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SPECTROPHOTOMETRIC DETERMINATION OF NIMODIPINE, NITRENDIPINE, LACIDIPINE IN TABLETS VIA DERIVATIZATION WITH PARA-DIMETHYLAMINOBENZALDEHYDE

Mariana Horyn, Liubomyr Kryskiw, Tetyana Kucher, Nadiya Zarivna, Nataliia Shulyak, Iryna Ivanchuk, Liliya Logoyda

The proposed approach *involves the interaction of NIM, NIT, and LAC directly with DABA reagent to produce coloured products with its further spectrophotometric analysis by the development of simple, available, and alternative spectrophotometric methods.*

Material and methods*. UV-visible double beam spectrophotometer Shimadzu UV-1800 (Japan) with included UV-Probe version 2.62 software was employed. Additional equipment included a precise analytical balance RAD WAG AS 200/C (Poland), an ultrasonic bath Elmasonic EASY 60H with a frequency of 40 kHz and a water bath VB-4 were used in the developed procedure. LAC, NIM and NIT (purity ≥ 98% (HPLC)) were supplied from Sigma-Aldrich Chemicals Co. (St. Louis, MO, USA). NIT 10 mg tablets, NIM 30 mg tablets were purchased from local drugstore. LAC 2 mg tablets were purchased from europharm.com.ua.*

Methanol was produced by Honeywell and had a purity of 99.9%. HCl conc. (fuming, ≥ 37% by Sigma Aldrich was used. DABA utilized in the experiment was analytical grade.

Results and discussion. *Simple, available and alternative visible spectrophotometric methods for the determination of nitrendipine (NIT), nimodipine (NIM), and lacidipine (LAC) in tablets through derivatization with the para-dimethylaminobenzaldehyde (DABA) have been developed. The optimal parameters for CCBs spectrophotometric analysis were as follows: detection wavelength – 577 nm for NIM, NIT and 616 nm for LAC, concentrated hydrochloric acid, 1.5 mL of 0.1% DABA solution, 15 min boiling at 100°C. The concentration was linearly proportional to absorbance values in the range of 25–175 μg/mL (NIT), 25–200 μg/mL (NIM), 20 – 200 μg/mL (LAC). Estimation of LOD and LOQ parameters were obtained as 3.75 μg/mL and 11.38 μg/mL (NIT), 4.43 μg/mL and 13.43 μg/mL (NIM), 6.30μg/ml and 19.1 μg/mL (LAC).*

Conclusions. *In this work, thorough scientific research was carried out with the presentation of the method of selection of the optimal reaction conditions and spectrophotometric methods for determining NIT, NIM, and LAC in tablets were developed. In addition, the three studied CCBs were quantified using easy-to-implement, simple, cost-effective spectrophotometric approaches. The proposed methods can be used as alternatives and arbitrage, which significantly expands the bank of analytical methods. Moreover, the described methods can be easily implemented for routine pharmaceutical analysis*

Keywords: *calcium channel blockers, nitrendipine, nimodipine, lacidipine, spectrophotometry, para-dimethylaminobenzaldehyde, assay, validation*

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1. Introduction

According to World Health Organization statistics, arterial hypertension has a prominent position as a metabolic risk factor for non-communicable disorders. 1,4-dihydropyridine calcium channel blockers (CCB) are a well-known group for the treatment of arterial hypertension. These drugs are useful agents for a variety of pathological conditions, including chronic stable angina and ischemic and coronary heart disorders [1–3]. Among them, nimodipine (NIM) is a commonly used agent that preferentially acts on cerebral vessels, especially in the brain [4, 5]. A range of analytical approaches have been employed for the assay of NIM in bulk, dosage forms, biological fluids, etc. In accordance with the requirements of the United States Pharmacopeia and the European Pharmacopeia for the determination of NIM titration with cerium sulfate, high-performance liquid chromatography (HPLC) was used [6, 7]. The literature review revealed that for NIM assay, such analytical methods as thin layer chromatography (TLC) combined with Raman spectroscopy, HPLC, reserve phase (RP)-HPLC, and liquid chromatography-tandem mass spectrometry (LC-MS) were applied [8–11]. For pharmacokinetic study and enantioselective determination of 1,4-dihydropyridine compounds, supercritical fluid chromatography and rapid capillary electrophoresis have been used [12, 13]. Lacidipine (LAC) is a wide-ranging lipophilic 1,4-dihydropyridine compound indicated for

use in monotherapy and combination therapy for the management of high blood pressure (HBP) [14, 15]. In addition, LAC has a positive impact on the endothelium of patients with hypertension. LAC is not referenced within any Pharmacopeias. Currently, micelle-enhanced spectrofluorimetric techniques for content testing of LAC and improving dissolution through deliberate formulation optimization were highlighted [16, 17]. According to the last data, lipid-based drug delivery systems are a prospect for hypertension care, including CCB agents with decreasing toxicity and enhancing biocompatibility [18]. Alternative approaches for the LAC assay in tablet dosage forms and biological samples were adopted via gas and liquid chromatography, titrimetric methods, etc [19–22]. Long-acting CCB agent Nitrendipine (NIT) is prescribed for hypertension therapy and manages to lower the cardiotoxicity of cocaine. Compared to other CCBs, it is slightly natriuretic and does not decrease glomerular filtration level. Also, neuroprotective enhancements in cognitive abilities were observed in combination therapy with NIT [23, 24]. According to Pharmacopeia monographs, the identification method for NIT includes infrared absorption spectroscopy and titration for its assay [7]. For the determination of NIT in bulk, biological liquids, and dosage forms, a multitude of chromatographic, spectrophotometric, and electrochemical procedures was highlighted [25–27]. Among them, the RP-HPLC technique was developed for the pharmacokinetic study of NIT liposomal gel. Long-lasting CCB agents, amlodipine (AML) and its enantiomer levamlodipine, are widely prescribed against hypertension [28, 29]. However, most of the previously described analytical procedures exhibit significant drawbacks, such as prolonged duration, high costs, or not being available for pharmaceutical analysis. Up till now, a few spectrometric procedures have been presented [30–32].

The necessity of the development of simple, available, and non-extractive spectrophotometric procedures is essential for the most quality control laboratories. Aldehydes are broadly used in the development of biochemical and analytical techniques [33, 34]. Comparison of the existing spectrophotometric procedures of 1,4-dihydropyridine CCBs with aldehydes is presented in Table 1.

Thus, the interaction of CCB with different reagents, such as aldehydes, has a lot of benefits. Among them, *para*-dimethylaminobenzaldehyde (DABA) is a frequently utilized reagent. According to the chemical structure it is a bifunctional aromatical substance. In scientific literature, it is also named as Ehrlich's reagent, 4-dimethylaminobenzaldehyde, DMAB, p-DAB, *p*-(dimethylamino)-benzaldehyde, N,N-dimethyl-4-aminobenzaldehyde, etc. Analytical application of DABA for the determination of a variety of compounds, including nanomaterials, organic medicines, and bioactive substances. In the utilization of DABA as an analytical reagent, the ability of its aldehyde component to be reduced to an alcohol or oxidized to a carboxylic acid, as well as the formation of condensation products, are applied [35–41].

Table 1

Comparison of the existing spectrophotometric procedures of 1,4-dihydropyridine CCBs with aldehydes

1,4-dihydropyridine CCB	NIM	LAC NIF	Cilnidipine	NIF NIM AML	NIM NIF
Used reagent	p-dimethyl-amino-cinnam-aldehyde	DABA	dimethyl-amino-cinnamalde-hyde	Vanillin	p-anis-aldehyde
Methodology	Schiff's base formation measured at 510.0 nm	Schiff's base formation measured at 615.7 nm	Coloured chromogen measured at 545.0 nm	Colored chromogen measured at 479.0 and 500.0 nm	Coloured product measured at 460.0 nm
Linear range, μg/mL	0.5–4.0	10.0–70.0	100–350	5.0–70.0	5.0–60.0
References	[35]	[36]	[37]	[38]	[39]

The proposed approach involves the interaction of NIM, NIT, and LAC directly with DABA reagent to produce coloured products with its further spectrophotometric analysis by the development of simple, available, and alternative spectrophotometric methods.

2. Planning of the research

Methodology of research of simple, available, and alternative spectrophotometric methods for the determination of NIM, NIT, LAC by interaction with DABA reagent includes:

1. Study of the recommendations of the State Pharmacopoeia of Ukraine (SPhU) and EP, analysis of scientific literature;

2. The study of methodology for choosing a reagent for the development of spectrophotometric methods.

3. Selection of the optimal conditions for the development of the spectrophotometric methods.

4. The application of the proposed spectrophotometric method for the determination of NIM, NIT, LAC by using DABA reagent to the analysis of tablets.

5. Validation of the spectrophotometric method for determination of NIM, NIT, LAC in tablets.

3. Materials and methods

Objects of study, solvents and equipment.

UV-visible double beam spectrophotometer Shimadzu UV-1800 (Japan) with included UV-Probe version 2.62 software was employed. Additional equipment included a precise analytical balance RAD WAG AS 200/C (Poland), an ultrasonic bath Elmasonic EASY 60H with a frequency of 40 kHz, and a water bath VB-4 were used in the developed procedure.

LAC, NIM and NIT (purity ≥ 98% (HPLC)) were supplied from Sigma-Aldrich Chemicals Co. (St. Louis, MO, USA). NIT 10 mg tablets, NIM 30 mg tablets were purchased from local drugstore. LAC 2 mg tablets was purchased from europharm.com.ua.

Methanol was produced by Honeywell and had a purity of 99.9%. HCl conc. (fuming, ≥ 37%) by Sigma Aldrich was used. DABA utilized in the experiment was analytical grade.

Procedure for preparation of standard stock solution of CCBs (*NIT, NIM, LAC*).

A standard stock solution of analyzed CRS CCBs drugs was prepared by dissolving 25.00 mg in 15 mL of methanol, followed by dilution to a final volume in a 25.00 mL volumetric flask.

Procedure for tablets for the determination of CCBs (*NIT, NIM, LAC*).

A precise weight and crushing of twenty tablets were performed. A 10.00 mL measuring flask was filled with a powder of crushed tablets containing 10.00 mg of the tested CCBs. Afterwards the samples were mixed with 5 mL of methanol, adjusted using the same solvent to the mark, and placed in an ultrasound bath for two minutes before being filtered with a Whatman No. 42 filter paper.

Procedure for preparation of DABA solution.

$6.7*10^{-3}$ M of DABA solution was prepared in a 25.00 mL measuring flask by dissolving 25.00 mg of DABA in 15 mL of HCl conc., mixed for 2 min, diluted to the mark with the same solvent, and mixed thoroughly.

4. Research results

4. 1. Methodology for choosing a reagent for the development of spectrophotometric methods

One of the promising reagents for the development of spectrophotometric methods for the determination of CCBs is aromatic aldehydes. DABA interacts with CCBs to form condensation products, which are called Schiff bases. Indian scientists [36] described the spectrophotometric determination of LAC in bulk and tablet dosage form via reaction with DABA. We became interested in this direction and evaluated this method for other CCBs, such as AML, nifedipine (NIF), levamlodipine (LAML), NIT, NIM and lercanidipine (LER). AML, NIF, LAML and LER did not interact with DABA. In comparison with the previous analytes described above, NIT, NIM and LAC interacted with DABA to form reaction products demonstrated on a Fig. 1. The absorption maxima for these drugs were located at 577 nm and 616 nm respectively.

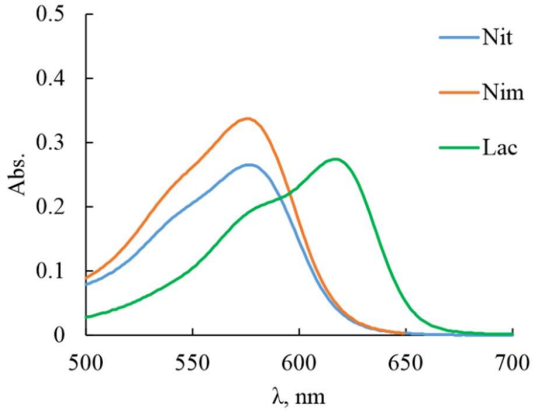

Fig. 1. Absorption spectra of CCBs reaction product with DABA 0.1% in HCl (C(NIT) = 100 μg/mL, C(NIM) = 125 μg/mL, C(LAC) = 100 μg/mL)

In addition, during the optimization of the conditions of the reaction, we established some advantages of the interaction of LAC with DABA in comparison with the method [36]. For example, in article [36], volume 50 ml was used, while we proposed 10 ml, which reduced the number of reagents used by five times and increased the score of «greenness» of the method.

4. 2. Selection of the optimal conditions for the development of the spectrophotometric methods

Therefore, the next necessary stage of our research was to study the optimal conditions for the interaction of NIM, NIT and LAC with DABA (choice of acid, amount of reagent, adding of extra components, time and heating temperature) for the development of spectrophotometric methods that are suitable for the pharmaceutical analysis. To select an acid as a solvent for the preparation of a reagent 0.1% DABA for NIM method were tested concentrated sulfuric, nitric, phosphoric, hydrochloric and boric acids (Table 2). Optimal solvent for the preparation of 0.1% DABA was hydrochloric acid.

Table 2

Selection of acid as the optimal solvent for preparation 0.1% DABA for the NIM method

H_2SO_4	HNO_3	H_3PO_4	HCl	HBr
The complex was not formed	The complex was not formed	The complex was not formed	A pink color complex was formed λ = 577 nm	A pink color complex was formed λ = 580 nm, non-stable over time

The interaction of NIM, NIT and LAC with a various volume of 0.1% DABA reagent ranging 1 to 3 mL in order to determine the best conditions has been studied. Fig. 2. shows the dependence of the absorbance on the amount of 0.1% DABA. The optimal amount was 1.5 mL of 0.1% DABA solution.

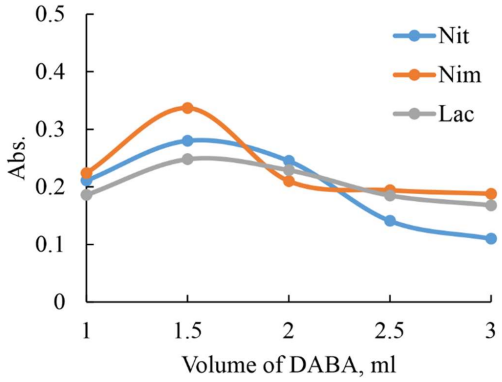

Fig. 2. The effect of the amount of added 0.1% DABA on the formation of reaction products (C(NIT) = 125 μg/mL, C(NIM) = 125 μg/mL, C(LAC) = 100 μg/mL)

According to the method [36], there was additional use of concentrated hydrochloric acid for the reaction. Therefore, the next stage of our research was the optimization of the amount of concentrated hydrochloric acid in the range 0–1.0 mL, in steps of 0.25 mL, as an additional component of the reaction. To achieve the task, the inter-

action of CCB with a concentration of 1 mg/mL and 0.1% DABA in concentrated hydrochloric acid was used during heating for 10 min at a temperature of 100°C. The dependence of the absorbance of the product of the reaction of NIM, NIT and LAC with 0.1% DABA on the amount of concentrated hydrochloric acid is shown in Fig. 3.

As can be seen in Fig. 4, the proposed method did not require the usage of additional concentrated hydrochloric acid, which had a positive impact on sample preparation, reducing the time of sample preparation and the number of reagents.

A necessary condition for the interaction of NIM, NIT and LAC with DABA was heating. The influence of the heating time was determined by the interaction of NIM, NIT and LAC with a concentration of 1 mg/mL and 0.1% DABA for 30 min (Fig. 4). The optimal heating time was 15 min.

The dependence of the absorbance of the product interaction of NIM, NIT and LAC with a concentration of 1 mg/ml and 0.1% DABA for 15 min on the heating temperature in the range of 80–100°C is shown in Fig. 5. As can be seen from Fig. 5. the optimal heating temperature was 100°C.

The stability of the analyzed CCBs reaction product was examined. It remained stable for 3 min, then gradually decreased (Fig. 6).

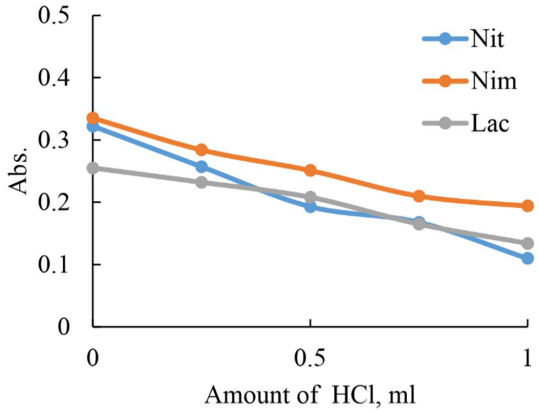

Fig. 3. The effect of the amount of added concentrated hydrochloric acid on the formation of reaction products (C(NIT) = 125 µg/mL, C(NIM) = 125 µg/mL, C(LAC) = 100 µg/mL)

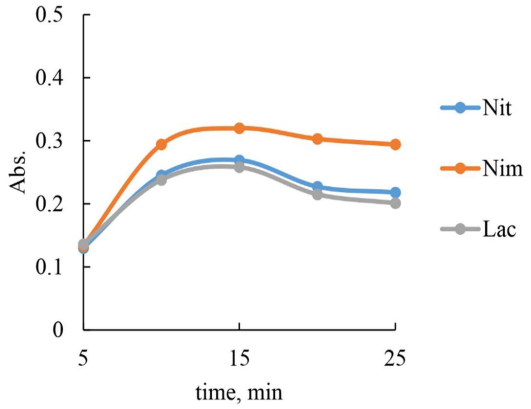

Fig. 4. Selection of heating time (C(NIT) = 100 µg/mL, C(NIM) = 125 µg/mL, C(LAC) = 100 µg/mL)

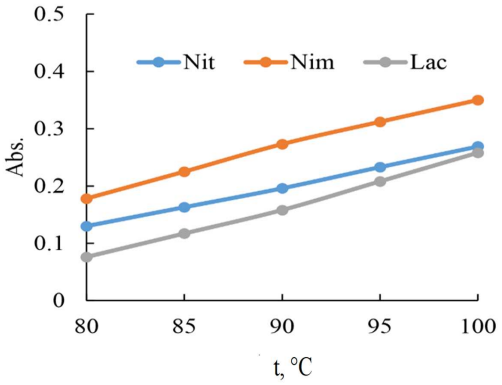

Fig. 5. Selection of heating temperature (C(NIT) = 100 µg/mL, C(NIM) = 125 µg/mL, C(LAC) = 100 µg/mL)

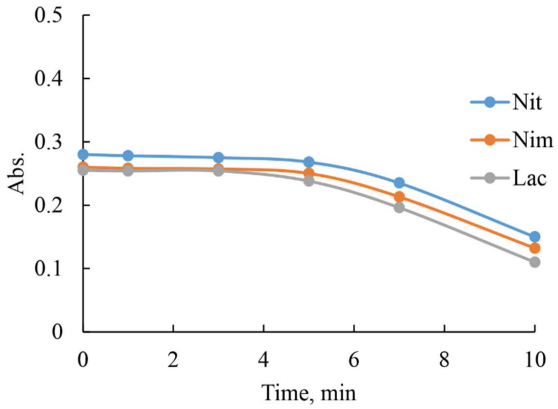

Fig. 6. Stability of reaction product in time (C(NIT) = 100 µg/mL, C(NIM) = 100 µg/mL, C(LAC) = 100 µg/mL)

The optimal parameters for CCBs spectrophotometric analysis via reaction with DABA were as follows: concentrated hydrochloric acid, 1.5 mL of 0.1% DABA solution, 15 min boiling at 100°C, detection wavelength for NIT, NIM 577.0 and 616 nm for LAC respectively.

4. 3. Application to tablets analysis

Table 3 illustrates quantification results for the tested drugs in tablets utilizing the DABA reaction. The accuracy and repeatability of the established analytical technique were acceptable.

Table 3

The results of the quantitative determinations of CCBs in tablets

Dosage form	NIT 10 mg	NIM 30 mg	LAC 2 mg
	Value		
1	9.961	29.983	1.958
2	10.156	30.435	2.044
3	9.932	29.734	1.954
4	9.825	30.482	1.965
5	10.077	30.356	2.05
6	10.177	29.638	2.007
Mean	10.021	30.105	1.996
SD	0.138	0.37	0.044
RSD	1.377	1.229	2.204

4. 4. Validation of the spectrophotometric methods

According to the guidelines of the International Conference on Harmonization (ICH) [42], the developed spectrophotometric procedure for determining the studied CCB drugs in tablets has been validated for such parameters as linearity, robustness, accuracy, precision and range of application.

Robustness.

During the method's development, robustness (absorbance stability, reagent volume, and heating duration) was evaluated. Prior research had demonstrated that adjustments made during the robustness study that are within ± 10% did not substantially alter the resulting absorbance (Table 4). All computed values range from 98.0 to 102.0% and satisfy the acceptance requirements.

Table 4

Robustness of the proposed procedure

Method parameters	Recovery* ± SD		
	NIT	NIM	LAC
Stability of solutions, min			
1	100.53 ± 1.1	100.01 ± 1.48	99.51 ± 0.68
2	99.91 ± 0.91	99.75 ± 1.74	101.14 ± 0.82
3	100.93 ± 0.75	99.38 ± 1.25	99.12 ± 0.47
Volume of reagent, mL			
1.35	99.67 ± 1.01	98.75 ± 0.5	99.61 ± 1.81
1.5	98.88 ± 0.75	100.69 ± 0.37	99.63 ± 0.98
1.65	100.2 ± 1.6	99.67 ± 0.79	99.39 ± 0.49
Heating time, min			
13.5	100.84 ± 0.63	100 ± 1.22	99.27 ± 1.34
15	100.68 ± 0.86	101.24 ± 0.04	100.04 ± 1.22
16.5	99.97 ± 1.15	100.58 ± 1.17	100.16 ± 1.39

*Note: *– average of the three determinations.*

Linearity.

Regression analysis was employed to evaluate the linearity of the suggested spectrophotometric approach for determining CCBs by its interaction with DABA, in compliance with ICH standards. In Table 5 and Fig. 7 display a few spectrum features and validation parameters for the evaluated spectrophotometric procedure. Linearity was studied over a wider range for quantification capabilities and for the Dissolution Test perspective.

It was demonstrated that whereas LAC determination had the widest range, NIT determination was the most sensitive. All analytes had correlation values of more than 0.9993, which suggests that the linearity of the analytical procedures was satisfactory.

Accuracy.

The accuracy of the suggested approach was assessed by looking at three drug concentration levels. As indicated in Table 6, the acquired findings demonstrated a considerable agreement between the tested and real ones, demonstrating the accuracy of the devised approach. The range of the average recovery percentage was 98.7% to 100.7%. Every concentration level had a recovery value that ranged from 98.0% to 102.0%. The RSD for every recovery value was less than 1.36%.

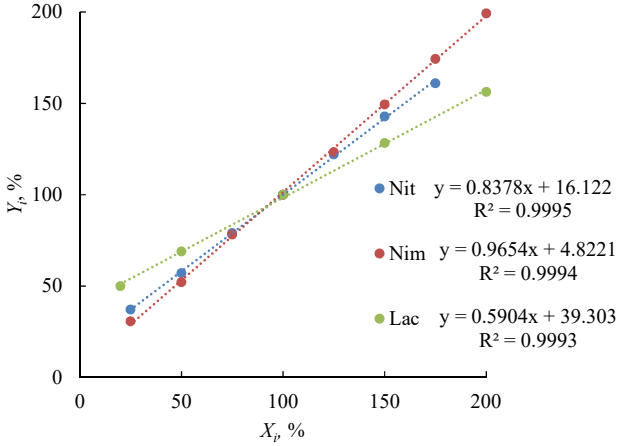

Fig. 7. Linearity study results

Table 5

Linearity results for the evaluated spectrophotometric procedures

Parameter	NIT	NIM	LAC
	Value		
Linearity, μg/mL	25–175	25–200	20–200
Correlation coefficient (R^2)	0.9995	0.9993	0.9993
Intercept ± SD*	$0.0451 \pm 2.67 \times 10^{-3}$	$0.0127 \pm 3.33 \times 10^{-3}$	$0.0998 \pm 2.86 \times 10^{-3}$
Slope ± SD	$0.0023 \pm 2.39 \times 10^{-5}$	$0.0025 \pm 2.83 \times 10^{-5}$	$0.0015 \pm 2.33 \times 10^{-5}$
LOD**, μg/mL	3.75	4.43	6.3
LOQ***, μg/mL	11.38	13.43	19.1

*Note: *SD – standard deviation; **LOD – limit of detection; ***LOQ – limit of quantitation.*

Table 6

Accuracy assessment of the proposed spectrophotometric determinations of CCBs using reaction with DABA

Conc level	NIT	NIM	LAC
	% Recovery*		
1	100.54	98.69	99.69
2	100.72	100.2	99.48
3	99.55	100.12	100.02
*Mean Recovery	100.27	99.67	99.73
SD	1.13	1.29	1.36

*Note: * – mean of three parallel determinations.*

Precision.

Using intra- and inter-day precision evaluation, the degree of agreement between the experimental results was evaluated. While intra-day precision was achieved by repeating the measurement of three analyte concentration levels at three separate times of the day, inter-day precision was achieved by monitoring the same concentrations for three consecutive days. Table 7 shows the results that were achieved.

Table 7

Intra- and inter-day precision assessment

CCB drug	Concentration level	% Mean Recovery* ± SD	
		Intra-day	Inter-day
NIT	1	100.66 ± 0.41	99.62 ± 0.91
	2	100.37 ± 0.81	100.61 ± 1.04
	3	99.08 ± 0.78	99.26 ± 0.92
NIM	1	99.58 ± 0.28	101.47 ± 0.29
	2	99.45 ± 1.51	100.48 ± 1.33
	3	100.77 ± 1.06	99.89 ± 1.89
LAC	1	100.38 ± 1.02	100.22 ± 1.39
	2	99.89 ± 1.43	99.11 ± 1.09
	3	100.28 ± 0.58	99.77 ± 1.08

*Note: * – mean of three determinations.*

5. Discussion of research results

Simple, available and alternative visible spectrophotometric methods for the determination of nitrendipine (NIT), nimodipine (NIM), lacidipine (LAC) in tablets through derivatization with the *para*-dimethylaminobenzaldehyde (DABA) have been developed. The optimal parameters for CCBs spectrophotometric analysis were as follows: detection wavelength – 577 nm for NIM, NIT and 616 nm for LAC, concentrated hydrochloric acid, 1.5 mL of 0.1% DABA solution, 15 min boiling at 100°C. The concentration was linearly proportional to absorbance values in the range of 25–175 μg/mL (NIT), 25–200 μg/mL (NIM), 20–200 μg/mL (LAC). Estimation of LOD and LOQ parameters were obtained as 3.75 μg/mL and 11.38 μg/mL (NIT), 4.43 μg/mL and 13.43 μg/mL (NIM), 6.30 μg/ml and 19.1 μg/mL (LAC).

In comparison with method [36], our modified technique for the determination of LAC made it possible to obtain a wider range of applications of the method, which definitely expands the scope of its application and optimized sample preparation, which significantly reduces the number of solvents. In addition, two spectrophotometric methods for the determination of NIT and NIM in tablets have been developed. All proposed methods can be used as alternatives and arbitrage, which significantly expands the bank of analytical methods.

Practical relevance. The proposed methods can be used as alternatives and arbitrage, which significantly expands the bank of analytical methods. Moreover, the described methods can be easily implemented for routine pharmaceutical analysis.

Study limitations. The developed spectrophotometric method can not be used to determine NIM, NIT and LAC in the presence of other antihypertensive APIs in medicines.

Prospects for further research. The next stage of research is planned to develop optimized chromatographic methods for the determination of calcium channel blockers in drugs.

6. Conclusion

In this work, thorough scientific research was carried out with the presentation of the method of selection of the optimal reaction conditions and spectrophotometric methods for determining NIT, NIM, LAC in tablets were developed. In addition, the three studied CCBs were quantified using easy-to-implement, simple, cost-effective spectrophotometric approaches. The proposed methods can be used as alternatives and arbitrage, which significantly expands the bank of analytical methods. Moreover, the described methods can be easily implemented for routine pharmaceutical analysis.

Conflict of interest

The authors declare that they have no conflict of interest in relation to this research, whether financial, personal, authorship or otherwise, that could affect the research and its results presented in this article.

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Data availability

The manuscript has no associated data.

Use of artificial intelligence

The authors confirm that they did not use artificial intelligence technologies when creating the current work.

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References

1. Hypertension. World Health Organization. Available at: https://www.who.int/health-topics/hypertension#tab Last accessed: 31. 05. 2024

2. McKeever, R. G., Patel, P., Hamilton, R. J. (2024). Calcium Channel Blockers. Treasure Island: StatPearls Publishing. Available at: https://www.ncbi.nlm.nih.gov/books/NBK482473/

3. Lin, Y., Ma, L. (2018). Blood pressure lowering effect of calcium channel blockers on perioperative hypertension. Medicine, 97 (48), e13152. https://doi.org/10.1097/md.0000000000013152

4. Pavasini, R., Camici, P. G., Crea, F., Danchin, N., Fox, K., Manolis, A. J. et al. (2019). Anti-anginal drugs: Systematic review and clinical implications. International Journal of Cardiology, 283, 55–63. https://doi.org/10.1016/j.ijcard.2018.12.008

5. Shadman, J., Panahpour, H., Alipour, M. R., Salimi, A., Shahabi, P., Azar, S. S. (2024). Investigating the therapeutic effects of nimodipine on vasogenic cerebral edema and blood-brain barrier impairment in an ischemic stroke rat model. Neuropharmacology, 257. https://doi.org/10.1016/j.neuropharm.2024.110054

6. Nimodipine. USP Monographs. Available at: https://doi.usp.org/USPNF/USPNF_M56650_05_01.html Last accessed: 31.05.2024

7. The European Pharmacopoeia (2022). European Directorate for the Quality of Medicines & HealthCare. Available at: https://www.edqm.eu/en/european-pharmacopoeia-ph.-eur.-11th-edition

8. Isse, F. A., Le, T., Mahmoud, S. H. (2021). Enantioselective assay of nimodipine in human plasma using liquid chromatography–tandem mass spectrometry. Biomedical Chromatography, 35 (2). https://doi.org/10.1002/bmc.4971

9. Mohamed, S., Riva, R., Contin, M. (2016). Simple and validated UHPLC–MS/MS analysis of nimodipine in plasma and cerebrospinal fluid of patients with subarachnoid haemorrhage. Journal of Chromatography B, 1028, 94–99. https://doi.org/10.1016/j.jchromb.2016.06.012

10. Riekes, M. K., Rauber, G. S., Kuminek, G., Tagliari, M. P., Cardoso, S. G., Stulzer, H. K. (2013). Determination of Nimodipine in the Presence of its Degradation Products and Overall Kinetics through a Stability-Indicating LC Method. Journal of Chromatographic Science, 51 (6), 511–516. https://doi.org/10.1093/chromsci/bms174

11. Feng, X. U., Xiaoxue, L. I., Li, L. I., Jicheng, L. U. (2018). Rapid detection of three chemical components added illegally into antihypertensive health food by TLC concentration in situ combined with Micro-Raman spectroscopy method. Chemical journal of Chinese Universities, 39 (6), 1172. https://doi.org/10.7503/cjcu20170735

12. Wang, W., Li, P., Fang, M., Li, X., Zhang, Y., Zhang, T. (2020). SFC-MS/MS Method for Simultaneous Determination of Nimodipine and 3-n-Butylphthalide in Beagle Plasma: Application to Pharmacokinetic Interaction Study. Bioanalysis, 12 (21), 1509–1519. https://doi.org/10.4155/bio-2020-0229

13. Galvão, A. F., Ajimura, T. O., Aguiar, F. A., Borges, K. B., Masetto de Gaitani, C. (2012). Stability-indicating methods for the enantioselective determination of dihydropyridines by high performance liquid chromatography and capillary electrophoresis. Analytical Methods, 4 (9), 2953. https://doi.org/10.1039/c2ay25055a

14. Lacidipine. PubChem. National Library of Medicine. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/5311217 Last accessed: 31.05.2024

15. Liu, X., Huang, Z., Zhang, Y., Shui, X., Liu, F., Wu, Z. et al. (2021). Lacidipine Ameliorates the Endothelial Senescence and Inflammatory Injury Through CXCR7/P38/C/EBP-β Signaling Pathway. Frontiers in Cardiovascular Medicine, 8. https://doi.org/10.3389/fcvm.2021.692540

16. Belal, F., Sharaf EL-Din, M., Tolba, M. M., Alaa, H. (2015). Micelle-enhanced spectrofluorimetric method for determination of lacidipine in tablet form; application to content uniformity testing. Luminescence, 30 (6), 805–811. https://doi.org/10.1002/bio.2823

17. Shen, J., Hu, A., Yang, Y., Nie, T., Huang, S., Cheng, Z. et al. (2024). Ternary solid dispersions of lacidipine: Enhancing dissolution and supersaturation maintenance through strategic formulation optimization. International Journal of Pharmaceutics, 654. https://doi.org/10.1016/j.ijpharm.2024.123989

18. Preeti, Sambhakar, S., Malik, R., Bhatia, S., Harrasi, A. A., Saharan, R., Aggarwal, G. et al. (2024). Lipid Horizons: Recent Advances and Future Prospects in LBDDS for Oral Administration of Antihypertensive Agents. International Journal of Hypertension, 1–54. https://doi.org/10.1155/2024/2430147

19. Dandu, G., Akkimi, P., Thirupathireddy, A., Venkateswara, B. (2019). Analytical method development and validation for the estimation of lacidipine in bulk and dosage form by RP-HPLC. Asian Journal of Chemical and Pharmaceutical Research, 7 (1), 1–6.

20. Sai Chebrolu, T., Kumar, L., Verma, R. (2021). Lacidipine: Review of Analytical Methods Developed for Pharmaceutical Dosage forms and Biological Fluids. Bioanalysis, 13 (12), 1011–1024. https://doi.org/10.4155/bio-2021-0024

21. Kisan Chatki, P., Tabassum, S. (2021). Analytical Methods of Dihydropyridines Based Calcium Channel Blockers - Amlodipine, Lacidipine, Isradipine, Nifedipine, Felodipine, Cilnidipine and its related formulations: A Review. Asian Journal of Research in Chemistry, 221–234. https://doi.org/10.52711/0974-4150.2021.00039

22. Chen, H., Li, L., Song, S., Du, Y., Jin, X., Ding, P. et al. (2018). Determination of lacidipine in human plasma by LC-MS/MS: Application in a bioequivalence study. Int. Journal of Clinical Pharmacology and Therapeutics, 56 (10), 493–500. https://doi.org/10.5414/cp203250

23. Nitrendipine. PubChem. National Library of Medicine. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/Nitrendipine Last accessed: 31.05.2024

24. Yusupova, K. H. F., Abdullaeva, G. J., Khamidullaeva, G. A., Ibrohimov, N. N. (2023). Neuroprotective efficacy of combined antihypertensive treatment with the inclusion of nitrendipine in patients with arterial hypertension. European Heart Journal, 44 (2). https://doi.org/10.1093/eurheartj/ehad655.2340

25. Mohammad, M. A.-A., Mahrouse, M. A., Amer, E. A. H., Elharati, N. S. (2021). Simultaneous determination of enalapril maleate and nitrendipine in tablets using spectrophotometric methods manipulating ratio spectra. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 244, 118894. https://doi.org/10.1016/j.saa.2020.118894

26. Sharma, A., Sharma, R., Singh Bora, K., Harikumar, S. L. (2022). Pharmacokinetic investigation of nitrendipine encapsulated niosomal gel in rat plasma by RP-HPLC method. Materials Today: Proceedings, 68 (4), 653–657. https://doi.org/10.1016/j.matpr.2022.05.301

27. Kawabata, K., Muraoka, H., Miyara, M., Kotake, Y., Nishi, H. (2023). Photodegradation profiling of nitrendipine: evaluation of active pharmaceutical ingredient, tablets and its altered forms. Analytical Sciences, 39 (11), 1791–1803. https://doi.org/10.1007/s44211-023-00400-x

28. Fares, H., DiNicolantonio, J. J., O'Keefe, J. H., Lavie, C. J. (2016). Amlodipine in hypertension: a first-line agent with efficacy for improving blood pressure and patient outcomes. Open Heart, 3 (2), e000473. https://doi.org/10.1136/openhrt-2016-000473

29. Li, X., Wang, C., Li, T., Liu, Y., Liu, S., Tao, Y. et al. (2020). Bioequivalence of levamlodipine besylate tablets in healthy Chinese subjects: a single-dose and two-period crossover randomized study. BMC Pharmacology and Toxicology, 21 (1). https://doi.org/10.1186/s40360-020-00459-6

30. Kryskiw, L., Horyn, M., Kucher, T., Zarivna, N., Poliak, O., Logoyda, L. (2024). Novel eco-friendly spectrophotometric determination of lercanidipine hydrochloride in tablets using methyl red. ScienceRise: Pharmaceutical Science, 3 (49), 47–53. https://doi.org/10.15587/2519-4852.2024.307263

31. Nguyen, T. D., Le, T. H., Nguyen, T. H., Hoang, T. T. M. (2022). Extractive spectrophotometric determination of nimodipine through ion-pair complex formation with bromothymol blue. Journal of Science and Technique, 17 (1), 5–16. https://doi.org/10.56651/lqdtu.jst.v17.n01.297

32. Alkhalil, R., Attal, A., Sakur, A. A. (2019). Spectrophotometric Determination of Amlodipine Besylate in Pure Form and Pharmaceutical Formulation using Amido Black. Research Journal of Pharmacy and Technology, 12 (7), 3389–3392. https://doi.org/10.5958/0974-360x.2019.00572.9

33. Abed, S. S. (2020). Cloud-Point Extraction and Spectrophotometric Determination of Nifedipine in Pharmaceutical Dosage Forms. Systematic Reviews in Pharmacy, 11 (7), 125–130.

34. Tulasamma, P., Venkateswarlu, P. (2016). Spectrophotometric determination of nifedipine in pharmaceutical formulations, serum and urine samples via oxidative coupling reaction. Arabian Journal of Chemistry, 9, S1603–S1609. https://doi.org/10.1016/j.arabjc.2012.04.025

35. Reddy, M. N., Murthy, T. K., Rao Kanna, K. V., Gopal Hara, A. V., Sankar, D. G. (2001). New spectrophotometric methods for the determination of nimodipine. Indian Drugs, 38 (3), 140–142.

36. Moorthi, C., Aju, M., Elsadig, Prezzy, Sumithira, G. (2011). Spectrophotometric determination of lacidipine in bulk and tablet dosage form. Journal of Applied Pharmaceutical Science, 1 (5), 209–213.

37. Gudavarthi, S. (2012). Rajiv Gandhi University of Health Sciences (India) ProQuest Dissertations & Theses.

38. Hamd, M. A. E., Derayea, S. M., Abdelmageed, O. H., Askal, H. F. (2013). A Novel Spectrophotometric Method for Determination of Five 1,4-Dihydropyridine Drugs in Their Tablets and Capsules Using Vanillin Reagent. American Journal of Analytical Chemistry, 4 (3), 148–157. https://doi.org/10.4236/ajac.2013.43020

39. Marzouq, M. A., El Hamd, M. A., Ahmed, S. A., Askal, H. F., Saleh, G. A. (2015). Spectrophotometric determination of some 1,4-dihydropyridine drugs in their pharmaceutical preparations and spiked human plasma. Der Pharma Chemica, 7 (8), 105–111.

40. 4- (diethylamino) benzaldehyde. PubChem. National Library of Medicine. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/7479 Last accessed: 31.05.2024

41. Mohamed, S., Yousif, E., Kadhom, M., Bufaroosha, M. (2024). Enhanced photostability of polyvinyl chloride films through antipyrine derivatives: a comprehensive study on UV resistance and degradation inhibition. Macromolecular Research, 33 (1), 85–103. https://doi.org/10.1007/s13233-024-00310-5

42. Validation of Analytical Procedures Q2 (R2) (2023). ICH. Available at: https://database.ich.org/sites/default/files/ICH_Q2%28R2%29_Guideline_2023_1130.pdf Last accessed: 24.06.2024

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Mariana Horyn, PhD, Assistant Professor**,** Department of Pharmaceutical Chemistry**,** I. Horbachevsky Ternopil National Medical University**,** Voli sq., 1, Ternopil, Ukraine, 46001

Liubomyr Kryskiw, PhD, Associate Professor, Department of Pharmaceutical Chemistry, I. Horbachevsky Ternopil National Medical University, Voli sq., 1, Ternopil, Ukraine, 46001

Tetyana Kucher, PhD, Associate Professor**,** Department of Pharmaceutical Chemistry**,** I. Horbachevsky Ternopil National Medical University**,** Voli sq., 1, Ternopil, Ukraine, 46001

Nadiya Zarivna, PhD, Associate Professor**,** Department of Pharmaceutical Chemistry**,** I. Horbachevsky Ternopil National Medical University, Voli sq., 1, Ternopil, Ukraine, 46001

Nataliia Shulyak, PhD, Senior Lecturer**,** Municipal Institution of Higher Education «Volyn Medical institute» of the Volyn Oblast Council**,** Lesi Ukrainky str., 2, Lutsk, Ukraine, 43016

Iryna Ivanchuk, PhD, Associate Professor**,** Department of Chemistry, Pharmaceutical Analysis and Postgraduate Education**,** Ivano-Frankivsk National Medical University, Halytska str., 2, Ivano-Frankivsk, Ukraine, 76018

Liliya Logoyda*, Doctor of Pharmaceutical Sciences, Professor, Head of Department**,** Department of Pharmaceutical Chemistry, I. Horbachevsky Ternopil National Medical University, Voli sq., 1, Ternopil, Ukraine, 46001

***Corresponding author:** *Liliya Logoyda, e-mail: logojda@tdmu.edu.ua*