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UV spectrophotometric method development and validation of Cilnidipine API and marketed pharmaceutical dosage form

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ABSTRACT

The present research work to develop and validate a simple, accurate, precise and economic method for estimation of Cinidipine in bulk and tablet dosage form by using UV spectroscopy. Ethanol was used as solvent for Cilnidipine. The UV spectrum of Cilnidipine showed λmax at 240nm and obeyed Beer-Lambert's law in the concentration range of 2-14µg/ml. The method was shown linear with line equation y=0.062x-0.012, with correlation coefficient r^2 =0.988. The accuracy values for Cilnidipine ranged from 97.8% to 100.06%. The %RSD of inter day precision was 0.52% to 1.92% (%RSD less than 2) and intra day precision was 0.672% to less than 2%.The system suitability studies in both pure and marketed formulation was within limits (%RSD Less than 2). The LOD & LOQ range was 0.0638µg/ml & 0.193µg/ml. Hence the proposed method is applicable for quantitative determination of bulk drug and pharmaceutical dosage form for routine analysis.

Keywords: Uv spectroscopy, Cilnidipine, ICH guidelines.

INTRODUCTION

Cilnidipine is a dihydropyridine calcium antagonist. It acts on N-type calcium channel that existing sympathetic nerve end besides acting on L-type calcium channel [1]. It is also indicated for the management of hypertension for end organ protection. Cilnidipine is chemically 3-(2-methoxyethyl) 5-(2E)-3-phenylprop-2-en-1-yl 2,6 dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate, with chemical formula $C_{27}H_{28}N_2O_7$ and molecular weight 492.528[2, 3].

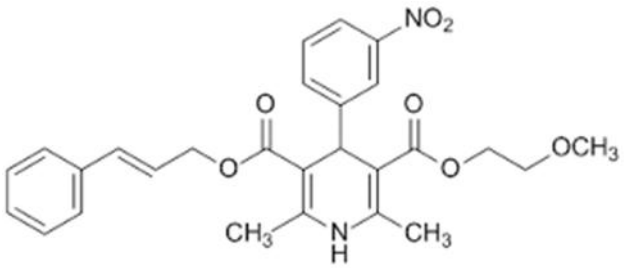

Figure 1: Structure of Cilnidipine

Literature survey has revealed that P.Ravisankar et al., 2018, developed a HPLC method development and validation. Dhwani Desai et al., 2016 were developed HPTLC method development and validation of Cilnidipine and metoprolol succinate in combined dosage form. Pankaj.P et al., 2012, developed a u.v method by using pure Cilnidipine. As such determination of Cilnidipine were reported by HPLC, HPTLC, UV methods as being used in combination with other drugs. In my present study it is directed to develop a simple, precise and accurate method by using ethanol as solvent, for the estimation of Cilnidipine in bulk and formulation as per ICH guide lines Q2 (R1).

MATERIALS AND METHOD

Materials

Pure standard of Cilnidipine powder was received as a gift sample from Aspire life sciences Pvt Ltd Mumbai, which was used as reference standard. The marketed formulation of Cilnidipine 10mg was purchased from local market.

- Ethanol: 99.9% Absolute analytical reagent (AR).
- Apparatus**:** UV visible spectrophotometer - spectro2080 model used.

Method development

Determination of λmax

The standard stock solution of 100µg /ml of Cilnidipine was prepared by weighing 10mg of drug and taken into 100ml volumetric flask and dilute with 99% ethanol and make up the final volume with ethanol. The sample was scanned in the range of 200-800nm to determine the wavelength of maximum absorbance Cilnidipine has found maximum absorption at 240nm (Figure 2).

Assay

Preparation of standard stock solution

100mg of standard drug of Cilnidipine was weighed and transferred into 100ml volumetric flask and make up the volume ethanol to 100ml to get the concentration of 1000µg /ml. From the above stock solution 100µg /ml and 10µg /ml was prepared.

Preparation of sample stock solution

Weigh 20 tablets individually and determine the average weight, triturate it to obtain homogenous mixture. An amount of powder equivalent to 10mg of Cilnidipine was taken into 10ml volumetric flask, dilute it with ethanol and sonicate for 20 mins, finally make up the volume to produce concentration of 1000µg /ml. The solution was filtered to remove the undissolved excipients. From the above stock solution 100µg /ml and 10µg /ml concentration was prepared.

Method validation [10]

Linearity

The ability of assay value to be directly proportional to the concentration of an analyte in the sample is called linearity. Linearity studies was performed by taking 100µg /ml standard stock solution of Cilnidipine and further diluted to obtain 2ug/ml-14µg /ml solutions (Table 2). The linearity curve was obtained by plotting the concentration on X-axis and absorbance on Y-axis and regression equation were calculated (Figure 3).

Precision

The system precision is a measure of the method variability. It was determined by performing three replicate analysis of the same working solutions, precision method was demonstrated by intraday and interday variation studies.The intra precision of the developed UV method was determined by preparing the sample of same batch in a determination with three concentrations (2,4,6µg /ml) and three replicates (n=3) each on same day i.e 1hours, 3hours, 6hours. The percentage RSD of the results was used to evaluate the method precision.The interday was determined by assaying the sample in triplicate (n=3) per day for three consecutive days (Table 4).

Accuracy

Accuracy of the method was ascertained by standard addition method at 3 levels. Standard quantity equivalent to 50%, 100% and 150% is to be added to the sample.From the standard stock solution of 10µg /ml take 1 ml into 3 different 10 ml volumetric flask and label as flask 1, flask 2 and flask 3 to flask 1 and 0.5ml of sample stock solution of 10 µg /ml. to flask 2 add 1ml of sample stock solution of 10µg /ml to flask 3 add 1.5 ml of sample stock solution and make up the final volume with ethanol to make 50%, 100% and 150% spiking (Table 5).

System suitability

A System suitability test of the spectrophotometer system was performed before each validation run. Six replicate reading of standard preparation was taken and %RSD of standard reading was calculated. Acceptance criteria for system suitability, %RSD of standard reading not more than 2% (Table 6).

LOD and LOQ

Detection limit is the smallest drug quantity which can be detected under normal test condition quantification limit is the lowest drug concentration that can be accurately and precisely determined.LOD and LOQ were determined based on standard deviation response and slope.

RESULTS AND DISCUSSION

Tabel 1: Assay analysis of Marketed formulation

Name	Label claim	Amount found	%Estimated	SD*	RSD*
Cinod -10	10mg	9.89	98.9	0.02	1.04

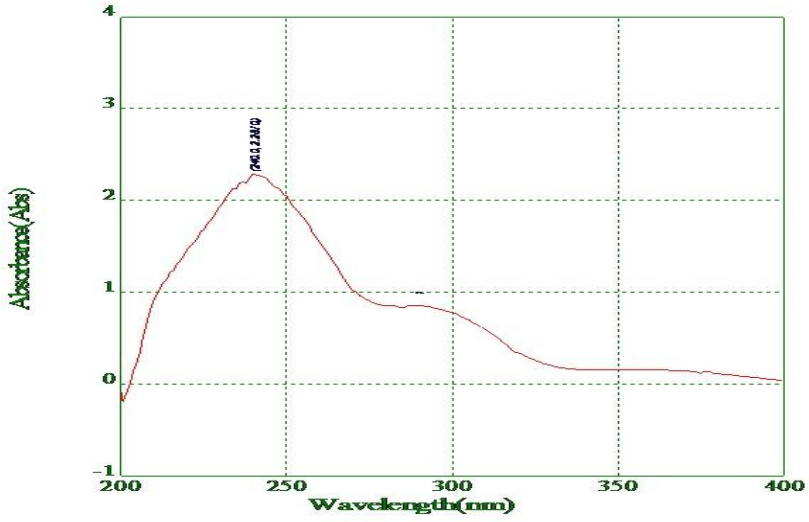

Figure 2: λmax measurement of standard stock solution of Cilnidipine

Table 2: Linearity data of Cilnidipine

Concentration (µg/ml)	Absorbance
2	0.119
4	0.234
6	0.346
8	0.457
10	0.672
12	0.754
14	0.84

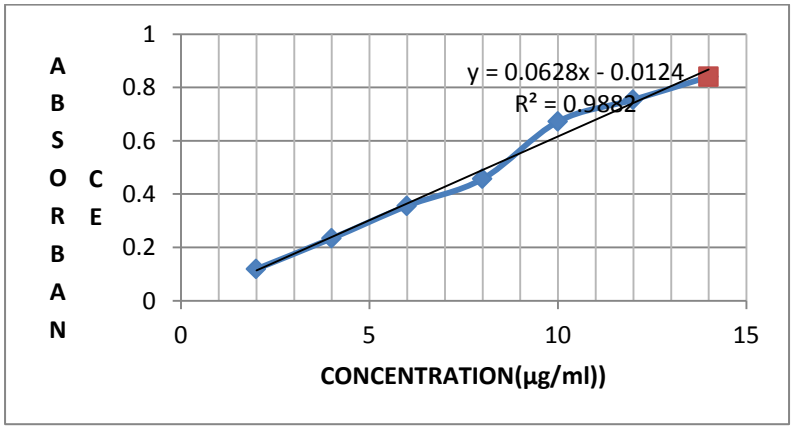

Figure 3: Calibration curve for Cilnidipine

Table 3: Statistical data of Cilnidipine

Parameter	Result
λmax (nm)	240
Beer's law Limits (µg/ml)	2-14
Regression equation	0.062x-0.012
slope	0.62
intercept	0.012
Regression coefficient (r2)	0.988
LOD	0.0638
LOQ	0.193
% Recovery	97.2-100.06

Table 4: INTRA –DAY and INTER- DAY Precision data of Cilnidipine

Concentration (µg/ml)	Inter- day precision				
	Absorbance				
	0 hour	**3 hours**	**6 hours**	**SD**	**% RSD**
2	0.119	0.116	0.121	0.002	0.706
4	0.234	0.239	0.214	0.013	1.92
6	0.356	0.359	0.367	0.005	0.525
	Intra- day precision				

	First day	Second day	Third day	SD	% RSD
2	0.112	0.122	0.126	0.007	2.003
4	0.214	0.216	0.227	0.002	1.065
6	0.354	0.355	0.367	0.007	0.672

Table 5: Accuracy determination of Cilnidipine

Concentration (µg/ml)				
% Recovery	**Formulation**	**Drug added**	**Drug found**	**% Recovery**
50	10	5	4.89	97.8
50	10	5	4.92	98.4
50	10	5	5.12	102.4
100	10	10	9.89	98.9
100	10	10	9.72	97.2
100	10	10	10.05	100.5
150	10	15	14.82	98.8
150	10	15	14.99	99.93
150	10	15	15.01	100.06

Table 6: Suitability determination of pure and marketed formulation Cilnidipine

Concentration (10µg/ml)	ASSAY	
	Standard	**sample**
0 hour	0.187	0.276
15 minutes	0.192	0.27
30 minutes	0.216	0.291
1 hour	0.247	0.263
3 hours	0.258	0.312
5 hours	0.267	0.319
8 hours	0.262	0.285
mean	1.629	2.016
SD	0.033	0.021
% RSD	2.08	1.04

LOD & LOQ

LOD = 3.3 * SD/S
SD = Standard deviation of slope
S= Slope of calibration
LOD = 3.3* 0.012/0.62 = 0.0638
LOQ = 10 * SD/S
LOQ = 10*0.012/0.62 = 0.193

CONCLUSION

An accurate UV spectroscopic method was developed and validated for the estimation of Cilnidipine in API and pharmaceutical dosage form. The quantification is a reliable and easily adopted method for routine quality control analysis.

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