FTIR SPECTROSCOPIC METHOD FOR QUANTITATIVE ANALYSIS OF CILNIDIPINE IN TABLET DOSAGE FORM

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ABSTRACT

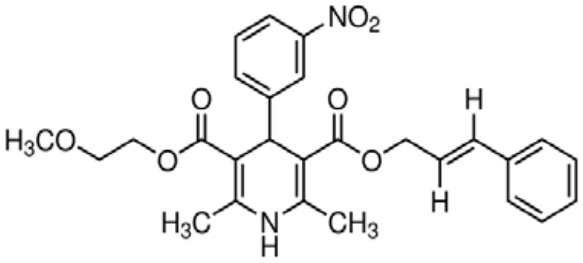
A Fourier transform infrared (FT-IR) spectrometric method was developed for the rapid and direct measurement of Cilnidipine in pharmaceutical drugs. Cilnidipine is newly discovered and very effective antihypertensive drug. Cilnidipine can be determined by various methods and now we are adding a new one that uses a Fourier transform infrared spectrophotometric technique. The method involves the measurement of absorbance of carbonyl group (C=O) peak at 1697 cm^{-1}. The proposed method was validated for pharmaceuticals in tablet form and %RSD was found to be less than two with recovery levels 99.8-102.5 and 99.8- 101.4 as per absorbance and peak area respectively.

Keywords: FT-IR, Cilnidipine, Carbonyl peak, Tablet formulation, FTIR.

INTRODUCTION

Cilnidipine(CIL)1,4-Dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinecarboxylic acid-2-methoxyethyl(2E)-3-phenyl-propenyl ester is a novel and unique dihydropyridine calcium channel blocker that possesses a slow onset, long-lasting vasodilating effect. CILis used in the treatment of hypertension[1] .CIL shows first pass mechanism. CILis used in combination with others drugs like Telmisartan(TEL), Olmesartan(OLME).

The structural formula for CIL is shown in following way.[2]



1, 4-Dihydropyridine (DHP), an important class of calcium antagonist, inhibits the influx of extracellular Ca^{+2}through L-type voltage-dependent calcium channels. **Cilnidipine** is a calcium channel blocker. Cilnidipine is the novel calcium antagonist accompanied with L-type and N-type calcium channel blocking function. Compared with other calcium antagonists, cilnidipine can act on the N-type calcium-channel that existing sympathetic nerve end besides acting on L-type calcium-channel that similar to most of the calcium antagonists. We can develop the new method for the quantitation of the Cilnidipine and Felodipine.FTIR can be used for the Quantitation purpose for the Cilnidipine. Infrared spectroscopy is a standard analytical method of provides the images of vibration of atoms of compound. Therefore it is also referred to as vibtational spectroscopy. IR spectrum is obtained by passing infrared radiation through the sample and determining what fraction of the incident radiation is absorbed and transmitted at a particular frequency.Literature survey reveals that the analytical method reported for quantitative estimation of the 1,4- Dihydropyridines are HPLC[3-5], UV[6], HPTLC[7], HPLC-MS[8], stability indicating HPLC method[10] etc. Comparative study was not done between 2 analytical methods for these drugs. This revealed that no analytical method is reported for the Quantitative estimation of the 1, 4- Dihydropyridines by FTIR except Amlodipine.So, the development and validation of the 1,4- Dihydropyridines by FT-IR is a novel , faster, easier, accurate, cheap, less time consuming method.

MATERIALS AND METHODS:

Chemicalsandreagents:

The reference samples of Cilnidipine were provided by pure chem limited Ankleshvar.Tablet used for analysis was Cillacar(Label claim: 10 mg) isprocuredfromthelocalmarket. Potassium bromide used was IR Grade. Chloroform used is of Analyticalgrade.

INSTRUMENTS AND FTIR CONDITION:

Instrument:

All spectral and absorbance measurements were made on I.R spectrophotometer (Bruker Optics alpha-T)

FTIR condition:

PARAMETERS	OPTIMISED CONDITIONS
Method of making pellets	Direct mixing method
Mode of measurement	Absorbance mode
Final wt. of pellet	150 mg
Peak selection	$1697cm^{-1}$
No. of scans	16 scans

Preparation of standard stock solution for FTIR

To the accurately weighed 30 mg of the drug, 300 mg of dried KBr was mixed with the aid of geometric mixing. This forms the stock solution of 100µg/mg. Mixing should be properly done so that each pellet formed contains uniformly distributed drug. This procedure was performed for all the three Dihydropyridines.

Preparation of standard working solution for FTIR

From the stock (100 µg/mg), 7.5, 15, 22.5, 30, 37.5, mg was weighed accurately and diluted to 150 mg with dried KBr to make the final concentration of 5, 10, 15, 20, 25µg/mg respectively. Mixing of the drug and dried KBr was done properly for uniform mixing.

RESULTS AND DISCUSSION:

Linearity and Range

The calibration curve was plotted over a concentration range of 5-25 µg/mg (Cilnidipine), Calibration curve was constructed by plotting absorbance and peak area of the C=O peak near to 1698 cm^{-1} against concentration and all the regression parameters were calculated. Then the spectrums of all individual concentration were overlaid to demonstrate the linearity. Each response was an average of five determinations.The limit of detection (LOD) is the lowest concentration of an analyte in a sample that can be detected and the limit of quantification (LOQ) is the lowest concentration of an analyte in a sample that can be quantitated. Both LOD and LOQ were experimentally verified and calculated using the following equation.

LOD = 3.3 (SD/Slope)

LOQ = 10 (SD/Slope)

Table 1: LOD and LOQ data of Cilnidipine by FT-IR Method

PARAMETER	CILNIDIPINE	
	Absorbance	Peak area
S.D. of the Y- intercept of the calibration curve	0.0085	0.061
Mean slope of the 3 calibration curve	0.1219	3.414
LOD(µg/mg)	0.22	0.050
LOQ(µg/mg)	0.60	0.17

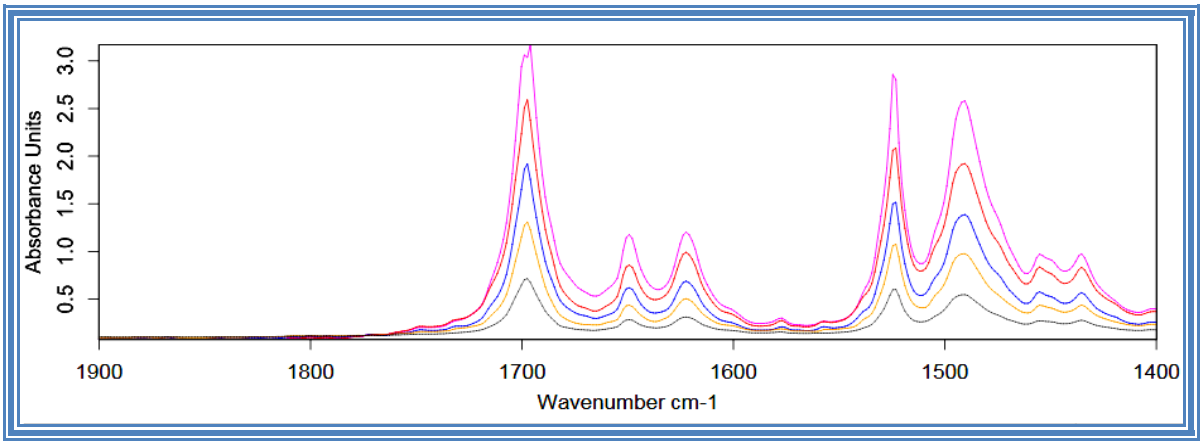


Figure 1: Overzoom Spectrum of Cilnidipine (FT-IR Method)

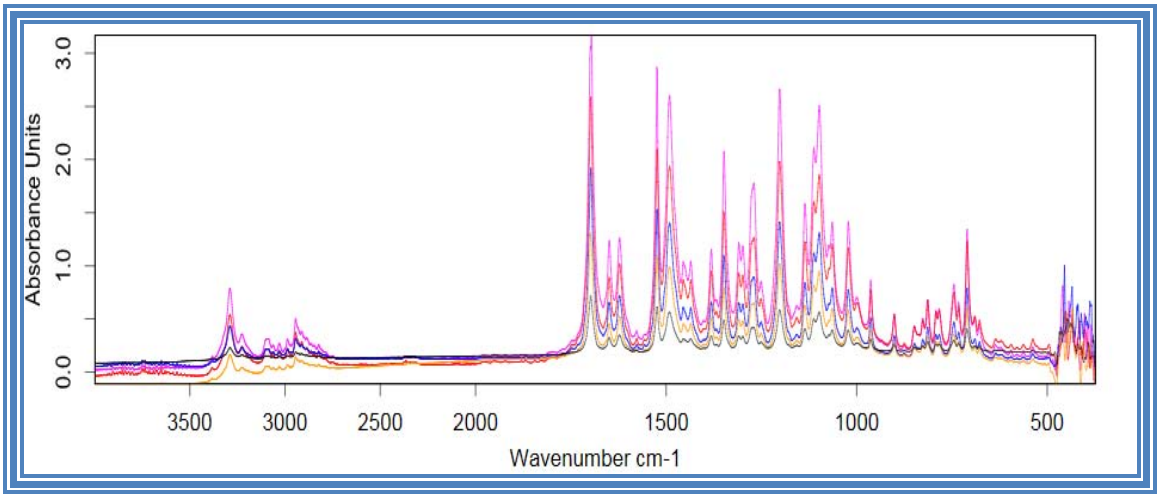


Figure 2: Overlay Spectrum of Cilnidipine (FT-IR Method)

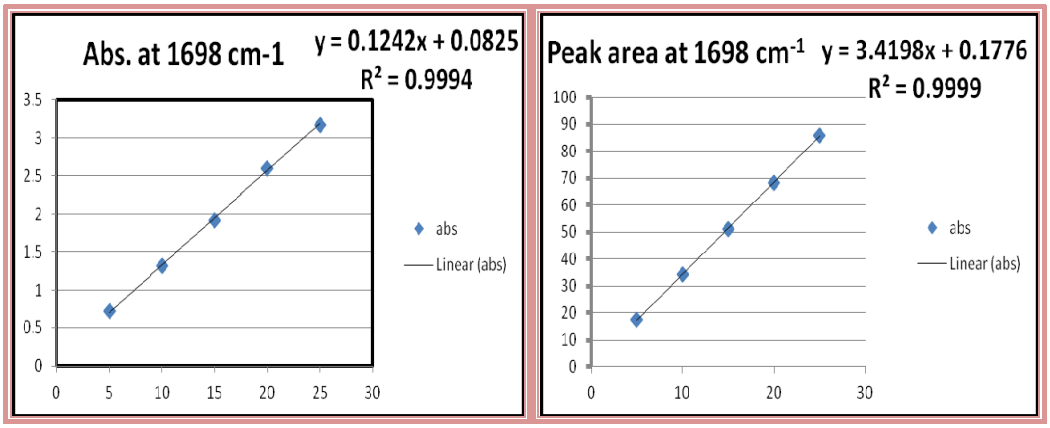


Figure: 3 Calibration Curve of Cilnidipine for Absorbance and Peak are

Table 2: IR Linearity Data of Cilnidipine for 150mg dilution with KBr

SR NO	CONC. (µg/mg)	ABSORBANCE ($1698CM^{-1}$) n=3	Mean ± SD	PEAK AREA ($1698CM^{-1}$) n=3	Mean ± SD
1	5	0.718	0.719 ± 0.0044	17.48	17.50 ±0.0047
2	10	1.312	1.31 ± 0.0122	35.30	34.22 ± 0.218
3	15	1.920	1.923 ± 0.00424	51.25	51.26 ±0.023
4	20	2.59	2.536 ±0.026	68.39	68.49 ± 0.126
5	25	3.180	3.156± 0.0176	85.94	85.50±0.333

Precision

To determine whether the proposed method is precise or not, it was confirmed by carrying out repeatability, Interday study and different analyst study for two Dihydropyridines. KBr pellets of different concentrations (lower, middle and higher of linearity range) were prepared and the absorbance & the peak area were recorded. Repeatability was checked by measuring the spectrum of any one concentration from the linearity range six times and calculating the %RSD. Then for interday& different analyst study, three different concentrations were measured on three days consecutive and by two different analyst respectively and calculating %RSD.

Table: 3 Repeatability data of 1, 4 - Dihydropyridines by FT-IR Method

SR NO	Cilnidipine	
	ABSORBANCE (10 µg/mg)	PEAK AREA
1	1.312	35.483
2	1.318	35.493
3	1.312	35.483
4	1.316	35.491
5	1.328	35.400
6	1.312	35.479
MEAN	1.314	35.485
RSD	0.0035	0.37
%RSD	0.273	1.02

Table: 4 Inter-day precision data of Cilnidipine by FT-IR Method

PARAMETER	CONC µg/mg)	DAY-1	DAY-2	DAY-3	MEAN	SD	%RSD
Absorbance	10	1.318	1.320	1.322	1.320	0.0063	0.477
	15	1.920	1.921	1.923	1.920	0.00124	0.06
	20	2.599	2.602	2.593	2.593	0.00339	0.127
Peak Area	10	35.306	35.315	35.493	35.371	0.0861	0.243
	15	51.257	51.309	51.301	51.280	0.022	0.042
	20	69.398	69.396	69.381	79.39	0.040	0.05

Table: 5 Different Analyst Study data of Cilnidipine by FT-IR Method

PARAMETER	CON (µg/mg)	ANALYST 1	ANALYST 2	MEAN	SD	%RSD
Absorbance	10	1.318	1.323	1.320	0.0025	0.189
	15	1.920	1.916	1.916	0.0020	0.104
	20	2.599	2.592	2.590	0.003	0.11
Peak Area	10	35.306	35.483	35.39	0.09	0.254
	15	51.257	51.309	51.283	0.026	0.050
	20	69.398	69.396	69.39	0.015	0.02

Accuracy

Accuracy study was carried out by calculating % Recovery of the Dihydropyridine by standard addition method. Known amounts of standard mixture of Cilnidipine (2, 5 and 8 µg/mg), were added respectively to a pre-quantified test mixture of Cilnidipine (5 µg/mg. The pellet of varying concentration prepared was measured thrice and the % recovery was calculated by measuring absorbance & peak areas and fitting these values into the regression equation of the calibration curve.

Table: 6 Accuracy data of Cilnidipine by FT-IR Method

Parameter	% of nominal amt.	Actual amt.	Spiked amt.	Total amt.	Amt. found (n=3)	recovery (n=3) %
Absorbance	80	5	4	9	9.02	100.22
	100		5	10	9.98	99.8
	120		6	11	11.20	102.5
Peak Area	80	5	4	9	29.314	99.89
	100		5	10	35.396	101.2
	120		6	11	40.126	101.4

Robustness

Robustness study was performed by varying few parameters deliberately. In FT-IR method, the parameters that were varied were the techniques that are used for recording the IR spectra. Three concentrations of each 1, 4-Dihydropyridine was measured and replicated thrice by KBr disc technique, liquid cell technique and lastly by keeping the air conditioner off.

Table 7: Robustness data of Cilnidipine by FT-IR Method

Parameter	Con(µg/ mg)	KBr technique	Liquid cell technique	Keeping A.C off	Mean	S.D	% RSD
Absorbance	10	1.312	1.390	1.310	1.335	0.0037	0.277
	15	1.920	1.929	1.922	1.923	0.0038	0.197
	20	2.599	2.593	2.600	2.597	0.003	0.115
Peak Area	10	35.306	35.310	35.306	35.307	0.0018	0.005
	15	51.257	51.262	51.260	51.259	0.0020	0.003
	20	69.398	69.400	69.396	69.398	0.0047	0.006

ANALYSIS OF THE MARKETED FORMULATION BY FT-IR SPECTROSCOPY

10 tablets of Cilnidipine (CILACAR-10 mg) were triturated after taking their average weight. The tablet powder equivalent to 1 tablet was transferred to the volumetric flask and dissolved in chloroform. The resulting solution (100µg/ml) was sonicated for 10 min and supernatant was filtered through whatman filter paper no. 41. Filtrate was evaporated and from the residue obtained 1 mg was accurately weighed, made up to 100 mg with dried KBr and triturated well. Then the dilution is further performed from this stock mixture to prepare the pellet of desired concentration. Thereafter the concentration of the sample was found from regression equation of calibration curve of respective 1, 4-dihydropyridines.

Table 8: Analysis of Marketed Formulation by FT-IR Method

Formulation	Amount of Drug taken (µg/mg)	Amt. found (µg/ml) (n=6)		%label claim	
		Absorbance	Peak Area	Absorbance	Peak Area
Cillacar	10	9.986	9.95	99.86%	99.66%

CONLUSION:

In the present investigation we have studied the possibility of quantification of Cilnidipine in single dosage formulation using FT-IR. From the data it is clear that FT-IR is capable of direct determination of Cilnidipine in the above formulations. The proposed FT-IR method was found to be simple, rapid, and reproducible and less time consuming compared to other analytical methods.

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