International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 16, Issue 4, 2024

Original Article

ANALYTICAL METHOD DEVELOPMENT, VALIDATION AND SOLUBILITY ESTIMATION OF NICARDIPINE HCL IN VARIOUS OIL SOLVENTS, SURFACTANTS AND COSURFACTANTS

RAHUL Y. PAGAR*, AVINASH B. GANGURDE

Department of Pharmaceutics, K. B. H. S. S. Trust's Institute of Pharmacy, Malegaon, Nashik-423105, Maharashtra, India
***Corresponding author: Rahul Y. Pagar; *Email: raahulpagar@gmail.com**

Received: 29 Apr 2024, Revised and Accepted: 05 Jun 2024

ABSTRACT

Objective: This study is focused on the development of an analytical method and the evaluation of the solubility of Nicardipine HCl (NHCL) in various oil solvents, surfactants, and cosurfactants using the saturated solubility determination method employing UV Spectrophotometry.

Methods: Lipophilic solvents such as Caprylic Capric, Soyabean oil, linseed oil, Coconut oil, Sunflower oil, Corn oil, Olive oil, Peanut oil, and Cottonseed oil were utilized, along with surfactants Tween 60 and Tween 80, and cosurfactants PEG 200 and Transcutol HP. Analytical validation parameters, including linearity and range, precision, limit of Detection (LOD), limit of Quantification (LOQ), ruggedness, robustness, and accuracy, were assessed according to the International Council for Harmonisation (ICH) guidelines. The solubility of NHCL in all of the aforementioned solvents was evaluated using the saturated solubility determination method.

Results: Linearity analysis revealed a linear relationship, determined by an R^2 value between concentration and absorbance. Intra-day precision demonstrates method reliability, with all Percent Relative Standard Deviation (%RSD) values ranging between 0.8426 and 1.9417%. LOD and LOQ values ranged between 1.1478 and 8.1632 µg/ml and 3.4783 and 24.7368 µg/ml, respectively. Ruggedness analysis exhibited good control over external experimental factors, with %RSD between 0.3433 and 1.9183%. Robustness assessment demonstrated consistent performance even with slight changes in environmental conditions, with %RSD between 0.5450 and 1.6443%. Accuracy study indicated % recovery values between 98.53 and 100.89%, suggesting minimal interference from excipients in the formulation.

Conclusion: Caprylic Capric, as an oil/triglyceride, exhibited a solubility of 0.94 mg/ml. Tween-80, as a surfactant, showed a solubility of 23.58 mg/ml, and Transcutol HP, as a cosurfactant, demonstrated a solubility of 38.18 mg/ml for NHCL

Keywords: Solubility, Bioavailability, Nicardipine HCl, Caprylic capric, Tween 80, Transcutol HP

DOI: https://dx.doi.org/10.22159/ijap.2024v16i4.51264 Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Nicardipine HCl (NHCL) falls under the category of dihydropyridine derivatives. NHCL represents the monohydrochloride salt of 2,6-dimethyl-5-methoxycarbonyl-3-(2-N-benzyl-methylamino) ethoxycarbonyl-4-(3-nitrophenyl)-1,4 dihydropyridine hydrochloride. This substance presents as a greenish-yellow crystalline powder with a subtle bitter taste and no discernible odour [1].

NHCL is a calcium channel blocker with potent vasodilator and antihypertensive characteristics. It undergoes rapid absorption primarily from the jejunum and ileum, key segments of the digestive tract [2]. It may be administered alone or in combination with an angiotensin-converting enzyme inhibitor. Additionally, NHCL dilates coronary arteries; thereby augmenting blood supply to the myocardium [3-5]. NHCL is classified as a BCS class II drug, indicating high permeability but low solubility. Water solubility significantly affects drug dissolution and bioavailability. Compounds with greater solubility typically exhibit enhanced absorption and increased bioavailability [6-18].

The solubility of BCS class II drugs can be improved through the dry emulsion techniques, employing lyophilization [19-25].

This study focuses on comprehensive exploration of the solubility behaviour of NHCL, an important cardiovascular drug, in a wide range of oil solvents, surfactants, and cosurfactants. By examining the solubility profiles across different solvents, this research will help for enhancing the bioavailability and efficacy of NHCL formulations. Furthermore, the inclusion of surfactants and cosurfactants in the investigation reflects a contemporary approach to pharmaceutical formulation, considering the importance of solubility enhancement techniques in improving drug delivery systems.

Moreover, the analytical method development and validation aspects underscore the rigor and reliability of the analytical techniques employed in quantifying NHCL concentrations. The validation process ensures the linearity, precision, LOD, LOQ, ruggedness, robustness, and accuracy of the analytical method, thus ensuring the credibility of the experimental results. This contributes to the scientific community by providing a validated analytical method that can be utilized for routine quality control analysis of NHCL formulations.

In essence, this study amalgamates analytical chemistry principles with pharmaceutical formulation science to address the critical need for robust analytical methods and enhanced solubility understanding in the development of NHCL formulations. Its comprehensive approach and scientific rigor make it a valuable contribution to both academia and the pharmaceutical industry, with potential implications for improving therapeutic outcome and patient care.

MATERIALS AND METHODS

Materials

NHCL, Caprylic Capric, and Transcutol HP were obtained as gift samples from Subhash Chemical Industries Pvt. ltd. Polyethylene glycol 200 (PEG-200), Tween-60, and Tween-80 were purchased from Vishal Chemicals. The Coconut Oil (Marico limited, Mumbai), Soyabean Oil (Pataldhamal Wadhwani Agri Tech Pvt. ltd.), Linseed Oil (Mahesh Agro Food Industries, Rajasthan), Corn Oil (Cargill India Pvt. ltd., Mumbai), Cottonseed Oil (Ashwin Vanaspati Industries Pvt. ltd.), Olive Oil (V. G. Kannan Foods Pvt. ltd., Mumbai), and Peanut Oil (Nav Maharashtra Agro Industries Pvt. ltd., Pune) were purchased from the suppliers.

Determination of λ max of NHCL in various solvent

A standard stock solution containing 100 µg/ml of NHCL was prepared by dissolving 10 mg of NHCL in Caprylic Capric, Soyabean Oil, Linseed Oil, Coconut Oil, Sunflower Oil, Corn Oil, Olive Oil, Peanut Oil, Cottonseed Oil, Tween-60, Tween-80, PEG-200, and Transcutol HP, and analysed on UV Spectrophotometer between 400-200 nm, and λ max was recorded.

Linearity and range

For the linearity study, five different dilutions of NHCL were prepared in each solvent as shown in table 1 and used for calibration curve plot (n=3). The intercept and slope for each solvent used were determined from the calibration curve.

Precision

Solutions of dilutions, as shown in table 2, were used to determine precision. Six samples (n=6) of the same concentration were used, and absorbance was recorded. Mean, Standard Deviation (SD), and % RSD were calculated.

Table 1: Solvent and different concentration (µg/ml) used for linearity study

Solvent	Concentration (µg/ml)	Solvent	Concentration (µg/ml)
Caprylic Capric	100, 150, 200, 250, 300	Corn Oil	50, 100, 150, 200, 250
Linseed Oil		Peanut Oil	
Sunflower Oil	50, 75, 100, 125, 150	Soyabean Oil	20, 40, 60, 80, 100.
Olive Oil	100, 120, 140, 160, 180	Cottonseed Oil	100, 150, 200, 250, 300
Tween-80	10, 20, 30, 40, 50	Tween-60	50, 70, 90, 110, 130
PEG-200	10, 15, 20, 25, 30	Transcutol HP	20, 40, 60, 80, 100

Table 2: Solvent and different concentration (µg/ml) used for precision study

Concentration (µg/ml)	Solvent	Concentration (µg/ml)	Solvent
200	Caprylic Capric and Cottonseed oil	150	Linseed Oil, Corn Oil and Peanut Oil
120	Olive Oil	100	Coconut Oil
90	Tween-60	75	Sunflower Oil
60	Soyabean Oil and Transcutol HP	30	Tween-80 and PEG-200

LOD and LOQ

LOD and LOQ were calculated for each used solvent by using formula for

$$\text{LOD} = \frac{3.3 \times \text{Standard Deviation}}{\text{Slope}} \text{LOQ} = \frac{10 \times \text{Standard Deviation}}{\text{Slope}}$$

Ruggedness

Solutions of dilutions, as shown in table 3, were used to study ruggedness. Two analysts at the same environmental condition and on the same instrument conducted the experiment. Three samples (n=3) of the same concentration were used, and absorbance was recorded mean absorbance, SD, and %RSD were calculated.

Table 3: Solvent and different concentration (µg/ml) used for ruggedness study

Concentration (µg/ml)	Solvent	Concentration (µg/ml)	Solvent
200	Cottonseed oil	150	Caprylic Capric, Corn Oil and Peanut Oil
125	Sunflower Oil		
100	Linseed Oil	120	Coconut Oil and Olive Oil
80	Soyabean Oil	90	Tween-60
30	Tween-80 and PEG-200	60	Transcutol HP

Robustness

Solutions of dilutions, as shown in table 4, were used to study robustness at two different temperature conditions (Room Temperature-36 °C and 20 °C). Six samples (n=6) of the same concentration were used, and absorbance was recorded. Mean absorbance, SD, and %RSD were calculated.

Accuracy/% recovery

Three different concentrations of 80%, 100%, and 120% of NHCL in each solvent were prepared using the label claim of the marketed product and bulk NHCL. Three samples (n=3) of each concentration were used, and absorbance was recorded. Mean absorbance, SD, and % Recovery were calculated [26-33].

Table 4: Solvent and different concentration (µg/ml) used for robustness study

Concentration (µg/ml)	Solvent	Concentration (µg/ml)	Solvent
200	Cottonseed oil	150	Caprylic Capric, Linseed Oil, Corn Oil and Peanut
120	Olive Oil		Oil
100	Coconut Oil	90	Tween-60
75	Sunflower Oil	60	Transcutol HP and Soyabean Oil
30	Tween-80 and PEG-200		

Saturated solubility study

Excess amounts of the drug were added to 10 ml of an appropriate solvent in glass vials. These vials were then placed on an orbital shaker and subjected to agitation for 48 h at a speed of 50 rpm, maintaining a constant temperature of approximately 37±0.5 °C. Subsequently, the resulting samples were filtered using syringe filters with a pore size of 0.22 µm. The filtrate was collected and appropriately diluted with the same solvent. The absorbance of the drug was then analysed using a UV-Visible Spectrophotometer at the pre-scanned λmax in the respective solvent (n=3). Finally, the mean absorbance values were converted into concentrations using a standard curve of the drug in the solvent [34].

RESULTS AND DISCUSSION

Linearity and Range

Table 4 represents the λ max, concentration range, and mean absorbance for different dilutions of the solvents used. Fig. 1 to 13

show concentration-versus-absorbance graphs, along with the corresponding R^2 values for each solvent.

Linearity, studied by the R^2 value, was found to be between 0.9873 and 0.9999, revealing a linear relationship between the concentration and absorbance of NHCL in various solvents. These values are close to those determined by Naik and Pai (2013) and Nagaraju *et al.* (2014), which were 0.991 and 0.997, respectively [35, 36]. Apridamayanti P. *et al.*(2024), discussed the significance of R^2 value in linearity study [37].

Table 4: λ max, concentration range, and mean absorbance for NHCL in solvents used

Caprylic Capric (λ max= 349 nm)					
Conc. (µg/ml)	100	150	200	250	300
mean Absorbance	0.1601±0.0043	0.2615±0.0060	0.3527±0.0038	0.4464±0.0092	0.5480±0.0099
Soyabean Oil (λ max= 345 nm)					
Conc. (µg/ml)	20	40	60	80	100
mean Absorbance	0.2762±0.0074	0.3225±0.0053	0.4057±0.0052	0.4966±0.0049	0.5875±0.0025
Linseed Oil (λ max= 376 nm)					
Conc. (µg/ml)	100	150	200	250	300
mean Absorbance	0.2092±0.0015	0.2891±0.0049	0.4248±0.0052	0.5749±0.0062	0.6894±0.0064
Coconut Oil (λ max= 349 nm)					
Conc. (µg/ml)	60	80	100	120	140
mean Absorbance	0.3628±0.0096	0.4668±0.0049	0.5403±0.0045	0.6195±0.0032	0.7248±0.0052
Sunflower Oil (λ max= 344 nm)					
Conc. (µg/ml)	50	75	100	125	150
mean Absorbance	0.1482±0.0044	0.3366±0.0050	0.5100±0.0088	0.6504±0.0047	0.7904±0.0016
Corn Oil (λ max= 376 nm)					
Conc. (µg/ml)	50	100	150	200	250
mean Absorbance	0.1032±0.0029	0.2240±0.0053	0.3364±0.0047	0.3960±0.0045	0.5004±0.0082
Olive Oil (λ max.= 330 nm)					
Conc. (µg/ml)	100	120	140	160	180
mean Absorbance	0.4038±0.0058	0.4570±0.0030	0.5118±.0040	0.5705±0.0055	0.6096±0.0083
Peanut Oil (λ max= 321 nm)					
Conc. (µg/ml)	50	100	150	200	250
mean Absorbance	0.1321±0.0043	0.2802±0.0035	0.3811±0.0041	0.5141±0.0050	0.6165±0.0071
Cottonseed Oil (λ max= 366 nm)					
Conc. (µg/ml)	100	150	200	250	300
mean Absorbance	0.1582±0.0046	0.2873±0.0061	0.3882±0.0072	0.5325±0.0083	0.6097±0.0076
Tween-60 (λ max= 371 nm)					
Conc. (µg/ml)	50	70	90	110	130
mean Absorbance	0.1650±0.0059	0.2293±0.0095	0.2604±0.0076	0.3151±0.0072	0.3569±0.0066
Tween-80 (λ max= 346 nm)					
Conc. (µg/ml)	10	20	30	40	50
mean Absorbance	0.1101±0.0047	0.3048±0.0073	0.4934±0.0076	0.6631±0.0073	0.8519±0.0080
PEG-200 (λ max= 358 nm)					
Conc. (µg/ml)	10	15	20	25	30
mean Absorbance	0.1026±0.0029	0.1582±0.0057	0.2220±0.0077	0.2850±0.0043	0.3579±0.0083
Transcutol HP (λ max= 351 nm)					
Conc. (µg/ml)	20	40	60	80	100
mean Absorbance	0.2009±0.0058	0.4001±0.0093	0.6080±0.0099	0.8010±0.0094	0.9975±0.0030

The data is expressed as a mean±SD, n=3

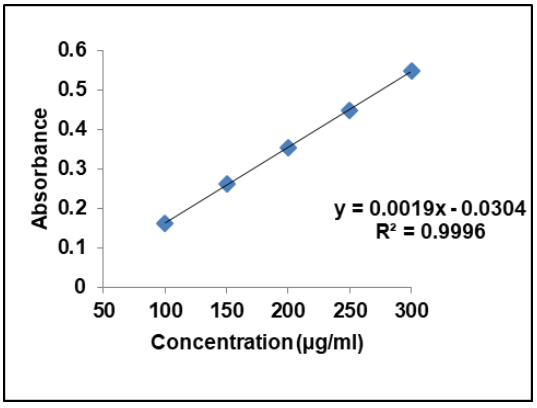

Fig. 1: NHCL in caprylic capric

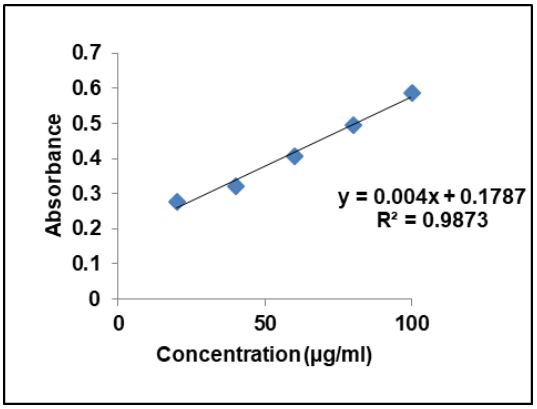

Fig. 2: NHCL in soyabean oil

Precision

Table 5 shows the Precision study and its % RSD for each solvent used.

Intra-day precision demonstrates method reliability, with all %RSD values ranging between 0.8426% and 1.9417%. According to Patil (2017) and Snyder *et al.* (2010), for a standard solution containing 100% analyte, the % RSD should be less than 2% to meet the acceptable precision criteria. This means that the variability in results obtained from repeated analyses of the standard solution should not exceed 2% of the mean value. When analyzing a sample solution with 1% analyte

content, the acceptable %RSD is specified to be below 2.7%. This slightly relaxed criterion reflects the lower concentration of analyte in the sample solution, allowing for a slightly higher degree of variability while still maintaining acceptable precision standards [38, 39].

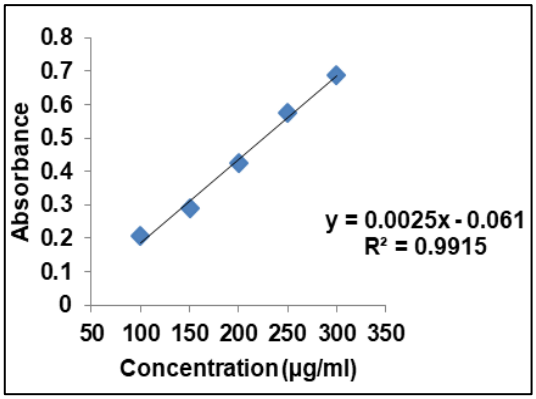

Fig. 3: NHCL in linseed oil

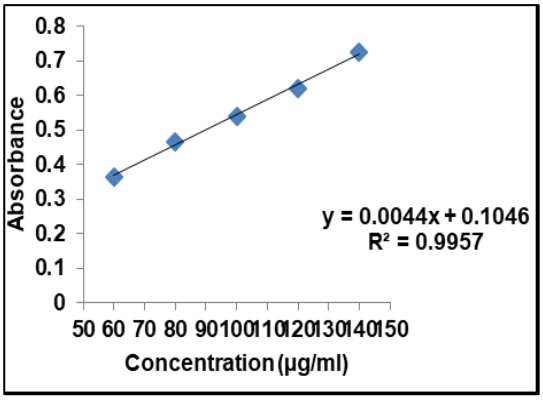

Fig. 4: NHCL in coconut oil

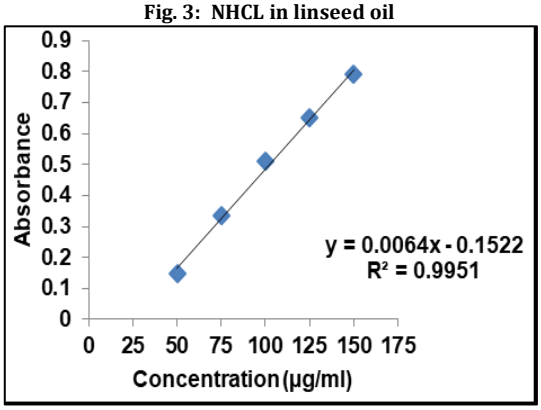

Fig. 5: NHCL in sunflower oil

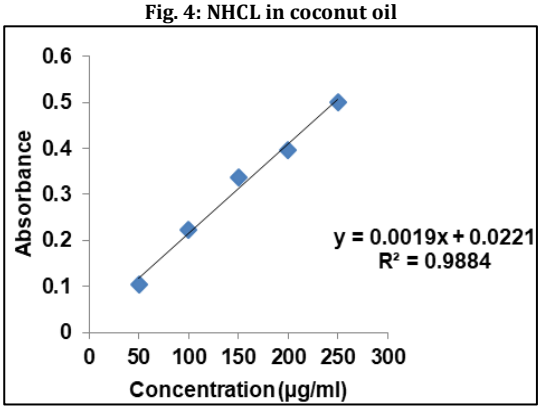

Fig. 6: NHCL in corn oil

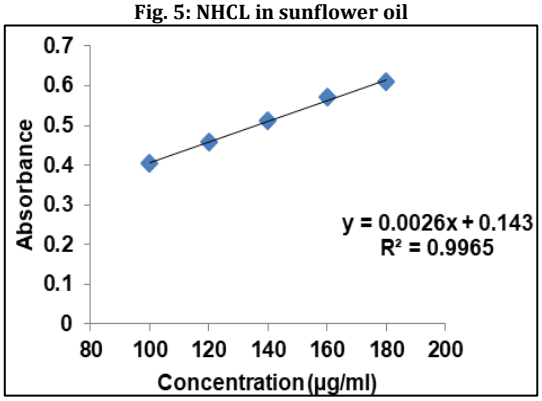

Fig. 7: NHCL in olive oil

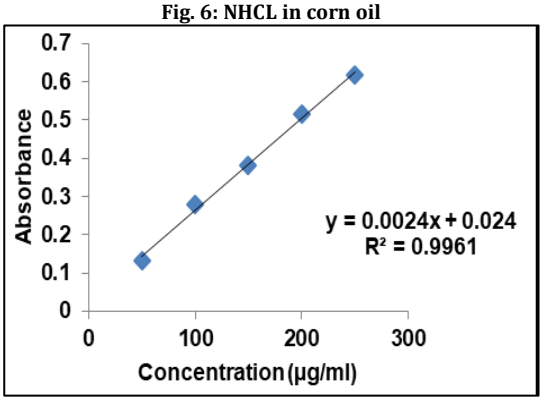

Fig. 8: NHCL in peanut oil

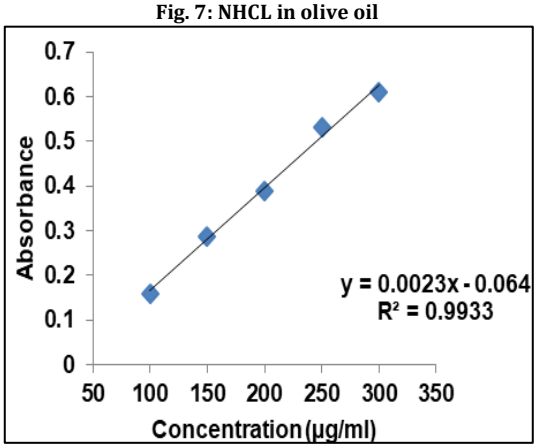

Fig. 9: NHCL in cottonseed oil

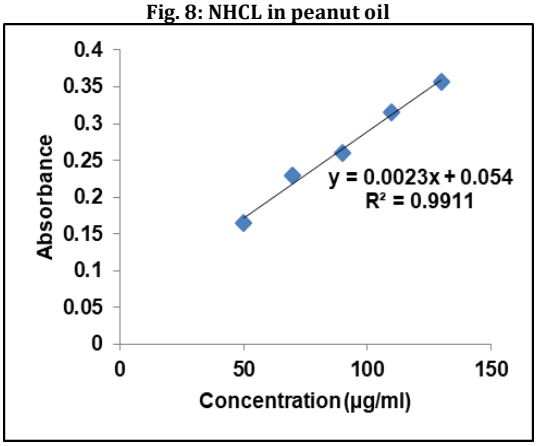

Fig. 10: NHCL in tween 60

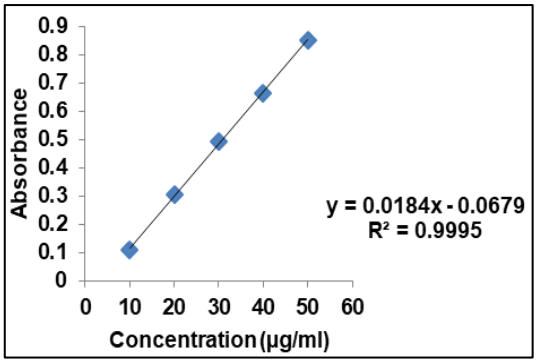

Fig. 11: NHCL in tween 80

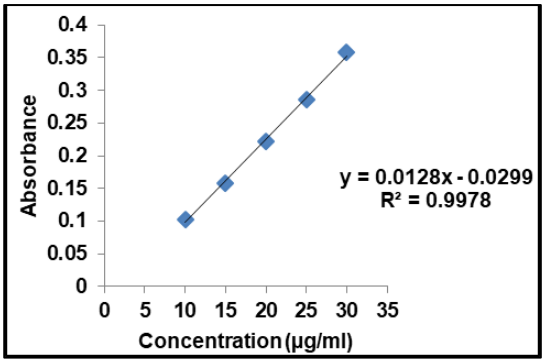

Fig. 12: NHCL in PEG200

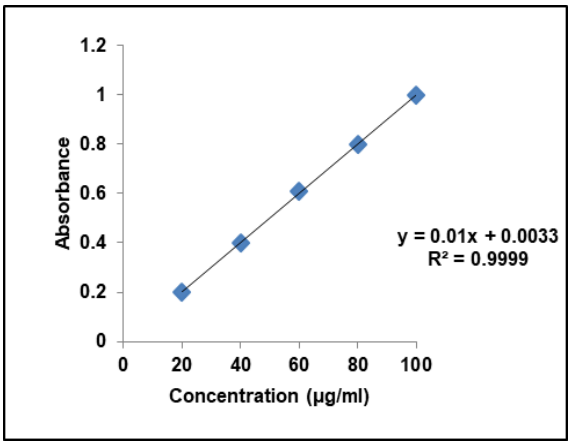

Fig. 13: NHCL in transcutol HP

Table 5: Precision study and its % RSD values for NHCL in solvents used

Solvent	Mean absorbance±SD*	%RSD
Caprylic Capric	0.3519±0.0047	1.2259
Soyabean Oil	0.4065±0.0037	1.6034
Linseed Oil	0.2866±0.0047	1.3558
Coconut Oil	0.5424±0.0039	0.8804
Sunflower Oil	0.3345±0.0041	0.8426
Corn Oil	0.3375±0.0037	1.1738
Olive Oil	0.4570±0.0033	1.0597
Peanut Oil	0.3842±0.0043	1.2025
Cottonseed Oil	0.3866±0.0052	1.1553
Tween-60	0.2638±0.0041	1.9417
Tween-80	0.4970±0.0064	1.1267
PEG-200	0.3581±0.0057	1.4729
Transcutol HP	0.6079±0.0070	1.1551

*The data is expressed as a mean±SD, n=6

Table 6: LOD and LOQ values for NHCL in solvents used

Solvent	LOD (µg/ml)	LOQ (µg/ml)
Caprylic Capric	8.1632	24.7368
Soyabean Oil	3.0525	9.2500
Linseed Oil	6.2405	18.8000
Coconut Oil	2.9250	8.8636
Sunflower Oil	2.1141	6.4063
Corn Oil	6.4263	19.4737
Olive Oil	4.1885	12.6923
Peanut Oil	5.9125	17.9167
Cottonseed Oil	7.4609	22.6087
Tween-60	5.8826	17.8261
Tween-80	1.1478	3.4783
PEG-200	1.4695	4.4531
Transcutol HP	2.3100	7.0000

LOD and LOQ

Table 6 shows the LOD and LOQ values for each solvent used.

The calculated LOD and LOQ values ranged between 1.1478 and 8.1632 µg/ml and 3.4783 and 24.7368 µg/ml, respectively. lOD and lOQ are derived from a linear regression analysis applied to a standard curve. These values indicate the method's sensitivity and the lowest concentration of NHCL that can be reliably detected and quantified with acceptable precision and accuracy [40].

Ruggedness

Table 7 shows Ruggedness study and its %RSD value for each solvent used by different analyst.

Ruggedness analysis exhibited good control over external experimental factors, with %RSD between 0.3433% and 1.9183%.

Table 7: Ruggedness study and its %RSD for NHCL in solvents used by different analyst

Solvent	Conc. (µg/ml)	Analyst	Mean absorbance±SD*	%RSD
Caprylic Capric	150	I	0.2659±0.0039	1.4643
		II	0.2608±0.0045	1.7066
Soyabean Oil	80	I	0.4966±0.0049	0.9892
		II	0.4929±0.0030	0.6135
Linseed Oil	100	I	0.2092±0.0015	0.7240
		II	0.2178±0.0037	1.7173
Coconut Oil	120	I	0.6195±0.0032	0.5131
		II	0.6149±0.0041	0.6634
Sunflower Oil	125	I	0.6504±0.0047	0.7298
		II	0.6516±0.0022	0.3433
Corn Oil	150	I	0.3364±0.0047	1.3854
		II	0.3336±0.0052	1.5544
Olive Oil	120	I	0.4570±0.0030	0.6476
		II	0.4529±0.0034	0.7594
Peanut Oil	150	I	0.3811±0.0041	1.0768
		II	0.3836±0.0022	0.5640
Cottonseed Oil	200	I	0.3882±0.0072	1.8570
		II	0.3840±0.0050	1.3091
Tween-60	90	I	0.2604±0.0023	0.8498
		II	0.2597±0.0050	1.9183
Tween-80	30	I	0.4934±0.0076	1.5419
		II	0.4875±0.0051	1.0368
PEG-200	30	I	0.3583±0.0037	1.0236
		II	0.3563±0.0044	1.2255
Transcutol HP	60	I	0.6080±0.0099	1.6276
		II	0.6090±0.0046	0.7473

*The data is expressed as a mean±SD, n=3

Robustness

Table 8 shows Robustness study and its % RSD of each solvent used at two different temperature conditions.

Robustness assessment demonstrated consistent performance even with slight changes in environmental conditions, with %RSD between 0.5450% and 1.6443%. The %RSD values fell within the acceptable range, indicating its reliability [41, 42].

Table 8: Robustness study and its %RSD for NHCL in solvents usedat two different temperature conditions

Solvent	Conc. (µg/ml)	Temperature	Mean absorbance±SD*	%RSD
Caprylic Capric	150	Room Temp.	0.2525±0.0029	1.1617
		20 °C	0.2547±0.0037	1.4625
Soyabean Oil	60	Room Temp.	0.4134±0.0036	0.8730
		20 °C	0.4065±0.0037	0.8987
Linseed Oil	150	Room Temp.	0.2934±0.0034	1.1455
		20 °C	0.2866±0.0047	1.6443
Coconut Oil	100	Room Temp.	0.5489±0.0047	0.8336
		20 °C	0.5424±0.0039	0.7110
Sunflower Oil	75	Room Temp.	0.3402±0.0041	1.2141
		20 °C	0.3345±0.0041	1.2257
Corn Oil	150	Room Temp.	0.3446±0.0039	1.1389
		20 °C	0.3375±0.0037	1.0970
Olive Oil	120	Room Temp.	0.4573±0.0025	0.5450
		20 °C	0.4570±0.0033	0.7281
Peanut Oil	150	Room Temp.	0.3872±0.0024	0.6128
		20 °C	0.3842±0.0043	1.1274
Cottonseed Oil	200	Room Temp.	0.3888±0.0044	1.1197
		20 °C	0.3866±0.0052	1.3468
Tween-60	90	Room Temp.	0.2536±0.0035	1.3889
		20 °C	0.2627±0.0041	1.5437
Tween-80	30	Room Temp.	0.4981±0.0056	1.1293
		20 °C	0.4970±0.0064	1.2807
PEG-200	30	Room Temp.	0.3560±0.0032	0.8947
		20 °C	0.3581±0.0057	1.5958
Transcutol HP	60	Room Temp.	0.6109±0.0039	0.6429
		20 °C	0.6079±0.0070	1.1490

*The data is expressed as a mean±SD, n=6

Accuracy/% recovery

Table 9 shows the % recovery values for each solvent used at 80%, 100% and 120% concentrations.

The accuracy study indicated % recovery values between 98.53% and 100.89%, suggesting minimal interference from excipients in the formulation. The capability to precisely recover known concentrations of the drug from the sample solution enhances confidence in the accuracy and suitability of the method [43].

Solubility estimation

Table 10 shows the solubility of NHCL in each solvent used.

Among the oils/triglycerides, Caprylic Capric exhibits the highest solubility, followed by coconut oil, soyabean oil, linseed oil, peanut oil, sunflower oil, olive oil, corn oil, and cottonseed oil, in descending order. As for surfactants, Tween-80 demonstrates the highest solubility, followed by Tween-60. Among the cosurfactants, Transcutol HP displays the highest solubility, followed by PEG-200.

Table 9: % recovery values for NHCL in solvents used at 80%, 100% and 120% concentrations

Solvent	Concentration	Mean conc. (µg/ml)±SD*	% Recovery
Caprylic Capric	180 µg/ml (80%)	179.0180±2.1862	99.45
	200 µg/ml (100%)	199.0042±1.9279	99.94
	220 µg/ml (120%)	219.8057±1.7199	99.91
Soyabean Oil	180 µg/ml (80%)	179.7038±1.9667	99.84
	200 µg/ml (100%)	199.5064±0.5552	99.75
	220 µg/ml (120%)	219.7607±1.1004	99.89
Linseed Oil	180 µg/ml (80%)	179.1205±1.9218	99.51
	200 µg/ml (100%)	200.1043±2.0082	100.05
	220 µg/ml (120%)	219.9647±1.0542	99.98
Coconut Oil	180 µg/ml (80%)	181.5981±1.3291	100.89
	200 µg/ml (100%)	199.6997±1.1405	99.85
	220 µg/ml (120%)	220.3178±1.1644	100.14
Sunflower Oil	180 µg/ml (80%)	177.3564±0.3345	98.53
	200 µg/ml (100%)	198.6161±1.9179	99.31
	220 µg/ml (120%)	218.4052±1.4161	99.28
Corn Oil	180 µg/ml (80%)	178.6710±1.4671	99.26
	200 µg/ml (100%)	199.5223±1.4236	99.76
	220 µg/ml (120%)	221.8568±1.7821	100.84
Olive Oil	180 µg/ml (80%)	180.2235±1.3469	100.12
	200 µg/ml (100%)	200.1447±1.0870	100.07
	220 µg/ml (120%)	221.0310±1.0095	100.47
Peanut Oil	180 µg/ml (80%)	178.6482±0.4795	99.25
	200 µg/ml (100%)	199.9764±2.0900	99.99
	220 µg/ml (120%)	219.8079±1.3022	99.91
Cottonseed Oil	180 µg/ml (80%)	179.6005±2.5452	99.78
	200 µg/ml (100%)	199.3700±1.2449	99.69
	220 µg/ml (120%)	219.5024±1.1784	99.77
Tween-60	180 µg/ml (80%)	179.6705±1.2568	99.82
	200 µg/ml (100%)	199.4661±1.0072	99.73
	220 µg/ml (120%)	219.4320±0.7813	99.74
Tween-80	36 µg/ml (80%)	35.9756±0.2878	99.93
	40 µg/ml (100%)	39.5007±0.0753	98.75
	44 µg/ml (120%)	43.8582±0.0806	99.68
PEG-200	36 µg/ml (80%)	35.9108±0.1903	99.75
	40 µg/ml (100%)	39.8322±0.2870	99.58
	44 µg/ml (120%)	43.6019±0.5236	99.10
Transcutol HP	72 µg/ml (80%)	71.7568±0.6422	99.66
	80 µg/ml (100%)	79.2883±0.2243	99.11
	88 µg/ml (120%)	87.6689±0.2113	99.62

*The data is expressed as a mean±SD, n=3

Table 10: Solubility of NHCL in solvents used

Solvent	Mean absorbance±SD of unknown*	Concentration of unknown (µg/ml)	Dilution	Solubility (mg/ml)
Caprylic Capric	0.1503±0.0040	94.13	10	0.94
Soyabean Oil	0.4180±0.0057	60.08	10	0.60
Linseed Oil	0.0674±0.0047	52.80	10	0.53
Coconut Oil	0.4319±0.0092	74.81	10	0.75
Sunflower Oil	0.1246±0.0049	43.56	10	0.44
Corn Oil	0.6887±0.0072	342.64	1	0.34
Olive Oil	0.2397±0.0081	37.21	10	0.37
Peanut Oil	0.1370±0.0073	47.38	10	0.47
Cottonseed Oil	0.6535±0.0077	311.75	1	0.31
Tween-60	0.4711±0.0054	176.85	100	17.69
Tween-80	0.3663±0.0058	23.58	1000	23.58
PEG-200	0.2924±0.0073	25.26	1000	25.26
Transcutol HP	0.3839±0.0069	38.18	1000	38.18

*The data is expressed as a mean±SD, n=3

CONCLUSION

Analytical method validation for each solvent was successfully conducted in accordance with ICH guidelines. Caprylic Capric, as an oil/triglyceride, Tween-80 as a surfactant and Transcutol HP as a cosurfactant, exhibited high solubility for NHCL.

ACKNOWLEDGEMENT

The authors are thankful to Subhash Chemical Industries Pvt. ltd. for providing the gift sample of Caprylic Capric, and Transcutol HP and KBHSS Trust's Institute of Pharmacy, Malegaon, Nashik for providing facilities to conduct the research.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

Rahul Y. Pagar: Conceptualization, Investigation, Data Analysis, Writing-original Draft.

Avinash B. Gangurde: Supervision, Data Analysis, Writing-reviewing and editing.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Singh BN, Josephson MA. Clinical pharmacology, pharmacokinetics, and hemodynamic effects of nicardipine. Am Heart J. 1990;119(2 Pt 2):427-34. doi: 10.1016/s0002-8703(05)80063-8, PMID 1967896.
2. Moursy NM, Afifi NN, Ghorab DM, El-Saharty Y. Formulation and evaluation of sustained release floating capsules of nicardipine hydrochloride. Pharmazie. 2003;58(1):38-43. PMID 12622251.
3. Sorkin EM, Clissold SP, Nicardipine. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy, in the treatment of angina pectoris, hypertension and related cardiovascular disorders. Drugs. 1987 Apr;33(4):296-345. doi: 10.2165/00003495-198733040-00002, PMID 3297616.
4. Selvam RP, Singh AK, Sivakumar T. Transdermal drug delivery systems for antihypertensive drugs-a review. Int J Pharm Biomed Res. 2010;1(1):1-8.
5. Elliott WJ, Ram CV. Calcium channel blockers. J Clin Hypertens (Greenwich). 2011;13(9):687-9. doi: 10.1111/j.1751-7176.2011.00513.x, PMID 21896151.
6. Chavda HV, Patel CN, Anand IS. Biopharmaceutics classification system. Syst Rev Pharm. 2010;1(1):62. doi: 10.4103/0975-8453.59514.
7. Charalabidis A, Sfouni M, Bergstrom C, Macheras P. The biopharmaceutics classification system (BCS) and the biopharmaceutics drug disposition classification system (BDDCS): beyond guidelines. Int J Pharm. 2019;566:264-81. doi: 10.1016/j.ijpharm.2019.05.041, PMID 31108154.
8. Mehta M, Polli JE, Seo P, Bhoopathy S, Berginc K, Kristan K. Drug Permeability-best practices for biopharmaceutics classification system (BCS)-based biowaivers: a workshop summary report. J Pharm Sci. 2023;112(7):1749-62. doi: 10.1016/j.xphs.2023.04.016, PMID 37142122.
9. Mehta S, Joseph NM, Feleke F, Palani S. Improving solubility of bcs class II drugs using solid dispersion: a review. J Drug Delivery Ther 2014;4(3):7-13. doi: 10.22270/jddt.v4i3.844.
10. Sarisaltik Yasin D, Teksin ZS. Biopharmaceutics classification system: evaluation on international guidelines and countries. J Lit Pharm Sci. 2018;7(2):160-74. doi: 10.5336/pharmsci.2018-61223.
11. Jindal K. Review on solubility: a mandatory tool for pharmaceuticals. Int Res J Pharm. 2017;8(11):11-5. doi: 10.7897/2230-8407.0811210, doi: 10.7897/2230-8407.0811210.
12. Kumar A, Rajesh M, Subramanian l. Solubility enhancement techniques: a comprehensive review. World J Bio Pharm Health Sci. 2023;13(3):141-9. doi: 10.30574/wjbphs.2023.13.3.0125.
13. Saxena C, Mishra GP. Comprehensive study about solubility enhancement techniques. IJBPAS. 2022;11(9). doi: 10.31032/IJBPAS/2021/11.9.6220.
14. Savjani KT, Gajjar AK, Savjani JK. ChemInform abstract: drug solubility: importance and enhancement techniques. ChemInform. 2013;44(26). doi: 10.1002/chin.201326246.
15. Coltescu AR, Butnariu M, Sarac I. The importance of solubility for new drug molecules. Biomed Pharmacol J. 2020;13(2):577-83. doi: 10.13005/bpj/1920. doi: 10.13005/bpj/1920.
16. Koch Weser J. Bioavailability of drugs (second of two parts). N Engl J Med. 1974;291(10):503-6. doi: 10.1056/NEJM197409052911005, PMID 4604153.
17. Stielow M, Witczynska A, Kubryn N, Fijałkowski L, Nowaczyk J, Nowaczyk A. The bioavailability of drugs-the current state of knowledge. Molecules. 2023;28(24):1-19. doi: 10.3390/molecules28248038, PMID 38138529.
18. Allam AN, El Gamal S, Naggar V. Bioavailability a pharmaceutical review. Int J Novel Drug Deliv Tech. 2011 Jan;1(1):77-93.
19. Patil D, Bachhav R, Gosavi D, Pagar R, Bairagi V. Formulation and evaluation of ezetimibe lyophilized dry emulsion tablets. J Drug Deliv Ther. 2019;9(3):630-5.
20. Gaidhani KA, Harwalkar M, Bhambere D, Nirgude PS. Lyophilization/freeze drying–a review. World J Pharm Res. 2015;4(8):516-43.
21. Pagar RY, Gangurde AB. Quality by design approach for development of lyophilized dry emulsion tablets (LDET). J Chem Health Risks. 2024;14(2):815-27.
22. Dhahir RK, Yassir AB, Al-Kotaji M, Rawas Qalaji M. Formulation and evaluation of olanzapine oral lyophilisates. Pharmakeftiki. 2024;36(1):64-79.
23. AlHusban F, Perrie Y, Mohammed AR. Formulation of multiparticulate systems as lyophilised orally disintegrating tablets. Eur J Pharm Biopharm. 2011;79(3):627-34. doi: 10.1016/j.ejpb.2011.05.014, PMID 21693189.
24. Shao H, Li B, Li H, Gao L, Zhang C, Sheng H. Novel strategies for solubility and bioavailability enhancement of bufadienolides. Molecules. 2021;27(1):51. doi: 10.3390/molecules27010051, PMID 35011278.
25. Corveleyn S, Remon JP. Formulation of a lyophilized dry emulsion tablet for the delivery of poorly soluble drugs. International Journal of Pharmaceutics. 1998;166(1):65-74. doi: 10.1016/S0378-5173(98)00024-6.
26. Maleque M, Hasan MR, Hossen F, Safi S. Development and validation of a simple UV spectrophotometric method for the determination of levofloxacin both in bulk and marketed dosage formulations. J Pharm Anal. 2012;2(6):454-7. doi: 10.1016/j.jpha.2012.06.004, PMID 29403782.
27. Ferraz RS, Mendonça EA, Silva JP, Cavalcanti IM, Lira Nogueira MC, Galdino SL. Validation of a UV-spectrophotometric analytical method for determination of LPSF/AC04 from inclusion complex and liposomes. Braz J Pharm Sci. 2015;51(1):183-91. doi: 10.1590/S1984-82502015000100018.
28. Pathade P, Sumrao A, Sonawane B, Shirode D, Shewale S, Shinde V. Development and validation of stability indicating UV spectrophotometric method for estimation of resveratrol in bulk and tablet dosage form. Int J Drug Deliv Technol. 2024;14(1):385-8. doi: 10.25258/ijddt.14.1.56.
29. Rajesh R. Stability-indicating RP-HPLC method development and validation for the analysis of doxepin hydrochloride in bulk and pharmaceutical dosage form. Int J Pharm Pharm Sci. 2024;16(4):27-35. doi: 10.22159/ijpps.2024v16i4.50126.
30. Bodke SS, Bhangale CJ, Bhandare SN. Stability indicating UPLC method for estimation of benazepril and hydrochlorothiazide in bulk and combined dosage form. Int J Pharm Pharm Sci. 2024;16(1):22-9. doi: 10.22159/ijpps.2024v16i1.49457.
31. Chauhan I, Singh L. Development and validation of a simple and cost-effective UV spectrophotometric method for quantifying linezolid. Int J App Pharm. 2024;16(3):211-6. doi: 10.22159/ijap.2024v16i3.50556.
32. Bhavya SK, Nandhini M. Simultaneous method development and validation of combined dosage form dapagliflozin and vildagliptin in bulk and combined tablet dosage form by UV spectrophotometer. Asian J Pharm Clin Res. 2024;17(4):53-9.
33. Jothula H, Navuluri S, Mulakayala NR. Stability based HPLC method for cyclophosphamide related substances in finished drug products: development and validation. Int J Curr Pharm Sci. 2024;16(3):42-51. doi: 10.22159/ijcpr.2024v16i3.4061.

34. Baka E, Comer JE, Takacs Novak K. Study of equilibrium solubility measurement by saturation shake-flask method using hydrochlorothiazide as model compound. J Pharm Biomed Anal. 2008;46(2):335-41. doi: 10.1016/j.jpba.2007.10.030, PMID 18055153.
35. Naik AD, Pai SP. Spectrophotometric method for estimation of linezolid in tablet formulation. Asian J Biomed Pharm Sci. 2013;3(21):4-6.
36. Nagaraju PT, Sreenivasa Rao M, Ravi Kumar C, Mabhasha D, Venu Gopal K, Murali Krishna NV. UV-spectrophotometric method development and validation for determination of linezolid in pharmaceutical dosage form. Res Rev J Pharm Anal. 2014;3(3):23-7.
37. Apridamayanti P, Pratiwi L, Sari R. The development and validation of analytical method for evaluating gallic acid in ethyl acetate fraction (eaf) of snedds formulation: quantitative analysis with *in vitro* assay. Int J App Pharm. 2024:57-65. doi: 10.22159/ijap.2024v16i2.49830.
38. Patil PN. HPLC method development-a review. SGVU J Pharm Res. 2017;2(1):243-60.
39. Snyder l, Kirkland J, Dolan J. Introduction to modern liquid chromatography. 3rd ed. John. NJ: Wileyandsonsinc; 2010.
40. Kaur T, Kaur S, Kaur P. Development and validation of UV spectrophotometric methods for determination of gemcitabine hydrochloride in bulk and polymeric nanoparticles. Int J App Pharm. 2017;9(5):60-5. doi: 10.22159/ijap.2017v9i5.19726.
41. Shirwar M, Birajdar S, Garad S, Kumbhar S. Development and validation of novel UV-visible spectrophotometric method for estimation of tepotinib in bulk and in pharmaceutical formulation. Int J Pharm Pharm Sci. 2023;15(9):32-6. doi: 10.22159/ijpps.2023v15i9.48431.
42. Singh S, Sharma N, Singla YP, Arora S. Development and validation of UV-spectrophotometric method for quantitative estimation of nefopam hydrochloride in polymethacrylate nanospheres. Int J Pharm Pharm Sci. 2015;8(1):414-9.
43. Swartz ME, Krull IS. Analytical method validation: accuracy in quantitation. LC GC N Am. 2005;23(1):46-52.