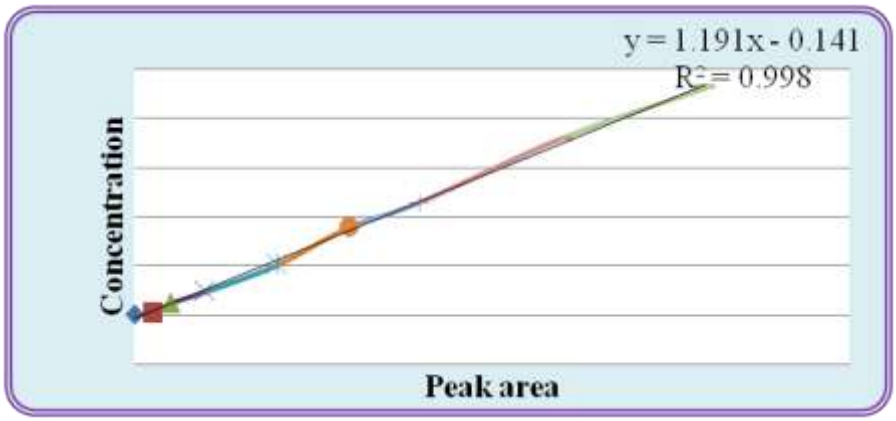


Table 11: Mean Serum Concentration of cilnidipine after oral administration of Optimized ORD CLN F11 and Marketed Formulation in rats

	ORD CLN F11		**Time (Minutes)**	**Marketed Formulation**	
Time (Minutes)	**Mean**	**SD**		**Mean**	**SD**
0	0	0.00	0	0	0
2	1.56	0.00	5	1.43	0.21
4	3.26	0.02	10	3.15	0.45
6	4.98	0.14	15	1.45	0.33
8	1.19	0.58	20	0.86	0.27
10	0.42	0.36	30	0.54	0.12
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Figure06: Mean Serum Concentration of cilnidipine after oral administration of Optimized ORD CLN F11 and Marketed Formulation in rats

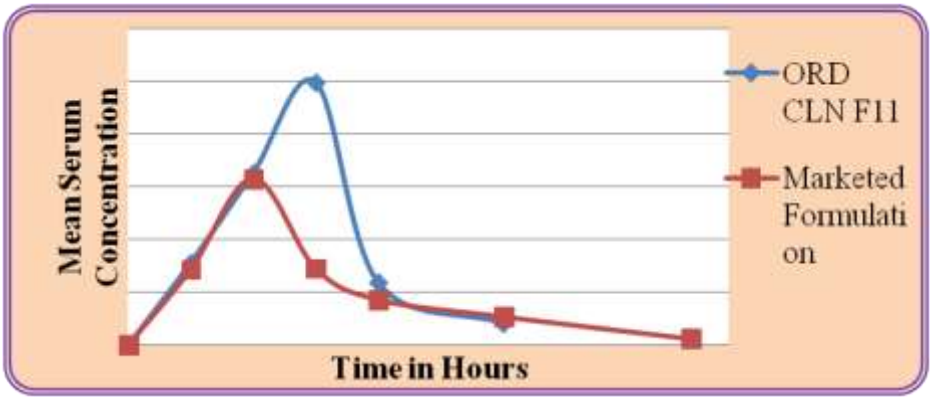


Table 12: Pharmacokinetic parameters of cilnidipine after oral administration of optimized cilnidipine solid dispersion loaded orodispersible tablets F11 and Marketed Formulations in rats

Parameter	**Marketed Formulation**	**ORD CLN F11**

C_{max}(µg/mL)	14.6±4.2	16.4±3.4*
T_{max} (h)	4.00	6.00
AUC_{Total}(µg.h/mL)	37.0±17.9	38.7±19.7*
$T_{1/2}$ (h)	11.3±0.32	13.98±0.67
MRT (h)	11.3±0.43	12.89±0.47#

Antihypertensive Studies

In rats with hypertension caused by DOCA salt, the current research demonstrated the significant antihypertensive activity of optimised cilnidipine solid dispersion-loaded orodispersible tablets. Through renin-angiotensin system stimulation, DOCA salt raises blood pressure. The decapeptide angiotensin I is produced when renin works on the 2-globulin angiotensinogen (renin substrate). Angiotensin-converting enzyme (ACE) cleaves this decapeptide to produce active angiotensin II (octapeptide), a powerful vasoconstrictor that causes hypertension. An aminopeptidase hydrolyzes angiotensin II to produce the potent heptapeptide known as angiotensin III. Demonstrated that significantly lowering high blood pressure was achieved after oral administration of optimised cilnidipine solid dispersion-loaded orodispersible tablets. Optimised cilnidipine solid dispersion-loaded orodispersible tablets provided a considerable anti-hypertensive effect in DOCA salt-induced hypertensive rats after 3 weeks of treatment.

When DOCA salt-induced hypertensive rats were given optimised cilnidipine solid dispersion-loaded orodispersible tablets, more anti-hypertensive activity was seen in comparison to the marketed tablet formulation as well as the cilnidipine pure drug due to increased solubility and increased amount of drug released.

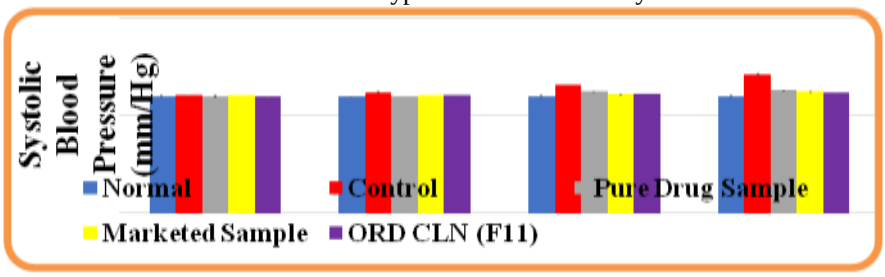
Determination of antihypertensive activity by DOCA salt model of hypertension

Table 13: Hypotensive activity of optimized cilnidipine solid dispersion loaded orodispersible tablets (F11)in DOCA salt-induced Hypertensive rats

Group	**Systolic Blood Pressure (mm of Hg)**			
	0 week	**I week**	**II Week**	**VI Week**
Normal	120.2±0.600	119.2±0.792	120.3±0.614	120±0.632
Control	120.8±0.307	124±0.730*	131.2±1.176*	142.1±0.881*
Pure Drug Sample	119.8±0.760	119.9±0.477*	124.5±0.666*	125.76±0.666*
Marketed Sample	121.2±0.477	121.2±0.447*	122.3±0.666*	124.5±0.600*
Optimized formulation (MDT F11)	119.5±0.477	121±0.749*	122.2±0.632*	123.6±0.670*

Mean±SEM, Tukey's test. *n*=6; ns – non-significant; * *P* <0.05 significant.

Figure 07: Hypotensive activity of optimized cilnidipine solid dispersion loaded orodispersible tablets (F11)in DOCA salt-induced Hypertensive ratsStability studies.



Mean±SEM, Tukey's test. *n*=6; ns – non-significant; * *P* <0.05 significant.

Stability studies

Stability studies were conducted for finally optimized formulation (ORD CLN F11) at accelerated temperature (40ºC/75% RH) of ORD tablet. accelerated temperature for three months. Mild variations were noticed in drug content, *In vitro* Disintegrating Time, Wetting Time, and % Drug Release (Table. 9.15), which indicated the resistance to stability problems during storage at

Table 14:Stability Studies of Optimized Formulation ORD CLN F11 at (40°C/75% RH)

Parameters	**0 Day**	**30 Days**	**60 Days**	**90 Days**
Drug content (%)*	100.74	100.39	100.03	100.3
In vitro Disintegrating Time (seconds)*	14	15.6	16	16
Wetting Time (seconds)*	23	24.3	24.9	25
% Drug Release	100.66	100.54	100.42	100.05

3. Conclusion

The current research has demonstrated that by making the poorly soluble drug cilnidipine as solid dispersions and preparing them using the spray drying method with carriers like chitosan and hydroxypropyl methylcellulose, the dissolution rate of the drug can be increased. ORD CLN F11 was chosen for the novel development of oral dispersible tablets based on the optimised formulations. Various super disintegrants were used in different concentrations to create oral dispersible tablets of CLN-loaded SD. When CCS was present in greater concentrations and the subliming agent was present, the drug release from ORD increased. The ORD formulation CLN F11 was chosen as the optimal formulation because it had the highest in vitro drug release, shortest disintegration time, excellent drug content, and in vivo studies in Wistar rats. The physical and drug release parameters of the ORD CLN F11 formulation did not significantly alter over the course of three months of storage.Therefore, ORD of CLN prepared using SD and CCS as super disintegrants may be the best method for increasing dissolution and consequently bioavailability of poorly water-soluble CLN, according to the findings of the current research. Comparing the optimised cilnidipine to the commercial tablet formulation as a reference drug, more antihypertensive action was seen.

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