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UV-VISIBLE SPECTROSCOPIC ANALYTICAL METHODS OF DIHYDROPYRIDINES BASED CALCIUM CHANNEL BLOCKERS AND ITS FORMULATIONS: A REVIEW

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ABSTRACT

1,4-Dihydropyridine derivatives such as nifedipine, amlodipine, lacidipine, felodipine, and related calcium channel blockers are widely used in the management of cardiovascular disorders. Accurate qualitative and quantitative analysis of these compounds is essential for quality control, pharmacokinetic studies, and regulatory compliance. Spectroscopic techniques have emerged as reliable, rapid, and cost-effective tools for the analysis of dihydropyridine drugs in bulk materials, pharmaceutical formulations, and biological matrices. This review provides a comprehensive overview of spectroscopic methods employed for the analysis of dihydropyridine derivatives, including ultraviolet–visible (UV–Vis) spectrophotometry, fluorescence spectroscopy, and mass spectrometry. The principles, analytical performance, advantages, and limitations of each technique are critically discussed with emphasis on method sensitivity, selectivity, and applicability. Recent advancements such as derivative spectrophotometry, spectrofluorimetric enhancements, and hyphenated spectroscopic techniques are also highlighted. The review aims to serve as a valuable reference for researchers and analysts involved in pharmaceutical analysis and method development for dihydropyridine-based drugs.

Keywords: *Calcium channel blocker, Dihydropyridine , Nifedipine,UV- Visibe Spectroscopy,*

INTRODUCTION

Hypertension represents a major global health concern, particularly among middle-aged and elderly populations. Epidemiological studies indicate that more than one billion individuals worldwide are affected by elevated blood pressure, which significantly contributes to cardiovascular and renal morbidity and mortality [1,2]. Effective management of hypertension is therefore critical for reducing long-term complications. Combination therapy using agents with different mechanisms of action has been shown to improve therapeutic outcomes and patient compliance [3,4].

Calcium channel blockers (CCBs) and angiotensin receptor blockers (ARBs) are frequently combined for the treatment of hypertension due to their complementary pharmacological effects [5,6]. Benidipine, a long-acting dihydropyridine calcium channel blocker, inhibits L-, N-, and T-type calcium channels and has been reported to exert both renal and cardiovascular protective effects [7,8]. Telmisartan, an angiotensin II receptor antagonist, lowers blood pressure by reducing systemic vascular resistance through selective AT1 receptor blockade. In addition, telmisartan exhibits partial peroxisome proliferator-activated receptor-γ (PPAR-γ) agonistic activity, which may offer metabolic benefits [9–10].

The widespread therapeutic use of dihydropyridine drugs necessitates the development of accurate and economical analytical methods for their determination in bulk drugs and formulations. UV–visible spectrophotometry is particularly attractive for this purpose, as it requires simple instrumentation, inexpensive reagents, and minimal sample preparation. Numerous spectrophotometric methods have been reported for the analysis of nifedipine and related drugs, based on condensation reactions, oxidative coupling, and reduction–oxidation mechanisms. These methods are well suited for routine quality control due to their acceptable precision, accuracy, and robustness. Spectrophotometric Determination of Dihydropyridine Drugs Several UV–visible spectrophotometric methods have been described for the determination of dihydropyridine calcium channel blockers in pharmaceutical preparations and, in some cases, biological matrices. The reported methods differ in reaction chemistry, wavelength of measurement, and instrumental setup, but generally rely on the formation of colored species that absorb in the visible region. Condensation reactions involving 1,4-dihydropyridine drugs and aromatic aldehydes in acidic media have been successfully employed, producing colored products with measurable absorbance. In such methods, reaction conditions such as reagent concentration, temperature, acidity, and reaction time are optimized to achieve maximum sensitivity and linearity.

Oxidative coupling reactions constitute another widely used approach. In these methods, the nitro group present in certain dihydropyridine drugs, such as nifedipine, is first reduced to the corresponding amino group. The reduced form then participates in oxidative coupling reactions with suitable chromogenic reagents, leading to the formation of intensely colored compounds. The absorbance of these products is measured at characteristic wavelengths, allowing quantitative determination.

Flow injection analysis (FIA) combined with spectrophotometric detection has also been explored for nifedipine estimation. The use of solid-phase reactors, such as immobilized manganese dioxide packed in a flow system, enables on-line oxidation reactions and improves sample throughput. These FIA-based methods offer advantages including reduced reagent consumption, enhanced reproducibility, and shorter analysis time.

Analytical Methods for Nifedipine

Nifedipine has been extensively studied due to its clinical importance and favorable spectroscopic behavior. Several methods are based on the reduction of the nitro group of nifedipine to an amino derivative using zinc in acidic medium. The resulting reduced form undergoes oxidative coupling with reagents such as pyrocatechol, 3-methyl-2-benzothiazolinone hydrazone (MBTH), or brucine in the presence of suitable oxidizing agents.

In one approach, reduced nifedipine reacts with pyrocatechol, which is oxidized by cerium(IV) or immobilized manganese dioxide to form a colored product measurable in the visible region. The use of a flow injection manifold with a solid oxidant reactor has been reported to provide a simple and sensitive procedure for nifedipine determination.

Alternative methods involve oxidative coupling of reduced nifedipine with MBTH in the presence of ferric chloride to form a green-colored chromogen, or with brucine–periodate systems to produce violet-colored products. These reactions yield stable colors with good linearity over defined concentration ranges, making them suitable for routine analysis.

Advantages and Limitations

UV–visible spectrophotometric methods offer several advantages, including low operational cost, ease of execution, and satisfactory analytical performance. The reagents used are generally inexpensive and readily available, and the instruments required are common in quality control laboratories. However, these methods may suffer from limited selectivity in complex matrices and often require careful optimization of reaction conditions to avoid interference.

Despite these limitations, spectrophotometric techniques remain valuable tools for the routine estimation of dihydropyridine drugs, particularly in settings where advanced chromatographic instrumentation is not available.

Table1: Details of the Methods, Maximum Absorption Wavelength and Optimised Conditions

Wavelength	Compound	Instrument	Method description	Optimisation of conditions	Ref
460 nm	nifedipine, nicardipine, nimodipine in pure form and pharmaceutical preparations. And spiked human plasma	Shimadzu model 1601PC, UV-Visible Spectrophotometer	condensation reaction of 1,4-DHP with p-anisaldehydein acidic medium and measuring the absorbance at 460 nm. The absorbance-concentration plot was rectilinear over the concentration range of 5-60 µg/mL with a minimum detection limit of 0.72-2.08 µg/mL.	1)Conc of anisaldehyde 5mg/ml (Absorbance increase with conc.) 2)Acid HCL 3)Temp. 80 °C 4)Time 20 min	11
432 nm 447 nm 458 nm 457 nm 464 nm	Nifedipine (NIF) Nicardipine (NIC), nimodipine(NIM	Jenway-6305 UV-Visible Spectrophotometer	treatment of 1,4-DHP drugs 10 ml with 1 ml TBAH base in DMSO. A yellow colour that formed can be regarded as anion	1)concentration range of 2.50-40.0 µg/mL 2)Reaction time 20 mins 3) Base TBAH 25 mg/mL (Trials on NaOH, KOH	12

	) Felodipine (FEL) Amlodipine(AML) in the tablets and capsules		formation between acidic N-H in 1,4-DHP drugs and TBAH alkali.	and tetraethylammonium hydroxide 4) solvent - dipolar aprotic solvents such as acetone, dimethyl formamide (DMF) or DMSO (Water and other protic solvent such as ethanol, methanol and propanol have a destructive effect on the formed chromogen.)	
500 nm 500 nm 500 nm 479nm	NIF NIC NIM FEL	Shimadzu model 1601PC, UV-Visible Spectrophotom eter (Shimadzu, Tokyo, Japan) and Jenway 6305, UV-Visible Spectrophotom eter,	coupling reaction between aldehydic group of vanillin and active methyl group which present in all the cited drugs in the acidic condition. Under optimized conditions form red coloured products. suggested mechanism involved one reaction step and did not depend on the presence of the -NO_3 group	1) concentration range-5 - 70 µg/mL 2) Vanillin Reagent concentration 0.5%, w/v for NIF, NIC, NIM ,FEL. And 2.0 % w/v for AML Prepared by dissolving in 2 ml methanol followed by 98 ml 35% W/V HCL 3)temperature up to 50˚C for 30 min, in case of NIF, NIC, NIM and FEL 70˚C for 35 min for AML	13
607nm	NIF Atenolol NIC NIM FEL AML besylate, metoprolol)	Shimadzu 1601PC, UV-visible spectrophotome ter , Jenway 6305, UV-visible spectrophotome ter	The method is based on addition of known excess of NBS to an acidified solution of 1,4-DHP drugs and determining the residual of NBS through its ability to bleach the colour of the used dye; the amount of NBS that reacted corresponded to the amount of drugs. Reaction between INC and NBS. INC has a blue colour in aqueous solution showed *λ*max at607 nmduetoitshighlyconjugat edstructure.	Concentration of NBS 0.02%w/v INS 0.07% w/v Time- Contact time with NBS min 20 mins can be extended to 45 mins Bleaching time with HClO4- 10 mins colour is stable for hours after this	14
233.1 nm 239.8 nm	**Telmisartan and Benidipine formulation**	Shimadzu 1650, Japan UV Vis Spectrophotom eter	Powdered tablet equivalent to 4 mg of BEN and 40 mg of TEL was dissolved in 50 mL of ethanol by sonicating for 15 min. The solution was filtered into another 100 mL graduated flask, the remainder was splashed with additional ethanol, and the absolute volume made 100 mL with ethanol.		15
218 nm	Lacidipine	Shimadzu UV - 1800 UV/VIS spectrophotome ter	Second order derivative method developed for the estimation of Lacidipine after dissolving in	Concentration - 100 mcg/ml.	16

			methanol , It was kept for ultrasonication for 30 min and filtered through Whatman filter paper No. 41.		
Method I(absorption) 525 Method II (Fluorescence (355)	NIF NIC NIM FEL AML	Shimadzu 1601PC, UV-visible spectrophotometer	In method I The drugs were oxidizable by KMnO4 in acidic solution this was evidenced from the decrease in the violet colour at 525 nm of the KMnO4 solution . The decrease in colour (ΔA) was used as a measure for the concentration of the drugs in their solutions. In method II; the oxidation resulting in release of cerium (III) which measured at emission 355 nm(Excitation at 255 nm)	Reagent concentration Method I Conc. 25 to 30 µg/ml KMnO4solution- 1.0 ml of 0.07% w/v above this no effect on absorbance Acid – 5.7 M Sulphuric acid (Trials on HCL, HNO3, Acetic Acid , Perchloric acid) heat of reaction Solvent- Water gave max absorbance after trial on acetone , ethanol, methanol and propanol Method II Conc. 0.1 to 1.0 µg/ml Con of Ce (IV) - 0.75 mg/ml above this Fluorescence intensity decreases. Temp.- Method 1- R.T Method 2- 40 ºC To 60ºC	17
297 nm	Telmisartan	Double beam UV/Vis spectrophotometer, Systronics UV- 1100		Solvent: Triethyl amine, methanol, distilled water in ratios of 5:10:85 Concentration Range: 10 50µg/mL Linearity (R2): 0.999	18
467nm	NIF	A digital double beam spectrophotometer a type of Shimadzu UV-VIS 260 peristaltic pump of six channels (Ismatec, Labortechnik-Analytic, type CH-8152,	The reduction of NIF with zinc in hydrochloric acid converted the nitro group into the corresponding amino group (Solomons, 1996). When a solution of reduced NIF was mixed with Pyrocatecol reagent and oxidized with Ce (IV) solution, an orange colour formed immediately.	Pyrocatecol Concentration- 2 x10-4M Ce(IV) Conc.- 8mM Flow rate - 1.4mL.min-1 Coil length - 75 cm Sample Volume - 150 µL	19
465 nm	NIF	Shimadzu UV–VIS 260 A peristaltic pump of six channels (Ismatec, Labortechnik-Analytic, type	Estimation NIF by use of immobilized MnO_2 on cellulose acetate support and packed in SPR which was inserted in FIA manifold. Pyrocatechol is oxidized by MnO_2(solid oxidant reactor) which then reacts with reduced NIF to produce coloured	Composition ratio (MnO_2: CA 1:9 Particles size of immobilized MnO2, mm Reactor length, cm Weight of particles packed inside the reactor, g Concentration of PC, $1x10^{-4}$ µg.mL^{-1} Flow rate, mLmin^{-1} Injection sample volume, µL Reaction coil, cm	20

			product measured spectrophotometrically.		
Method A- 685nm Method B – 546nm	NIF	Shimadzu UV–visible double beam spectrophotometer (model 2450)	Two proposed methods are based on the reduction of the nitro group to amino group of the drug. The resulting amine was then subjected to proposed meth-ods. Method A is based on the oxidation followed by coupling of nifedipine with 3-Methyl-2-ben-zothiazolinone hydrazone (MBTH) in presence of ferric chloride ($FeCl_3$) to form green colored chromogen Method B is based on the oxidative coupling reaction between the corresponding drug and brucine – NaIO4 to form violet colored chromogen at 546 nm.	Acid -Method A-HCl gave stable colour Method B – 0.1 M Sulphuric Acid	21

CONCLUSION

UV–visible spectrophotometric methods provide practical and reliable approaches for the determination of 1,4 dihydropyridine-based calcium channel blockers in pharmaceutical formulations. In particular, flow injection spectrophotometric analysis incorporating solid-phase reactors offer a sensitive and efficient strategy for nifedipine estimation. The reviewed methods demonstrate acceptable accuracy, precision, and cost-effectiveness, supporting their application in routine quality control. Continued improvements in reagent systems and flow-based techniques may further enhance the sensitivity and applicability of spectrophotometric methods for antihypertensive drug analysis.

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