Available online on 15.12.2023 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Research Article

Revolutionizing Drug Delivery: Nicardipine Nanosuspension Formulation and In-Vitro Evaluation

Risha Miskan [1]*, S M Shahidulla [2], Sana Sultana [1]

[1] *Research Scholar, Department of Pharmaceutics, Deccan School of Pharmacy, Osmania University, Hyderabad, India*

[2] *Professor, Department of Pharmaceutics, Deccan School of Pharmacy, Osmania University, Hyderabad, India*

Article Info:

Article History:

Received 11 Sep 2023
Reviewed 02 Nov 2023
Accepted 26 Nov 2023
Published 15 Dec 2023

Cite this article as:

Miskan R, Shahidulla SM, Sultana S, Revolutionizing Drug Delivery: Nicardipine Nanosuspension Formulation and In-Vitro Evaluation, Journal of Drug Delivery and Therapeutics. 2023; 13(12):137-147

DOI: http://dx.doi.org/10.22270/jddt.v13i12.6134

*Address for Correspondence:

Risha Miskan, Research Scholar, Department of Pharmaceutics, Deccan School of Pharmacy, Osmania University, Hyderabad, India

Abstract

Nicardipine hydrochloride, is a potent calcium channel blocker, is commonly used in the management of hypertension and angina. It is a BCS class II drug which has low aqueous solubility and high permeability. In the present study, an attempt was made to formulate and evaluate nanosuspension of Nicardipine hydrochloride using different stabilizers, namely Tween 80, PVP K30, Poloxamer 188 by using Nanoprecipitation method with the objective to improve solubility and enhance dissolution of Nicardipine hydrochloride. Prepared nanosuspensions were evaluated for drug-excipient compatibility, particle size, PDI (Polydispersity Index), Zeta potential, Drug content, Saturation solubility, *In-vitro* release study, Scanning electron microscopy (SEM). FTIR (Fourier Transform Infrared Spectroscopy) studies revealed the compatibility of the drug with excipients. Nanosuspension (F3), which had the lowest particle size and the highest % Drug Release, was selected as the optimum formulation. It showed the droplet size, PDI, ZP,% Drug content and %Drug release of 150.4 nm,0.243, -30.6 mV,95.52%,91.24%. Kinetic release profiles of the NS F3 revealed that it followed First order kinetics. This study showed the ability of nanosuspension system in improving the solubility and drug release of Nicardipine.

Keywords: Nicardipine, Nanosuspension, Solubility, % Drug Release, % Drug content, Scanning electron microscopy.

1. INTRODUCTION

A major challenge in the formulation of new chemical entities and generics is their low aqueous solubility, a common physico-chemical property shared by most new candidates in drug discovery. Compounds with slow dissolution rates face limitations in absorption and oral bioavailability when administered orally.Oral bioavailability is influenced by several factors. To enhance the biopharmaceutical properties of drugs, various technologies are commonly applied, including micronization, nanosizing, crystal engineering, solid dispersions, and encapsulation within molecules such as cyclodextrins, lipids (e.g., solid lipid nanoparticles and liposomes), and other colloidal drug delivery systems like microemulsions and self-emulsifying drug delivery systems. The Biopharmaceutics Classification System (BCS) is a scientific classification system designed to categorize active compounds based on their aqueous solubility and in vivo bioavailability. BCS considers two fundamental factors, solubility and intestinal permeability, to predict the oral drug absorption of solid dosage forms.[1]

Nicardipine, a prominent cardiovascular medication, belongs to BCS class 2 and functions as a calcium channel blocker for short-term treatment of hypertension and angina. Its low solubility limits bioavailability, but nanosuspensions can enhance dissolution and absorption. These nanosuspensions maintain stability, prevent aggregation, and improve long-term efficacy. They expand drug options, reduce toxicity through lower doses, and enhance formulation stability, reducing the need for preservatives. This technology opens new avenues for drug development and patient treatment.[2]

Nanosuspensions refer to colloidal dispersions of submicron-sized active particles, where the stability of these nanocrystals is maintained through the use of suitable polymers and/or surfactants. In liquid form, the preservation of particle size distribution over extended storage periods presents several challenges, attributed to factors like chemical instability, reactivity, or potential drug leakage. A novel approach involves formulating nanosuspensions within gel matrices to enhance dermal penetration. The micronization of active substances results in a considerable increase in total specific surface area, consequently elevating dissolution and diffusion rates. Nonetheless, it's worth noting that for certain compounds, micronization may not yield significant benefits efficiently.[3]

2. MATERIAL AND METHODS

Drug was purchased from Lupin Pharmaceuticals. Poloxamer 188 was procured from Merck Limited, Mumbai, India, and employed in the research. PVP k-30, an essential component in the study, was also purchased from Merck Limited in Mumbai, India. Tween80, Methanol was sourced from Merck Limited in Mumbai, India.

Pre-formulation studies

Physico-Chemical properties of Nicardipine

Organoleptic properties:

The sample of Nicardipine Hydrochloride was studied for organoleptic characteristics such as color, odour, taste and appearance.[4]

Determination of Nicardipine Melting point

Melting point of Nicardipine Hydrochloride was determined by taking a small amount of sample in a capillary tube closed at one end and placed in melting point apparatus. The melting point was noted in triplicate and average value was noted.[5]

Determination of Nicardipine Solubility

By placing an excess of the drug in a conical flask with 5ml of solvent, a solubility test is conducted. Following the addition of an excessive amount of the drug, the solution is held at room temperature for shaking in an orbital shaker (remi). Samples are taken. The samples were diluted accordingly with the same solvent after being filtered using Whatman filter paper, and their concentration was assessed using UV-VIS spectroscopy[6]

Drug-Excipients compatibility studies:

Drug-excipient compatibility was performed to examine any feasible interactions linked with drug and other excipients in formulation.

FTIR Spectroscopy

Spectroscopy is an analytical technique used to identify drug substances by monitoring the functional groups exist in the compound. FTIR spectra of Nicardipine (pure) and its mixtures were done by using FTIR spectrometer (Bruker,Germany).The samples were mixed thoroughly with KBr and the spectrum was analyzed in resolution of 4/cm and frequency range of 4000 to 400 cm^{-1}.[7]

Analytical method development for Nicardipine:

Using UV spectroscopy

Determination of absorption maxima

Dissolve **100** mg of drug in **100**ml of methanol - **1000**mcg/ml (Stock 1)

Pipette out **10** ml from above stock solution and dilute to **100**ml, using 0.1N HCl.

- 100mcg/ml(stock 2)

From the above solution pipette out 2,4,6,8,10,12 ml into 10ml volumetric flask and makeup the volume with 0.1N HCL to give various concentrations such as 2,4,6,8,10 µg/ml.

Scan for maximum absorbance using UV spectrophotometer in range **200-400nm.**

The spectral data from this scan was used for the generation of standard curve.[8,9]

Calibration curve of Nicardipine

Primary stock solution (1000mcg/ml) is prepared and then secondary stock solution (100mcg/ml) is formulated from the primary stock solution.

From the above solution pipette out 2,4,6,8,10 ml into 10ml of volumetric flask and volume made up using 0.1N HCl to give various concentrations such as 2, 4, 6, 8, 10 µg/ml were made for calibration curve plotted by recording absorbance of secondary stock solution in UV spectrophotometer at 240 nm.

All the experiment was carried out in triplicate. [10,11]

Formulation and Development

Design Of Experiment

A Central Composite Design (CCD) is used for quadratic modeling in response surface methodology (RSM), requiring fewer experiments. It assesses two factors, PVP and Tween 80, at high and low levels to study their effects on particle size and drug release. Nine runs were performed and statistically analyzed using Sigmatech® software, with randomization to prevent bias.[12]

Table 1: Low and High Values of independent variables

Variable Index	Independent variable	Low (-)	High (+)
X1	PVP	20	40
X2	Tween 80	2	4

I. Preparation of Coarse Suspension

The organic phase was gradually added to aqueous phase under magnetic stirring. The formulated suspension was then subjected to sonication to reduce the particle size using the ultrasonic probe sonicator for 30 min.

II. Preparation of Nanosuspension

The coarse suspensions were introduced into microfluidizer. Each formulation was subjected to 10 cycles at 25000psi where the intensifier applies the force which leads to collision within the particles and also with the walls of micro-channels results in reduction of particle size. The formulations were collected and characterized for particle size, zeta potential and *In-vitro* drug release.[13]

Table 2: Software generated Formulations

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Nicardipine(mg)	20	20	20	20	20	20	20	20	20
Poloxamer 188	1	1	1	1	1	1	1	1	1
PVP K30	20	40	20	40	30	10	50	30	30
Tween 80(ml)	2	2	4	4	3	3	3	1	5
Methanol	2	2	2	2	2	2	2	2	2
Water(ml)	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

EVALUATIONS

Analysis of Average Particle size and Polydispersity index (PDI)

▪ **The droplet size/particle size** of the formulations generated by the CCD were measured by using Malvern Zetasizer. This instrument works generally by photon correlation spectroscopy, which measures scattering of light due to the Brownian motion in between the droplets or particles.

▪ Multiple light scattering effects were avoided during analysis by using a 10% diluted nanosuspension sample.[14]

Polydispersity index

The Surface charge and charge density of Nanosuspension droplets was determined using Malvern Zetasizer. If the PDI values of the oral nanosuspension formulations are less than 0.5, it indicates the homogeneity of the droplet size distribution as previously reported. Samples were considered to be polydisperse when the polydispersity index was higher than 0.2.[15]

Zeta Potential:

Zeta potential and electrical conductivity were also measured using Malvern Zetasizer. Zeta Potential is an important parameter to analyze the longterm stability of the nanosuspensions. Zeta Potential refers to the surface charge of the particles. It indicates the degree of repulsion between closely charged particles in the dispersion, which prevents aggregation of the particles. The nanosuspension with high zeta potential value of +ve or -ve >30 is considered to be electrically stable, while nanosuspensions with low zeta potential value. tend to coagulate. The zeta potential results of all 9 formulations are discussed in chapter.[16]

% DRUG CONTENT

To determine the drug content in the formulation, the percentage of drug incorporated/entrapped in each formulation was measured and calculate. Each 1 ml prepared nanosuspension sample was diluted with methanol and centrifuged at 3500 rpm for 30 minutes. After centrifugation, the supernatant clear layer was removed and filtered. The samples were measured at 240 nm using UV-VIS spectroscopy. Results were noted in triplicate and averaged.[17]

***IN-VITRO* DRUG RELEASE STUDIES**

The *in-vitro* release of Nicardipine nanosuspension was carried out in USP dissolution test apparatus using paddle method at a rotation speed of 50 RPM and 0.1N HCL is used as the dissolution medium. The volume and temperature of dissolution medium were 900 ml and 37.0 ± 0.2 °C, respectively. Samples (5 ml) were withdrawn for a period of 2hrs and at each specified time intervals of 15, 30, 45, 60,90,120 and were filtered. The filtered samples were analyzed at 240 nm using UV spectrophotometer. All the determination was made in triplicate.[18]

KINETIC RELEASE STUDY

To study the drug release mechanism from the optimized formulation of Nicardipine Nanosuspension F3, the % drug release data were fitted to the following equations:

Zero-order equation:

$Qt=Q_0+k_0t$

Where, Q_0 is the initial drug amount in the solution, Qt is the drug release amount in time t.

First-order equation:

$lnQt=lnQ_0+k1t$

Where, Q_0 is the initial drug amount in the solution, Qt is the drug release amount in time t, and k_1 is the first order release rate constant.

Higuchi's equation:

$Q=k_Ht1/2$

Where, k_H is the Higuchi diffusion rate constant and Q is the drug release amount at time t.

Korsmeyer Peppas equation:

$Mt/M\infty=Ktn$

Where, M_∞ is the released drug amount at time, Mt is the released drug amount at time t, n is the diffusion exponent demonstrating drug release mechanism and k is the kinetic constant.[19]

SCANNING ELECTRON MICROSCOPY

SEM was used to scan the atomic surface of optimized Nicardipine nanosuspension, which was under the view of an electron microscope, for shape and size. The surface morphology of the samples was investigated for liquid sample F3, it was prepared by the droplet evaporation technique. A droplet of liquid was deposited on double-sided carbon tape and dried at room temperature for the evaporation of water and then coated with gold and examined with a scanning electron microscope (JEOL,USA).[20,21]

SHORT TERM STABILITY ASSESSMENT:

These studies were conducted with optimized formulations. Taken the nanosuspensions in glass vials at a temperature of 4°C & 25°C. The samples were withdrawn at 0, 1, 5, 12, 20, 30 days for studying droplet size and drug content and it was noted down.[22,23]

3.RESULTS AND DISCUSSION

The primary objective of this study was to create a Nanosuspension of Nicardipine utilizing different polymers. Each of the formulations underwent an assessment of their physicochemical characteristics and were subjected to in vitro studies to analyze drug release patterns.

PHYSICOCHEMICAL ATTRIBUTES OF NICARDIPINE

Table 3: Organoleptic properties

S.no	Test	Description
1	Colour	Pale yellowish powder
2	Odour	Odourless
3	Appearance	Powder
4	Taste	Bitter taste

Melting point: The M.P of Nicardipine was found to be 171 °C which was observed to be in the standard reference range according to the literature.

Table 4: Melting Point of Nicardipine

S.no	Pure drug	Reference range	Observed value
1.	NICARDIPINE	168 - 175°C.	171°C.

Solubility studies

The absorbance of the drug was measured with UV Visible Spectrophotometer at 240 nm and its concentration was calculated, the highest solubility was found to be in methanol i.e 81.8 µg/mL

Table 5: Solubility studies of drug in different solvents

S.no	Solvents	Solubility (µg/ml)
1	Water	2.5 ± 0.13
2	6.8 phosphate buffer	20.3 ± 0.39
3	Methanol	81.8 ± 0.84
4	DMSO	45.1± 0.30
5	0.1N HCL	76.5 ± 0.53

Results are expressed as mean ± S.D (n = 3)

UV-Spectroscopic examination of drug

Determination of λ max for Nicardipine in 0.1N HCL by UV:

The Nicardipine solution underwent spectral analysis within the wavelength range of 200-400 nm, uncovering notable absorbance specifically at 240 nm. Due to the distinct and highest peak in the absorption spectrum occurring at 240 nm, this wavelength was selected for detection when using methanol as the solvent.

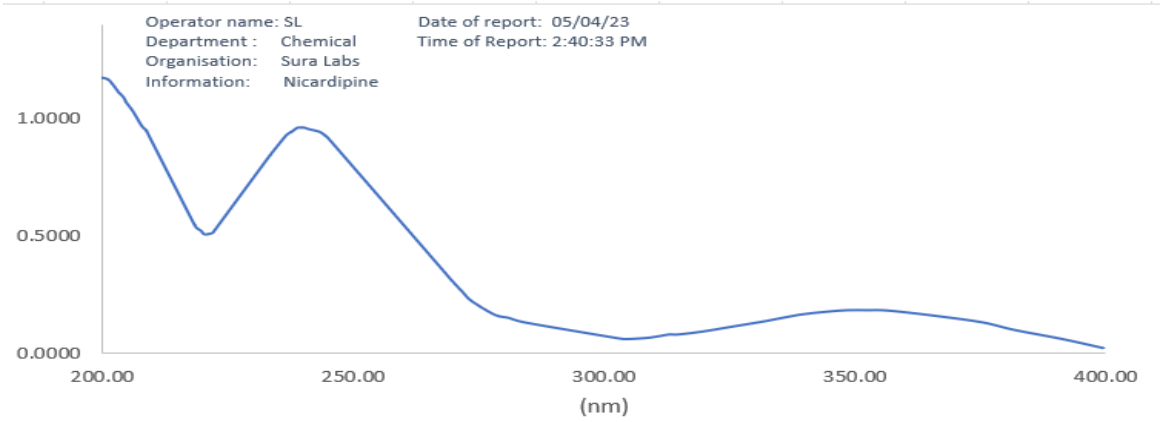


Figure 1: Spectra for Nicardipine Wavelength Optimization

Standard Calibration curve of Nicardipine in 0.1N HCL:

Table 6: Table showing absorbance values at multiple concentrations

Concentration (µg/ml)	Absorbance
0	0
2	0.163±0.014
4	0.322±0.057
6	0.471±0.010
8	0.631±0.105
10	0.782±0.081
12	0.931±0.04

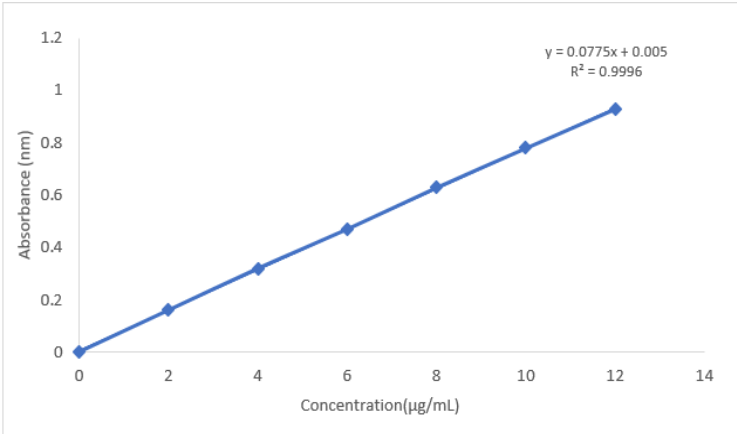


Figure 2: Calibration Curve Data of Nicardipine In 0.1N HCL

From the prepared stock solution, various dilutions of the sample solutions were prepared and analyzed at 240 nm. The different dilutions showed absorbance values and the standard graph was obtained by taking concentration on X-axis and Absorbance on Y-axis.

Y=0.0775x + 0.005 R^2Value Was Ascertained to be 0.9996.

FTIR REPORTS

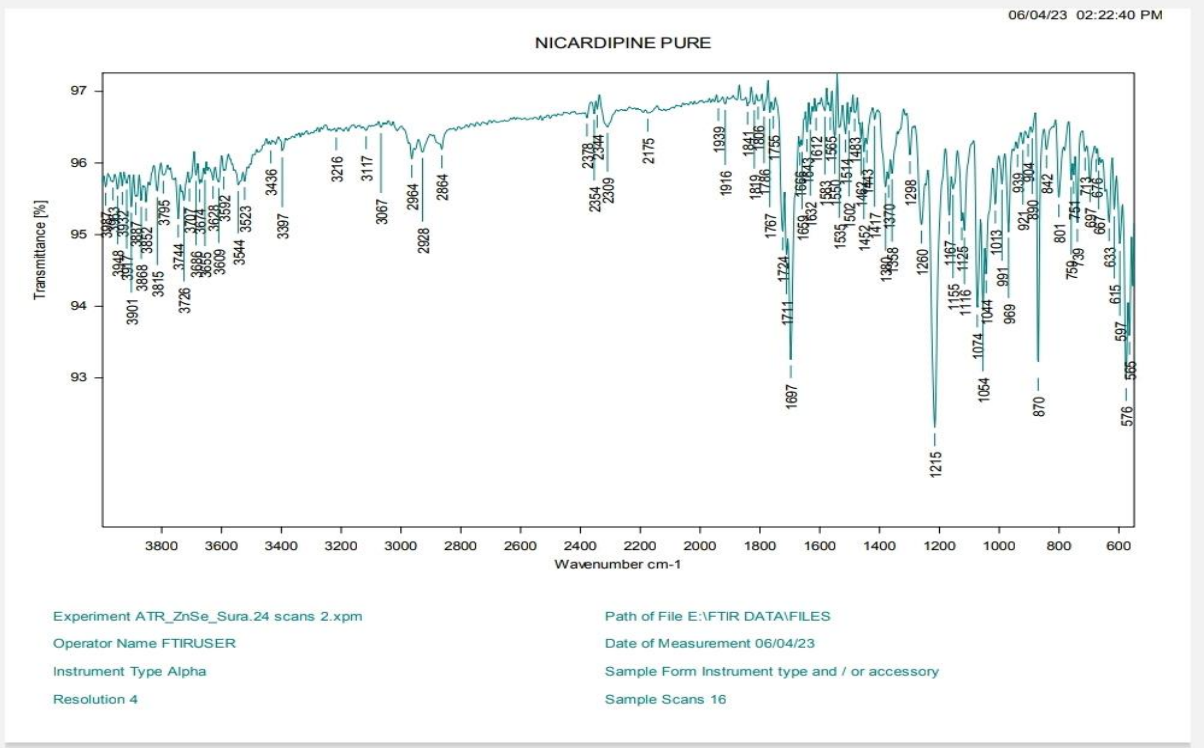


Figure 3: FTIR RESULTS

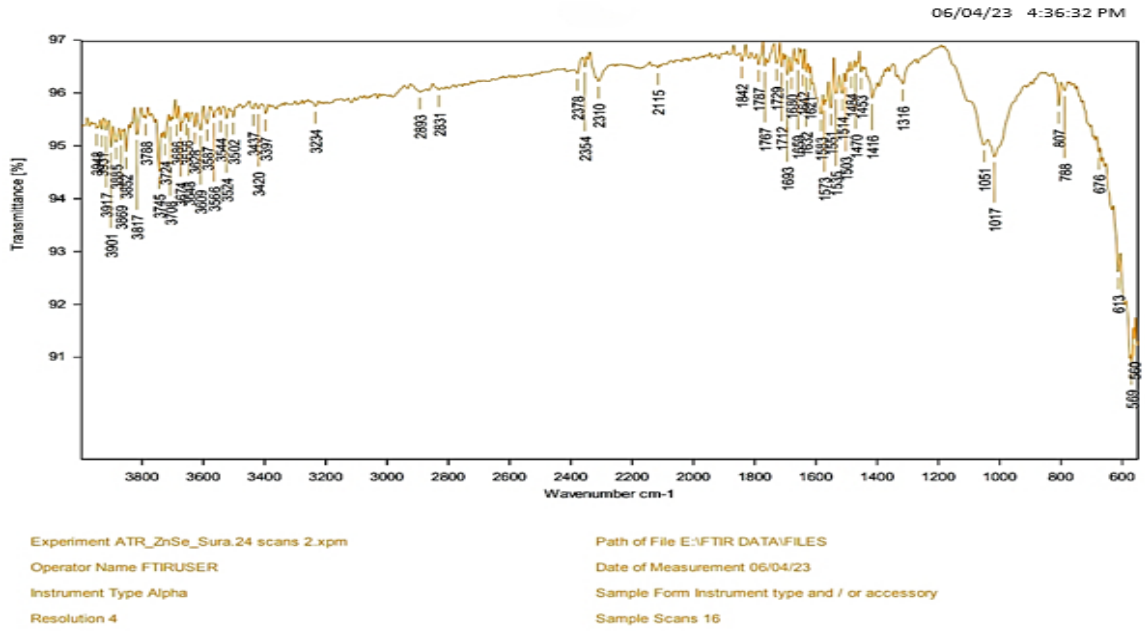


Figure 4: FTIR Spectra for Pure Nicardipine Along with Poloxamer 188, PVP – K30, Tween 80

The FTIR spectrum of Nicardipine-excipients mixture was confirmed by FTIR. The spectrum of Nicardipine-excipients mixture showed presence of its characteristic absorption peaks of; –NH stretch at 3240 cm^{-1}, C-H stretch at 2893 cm^{-1}, C=O stretch at 1693 cm^{-1}, Nitro group stretch at 1316 cm^{-1}, C=C stretch at 1642 cm^{-1}, C-N stretch at 1261 cm^{-1}.The spectral data shows that the major peaks were obtained as closer values and that there were no important changes in IR peaks from the physical mixtures of nicardipine and excipients.

Experimental Design and Optimization

Nanosuspensions were prepared using probe sonicator and High pressure homogenizer (Microfluidizer)

Figure 5: Samples of Coarse Suspension

Figure 6: Samples of Nanosuspension

The prepared formulations were optimized using 2^2 CCD which gives a total of 9 formulation values including midpoint value. The independent variables selected for optimization were PVP K30 (X1) and TWEEN 80 (X2) and the dependent variables were Particle size and %Drug release.

Central Composite Plan

Project Name : nic nano

y1 y2

Sl No..	Combinations	X1	X2	particle size	dr
1	I	20	2	159.4	87.13
2	X1	40	2	165.2	85.09
3	X2	20	4	150.4	91.24
4	X1X2	40	4	282.6	74.62
5	Mid Point	30.0	3.0	186.2	79.51
6	X1At -2 L	10.0	3.0	292.1	71.03
7	X1At +2 L	50.0	3.0	191.8	78.42
8	X2At -2 L	30.0	1.0	179.3	83.53
9	X2At +2 L	30.0	5.0	157.2	89.01

Back Save Print Cl... Analysis

Figure 7: Formulation, Particle Size And % Drug Release Table of F1-F9 Formulations

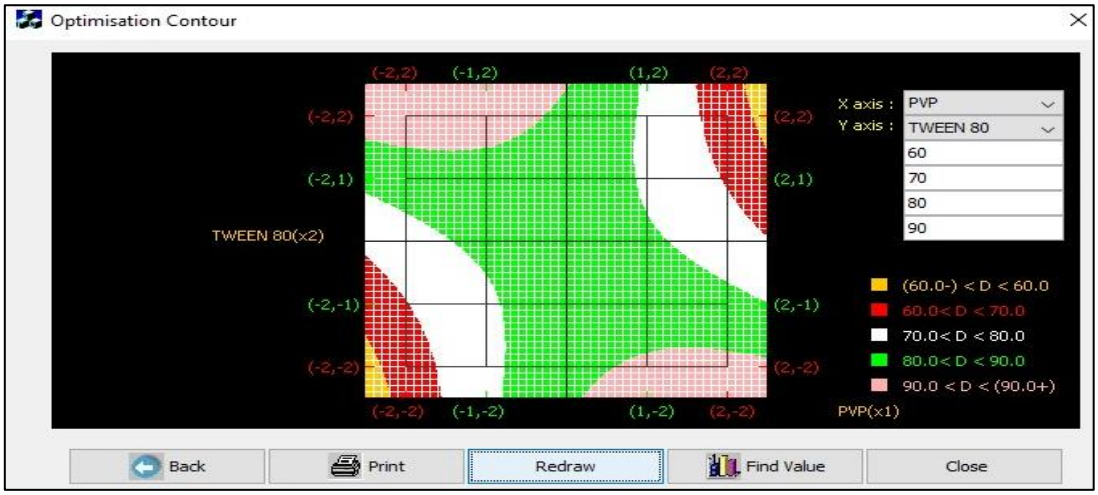


Figure 8: Contour Plot showing Optimized formulation

The findings and observations were verified by analyzing the contour plot depicting Particle Size and % Drug Release. Fig. No (8) illustrates this contour plot, highlighting the interactions between PVP K30 and TWEEN 80. Notably, it reveals an optimal design space, ranging from 80% to 90%.

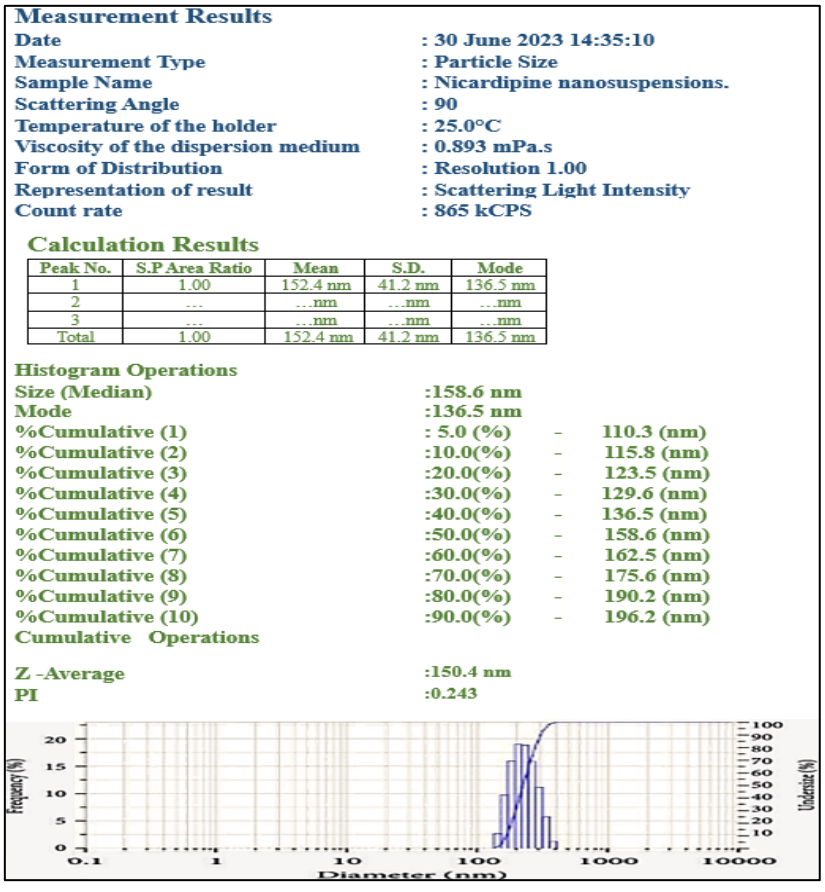
EVALUATIONS

Average Particle size & polydispersity index (PDI) analysis:

The lowest particle size of 150 nm was obtained for F3 formulation with a PDI of 0.243.

Table 7: The Particle sizes and PDI values of all formulations

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9
P. Size (nm)	159.4	165.2	150.4	282.6	186.2	292.1	191.8	179.3	157.2
PDI	0.329	0.362	0.243	0.527	0.453	0.559	0.513	0.451	0.256



Measurement Results

Date	: 30 June 2023 14:35:10
Measurement Type	: Particle Size
Sample Name	: Nicardipine nanosuspensions.
Scattering Angle	: 90
Temperature of the holder	: 25.0°C
Viscosity of the dispersion medium	: 0.893 mPa.s
Form of Distribution	: Resolution 1.00
Representation of result	: Scattering Light Intensity
Count rate	: 865 kCPS

Calculation Results

Peak No.	S.P Area Ratio	Mean	S.D.	Mode
1	1.00	152.4 nm	41.2 nm	136.5 nm
2	...	...nm	...nm	...nm
3	...	...nm	...nm	...nm
Total	1.00	152.4 nm	41.2 nm	136.5 nm

Histogram Operations

Size (Median)	:158.6 nm		
Mode	:136.5 nm		
%Cumulative (1)	: 5.0 (%)	-	110.3 (nm)
%Cumulative (2)	:10.0(%)	-	115.8 (nm)
%Cumulative (3)	:20.0(%)	-	123.5 (nm)
%Cumulative (4)	:30.0(%)	-	129.6 (nm)
%Cumulative (5)	:40.0(%)	-	136.5 (nm)
%Cumulative (6)	:50.0(%)	-	158.6 (nm)
%Cumulative (7)	:60.0(%)	-	162.5 (nm)
%Cumulative (8)	:70.0(%)	-	175.6 (nm)
%Cumulative (9)	:80.0(%)	-	190.2 (nm)
%Cumulative (10)	:90.0(%)	-	196.2 (nm)

Cumulative Operations

Z -Average	:150.4 nm
PI	:0.243

Figure 9: Average Particle Size & PDI Of Optimized Formulation F3

Zeta Potential

The highest zeta potential value of -30.6 mV was observed to be of F3 formulation, which indicates that it is a stable nanosuspension.

Table 8: Zeta Potential

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9
Zeta Potential (mV)	-26.4	-23.6	-30.6	-19.4	-21.3	-17.64	-20.8	-22.3	-27.5

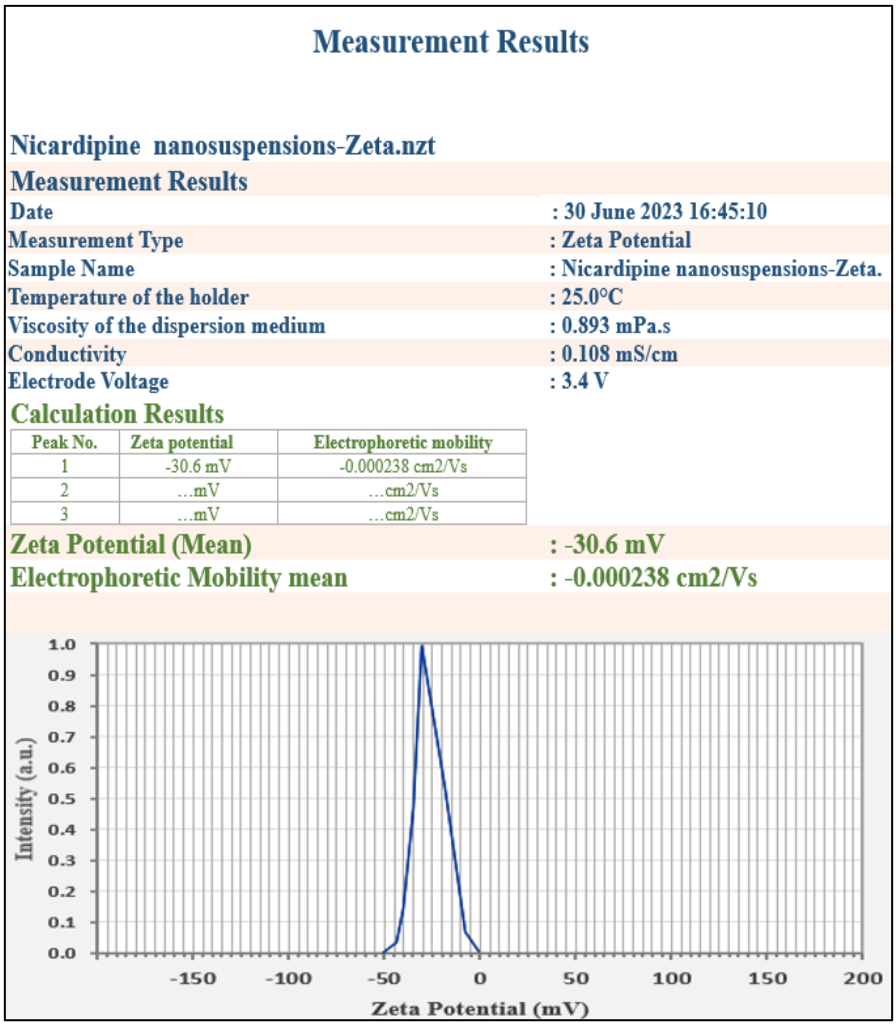


Figure 10: Zeta Potential of Optimized Formulation F3

% Drug Content

The highest % DC of 95.52% w/vof the nanosuspension with ± 0.06 standard deviation was found in F3.

Table 9: % Drug Content

Formulation	% Drug Content
F1	92.51 ± 0.19
F2	91.26 ± 0.81
F3	95.52 ± 0.06
F4	87.73 ± 0.08
F5	89.21 ± 0.75
F6	85.04 ± 0.93
F7	88.59 ± 0.87
F8	90.39 ± 0.29
F9	93.13 ± 0.76

***IN-VITRO* DRUG RELEASE STUDIES**

The cumulative drug release, F3 nanosuspension shows 91.24%, release at the end of the 120th min. It was observed that as the particle size increases, the release rate decreases.

Table 10: % Drug Release of Nicardipine nanosuspension

Time (mins)	F1	F2	F3	F4	F5	F6	F7	F8	F9
15	17.93 ±0.29	15.25 ±0.53	23.04 ±0.12	20.35 ±0.81	17.25 ±0.19	19.62 ±0.08	20.82 ±0.17	20.81 ±0.81	21.73 ±0.03
30	33.17 ±0.65	30.64 ±0.23	31.42 ±0.76	35.62 ±0.92	31.46 ±0.54	31.62 ±0.75	34.53 ±0.89	39.42 ±0.90	39.46 ±0.75
45	47.82 ±0.43	56.23 ±0.90	49.51 ±0.45	42.59 ±0.37	38.39 ±0.09	48.93 ±0.29	47.62 ±0.98	52.92 ±0.23	46.39 ±0.09
60	51.64 ±0.83	59.49 ±0.74	57.95 ±0.63	49.91 ±0.88	54.62 ±0.76	56.92 ±0.96	51.64 ±0.19	59.59 ±0.71	58.46 ±0.61
90	71.81 ±0.72	74.81 ±0.88	79.36 ±0.51	66.51 ±0.02	69.51 ±0.96	61.23 ±0.67	69.91 ±0.63	69.43 ±0.32	77.82 ±0.34
120	87.13 ±0.87	85.09 ±0.98	91.24 ±0.65	74.62 ±0.82	79.51 ±0.12	71.03 ±0.16	78.42 ±0.88	83.53 ±0.34	89.01 ±0.08

Results are expressed as mean ± S.D, n=3 nanosuspension

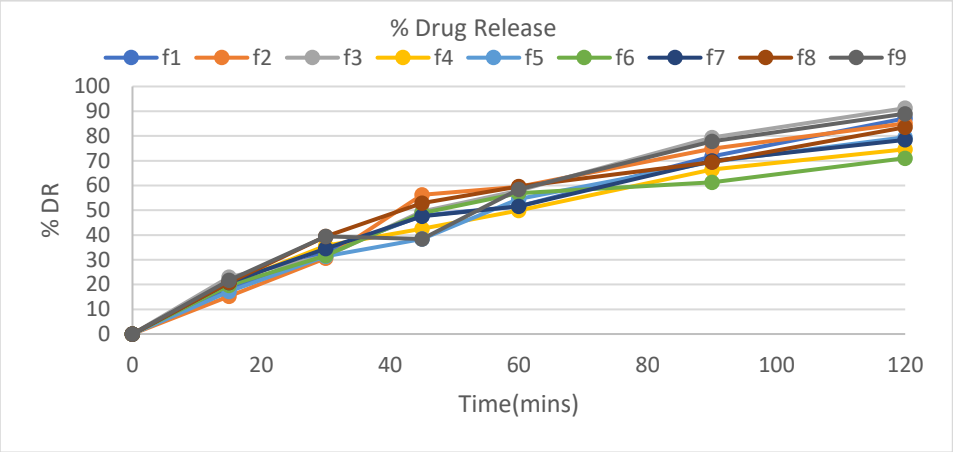


Figure 11: *In-vitro* Dissolution Studies Graph

OPTIMIZED FORMULA EVALUATIONS

Table 11: The DOE, Formulation & Optimization:

Formulation	Particle Size (nm)	PDI	Z.P (mV)	DC (%)	DR (%)
NSF1	159.4	0.329	-26.4	92.51	87.13
NSF2	165.2	0.362	-23.6	91.26	85.09
NSF3	150.4	0.243	-30.6	95.52	91.24
NSF4	282.6	0.527	-19.4	87.73	74.62
NSF5	186.2	0.453	-21.3	89.21	79.51
NSF6	292.1	0.559	-17.64	85.04	71.03
NSF7	191.8	0.513	-20.8	88.59	78.42
NSF8	179.3	0.451	-22.3	90.39	83.53
NSF9	157.2	0.256	-27.5	93.13	89.01

Kinetic Release Profiles

The kinetic release profiles indicates that the kinetics of % DR data were fitted to the zero-order and 1st order. The profiles shows that the optimized formula F3 followed First order kinetics (**fig. no. 12**) with an R^2 valueof 0.973.

Table 12: Release kinetics for optimized formulation

PLOT	SLOPE	INTERCEPT	COR-RELATION	R^2
ZERO ORDER (% CDR Vs T)	0.743622754	9.259401198	0.982128483	0.964576357
FIRST ORDER (Log % RemainVs T)	-0.008626373	2.05887741	-0.986431428	0.973046962

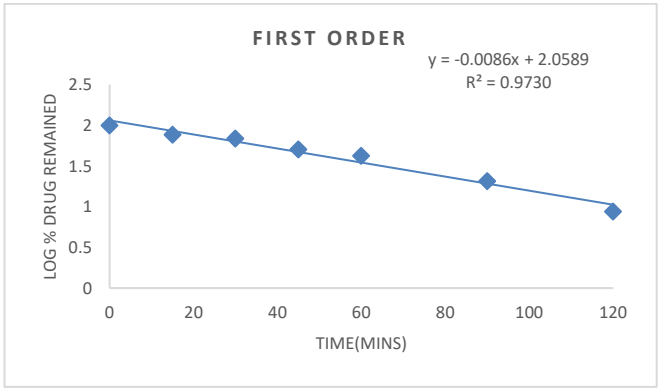


Figure 12: First Order Kinetics

Figure 13: Zero Order Kinetics

Scanning Electron Microscopy

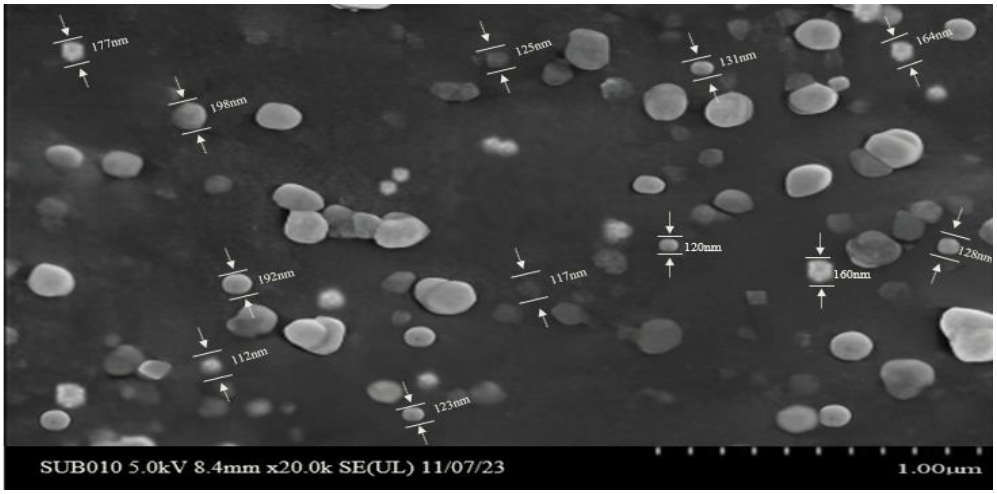


Figure 14: Scanning Electron Microscopy Study

The SEM studies of the optimized Nicardipine nanosuspension formula F3 showed showed smooth uniform particles within the nano size (Fig. No. 14) and the result obtained is found to be satisfactory.

Short term Stability assessment of optimized nanosuspension

The droplet sizeand % drug content showed slight change over time but it was found to be negligible.

Table 13: Short term stability study of optimized nanosuspension F3

Assessment Parameter	Temperature	Number of days					
		Day 0	Day 1	Day 5	Day 12	Day 20	Day 30
Droplet Size (nm)	4 ˚C	150.4	150.6	151.2	151.8	152.7	153.5
	25 ˚C	150.4	152.2	159.3	165.1	172.2	181.7
% Drug Content	4 ˚C	95.5	95.5	95.4	95.2	94.9	94.5
	25 ˚C	95.5	95.4	95.4	95.0	94.7	94.4

CONCLUSION

In conclusion, this study successfully developed nanosuspensions of Nicardipine hydrochloride, a challenging drug due to its low solubility. By utilizing different stabilizers and the nanoprecipitation method, we improved its solubility and dissolution properties. The drug and excipient compatibility was confirmed by FTIR studies. Nanosuspension F3, with small Particle size of 150.4 nm, low PDI (0.243), and a highly negative Zeta potential (-30.6 mV), demonstrated excellent stability and uniformity. It also boasted a high Drug content of 95.52%, ensuring proper dosing. Most importantly, these nanosuspensions substantially enhanced Nicardipine hydrochloride's solubility and dissolution rates, crucial for its therapeutic effectiveness. Nanosuspension F3, following First order kinetics, emerged as the optimized formulation. This research highlights the potential of nanosuspension systems to overcome solubility challenges and improve drug delivery, offering promising prospects for enhancing cardiovascular medication effectiveness and patient care.

REFERENCES

1. Kawabata Y, Kwada K, Nakatani M, SYamada S, Onoue S, Formulation design for poorly water-soluble drugs based on biopharmaceutics classification system: basic approaches and practical applications, Int. J. Pharm, 2011;420(1): 1-10. https://doi.org/10.1016/j.ijpharm.2011.08.032 PMid:21884771

2. Kumar S, Singh P, Various techniques for solubility enhancement: an overview, Pharma Innov. J, 2016; 5(1):23-28.

3. Wang Y, Zheng Y, Zhang L, Wang Q, Zhang D,Stability of nanosuspensions in drug delivery, J Control Release, 2013;172(3):1126-41. https://doi.org/10.1016/j.jconrel.2013.08.006 PMid:23954372

4. Shen C, Shen B, Liu X, Yuan H, Nanosuspensions based gel as delivery system of nitrofurazone for enhanced dermal bioavailability, J. Drug Deliv. Sci. Technol, 2018;43: 1-11. https://doi.org/10.1016/j.jddst.2017.09.012

5. Jane M, Agrawal S, Khan A, Formulation And Evaluation Of Nanosuspension Of Valsartan, Int J Curr Pharm Res, 2018;10(2):68-74. https://doi.org/10.22159/ijcpr.2018v10i2.25874

6. Bhalekar R. Mangesh, Madgulkar R. Ashwini, Shaikh G.Shagufta, Formulation and Evaluation of Chitosan- Based Mucoadhesive Buccal Patch of prochlorperazine Maleate, An International Journal of Pharmacy and Pharmaceutical Research, 2018;12(4):61-73.

7. Vinod K.R, Santhosha D, Anbazhagan. S, Formulation And Evaluation of Piperine Cream a New Herbal Dimensional Approach For Vitiligo Patients, International Journal Of Pharmacy And Pharmaceutical Sciences, 2011;3(2):29-33.

8. Pandey N, Dr. Sah AN, Mahara K, Formulation and evaluation of floating microspheres of nateglinide, Int J Pharm Sci Res, 2016;7:453-464.

9. Jassem NA, Rajab NA, Formulation and in vitro evaluation of azilsartan medoxomil nanosuspension, Int J Pharm Pharm Sci, 2017;9(7):110-119. https://doi.org/10.22159/ijpps.2017v9i7.18917

10. Sumathi R, Tamizharasi S, Sivakumar T, Formulation and evaluation of polymeric nanosuspension of naringenin, Int J Appl Pharm, 2017;9(6):60-70. https://doi.org/10.22159/ijap.2017v9i6.21674

11. Anjane M, Agrawal S, Khan A, Formulation and evaluation of nanosuspension of Valsartan, Int J Curr Pharm Res, 2018;10(2):68-74. https://doi.org/10.22159/ijcpr.2018v10i2.25874

12. Karakucuk A, Celebi N, Teksin ZS, Preparation of ritonavir nanosuspensions by microfluidization using polymeric stabilizers: I. A Design of Experiment approach, Eur J Pharm Sci, 2016;95:111-121. https://doi.org/10.1016/j.ejps.2016.05.010 PMid:27181836

13. Jawahar, N. & S.N, Meyyanathan & Senthil, Vel & Kuppusamy, Gowthamarajan & Elango, K, Studies on physico-chemical and pharmacokinetic properties of olanzapine through nanosuspension, Journal of Pharmaceutical Sciences and Research, 2013;5(10):196-202.

14. Patel DJ, Pandya VM, Patel JK, International Journal of Pharmaceutical Research, 2009;5(2):3318-3324.

15. Liu D, Pan H, He F, Wang X, Li J, Yang X, Effect of particle size on oral absorption of carvedilol nanosuspensions: In vitro and in vivo evaluation, Int J Nanomedicine, 2015;10:6425-6434. https://doi.org/10.2147/IJN.S87143 PMid:26508852 PMCid:PMC4610768

16. Yuancai D, Wai KN, Jun H, Shoucang S, Reginald BHT, A continuous and highly effective static mixing process for antisolvent precipitation of nanoparticles of poorly water-soluble drugs, Int J Pharm, 2010; 386(1-2):256-261 https://doi.org/10.1016/j.ijpharm.2009.11.007 PMid:19922777

17. Patravale V.B, Date A.A, Kulkarni R.M. Nanosuspensions: A Promising Drug Delivery Strategy, Journal of Pharmacy Pharmacology, 2004;56(7): 827-840. https://doi.org/10.1211/0022357023691 PMid:15233860

18. Vyas Himanshu D, Parmar Ghanshyam, Shah Nirmal, Chauhan Sachin, Seth A K, Formulation and evaluation of fast dissolving film of methylcobalamin, An International Journal of Pharmaceutical Sciences, 2015;6(4):50-68.

19. Murthy KVR, Raju V, Development and validation of new discriminative dissolution method for carvedilol tablets, Indian J Pharm Sci, 2011;73(5):527-536. https://doi.org/10.4103/0250-474X.99000 PMid:22923865 PMCid:PMC3425064

20. Bajaj A, Rao MRP, Pardeshi A, Sali D, Nanocrystallization by evaporative antisolvent technique for solubility and bioavailability enhancement of telmisartan, AAPS Pharm SciTech, 2012;13(4): 1331-1340. https://doi.org/10.1208/s12249-012-9860-x PMid:23054986 PMCid:PMC3513472

21. Yasemin, Budama-Kilinc, Piperine Nanoparticles for Topical Application:Preparation, Characterization, In vitro and In silico Evaluation,Chemistry Select, 2019;4(40):11693- 11700. https://doi.org/10.1002/slct.201903266

22. Vijay Agarwal1,and Meenakshi Bajpai, Preparation and Optimization of Esomeprazole Nanosuspension using Evaporative Precipitation-Ultrasonication, Tropical Journal of Pharmaceutical Research, 2014;13(4):497-503. https://doi.org/10.4314/tjpr.v13i4.2

23. Dolenc A, Govedarica B, Kocbek P, Srčič S, Kristl J, Nanosized particles of orlistat with enhanced in vitro dissolution rate and lipase inhibition, International journal of pharmaceutics, 2010;396(1-2):149-155. https://doi.org/10.1016/j.ijpharm.2010.06.003 PMid:20540997