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Development and Validation of UV Spectrophotometric Method for the Estimation of Cilnidipine and Valsartan in Bulk and Pharmaceutical Formulations

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Abstract : A simple, rapid, accurate, precise, specific and economical spectrophotometric method for simultaneous estimation of Cilnidipine and Valsartan in combined tablet dosage form has been developed. Its employs Formation and solving of simultaneous equation using two wavelengths 240.20nm and 250nm using methanol as solvent. This method obeys Beers law in the employed concentration range 2-12µg /mL and 8-40 µg /mL for Cilnidipine and Valsartan respectively. Coefficient of correlation (R^2) was 0.999for Cilnidipine and 0.999 for Valsartan. This method can be adopted in routine analysis of Cilnidipine and Valsartan in bulk and tablet dosage form and it involves relatively low cost solvent and no complex extraction technique.

Key Word : Cilnidipine, Valsartan, Simultaneous equation.

Introduction [1-12]

Cilnidipine chemically, 1,4Dihydrogen -2, 6dimethyl1-4(3nitrophenyl-3,5pyridinecarboxylic acid 2-methoxyethyl (2E)-3-phenyl ester is a dual blocker of L-type of Voltage-gated calcium channel in vascular smooth muscle and N-type of calcium channels in sympathetic nerve terminals that supply blood vessels.

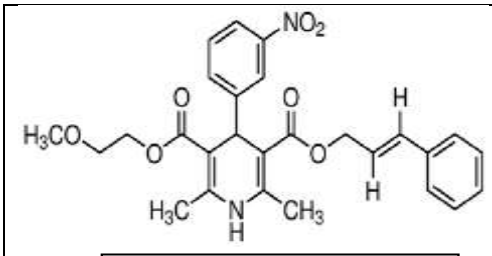

Fig no-1 Cilnidipine

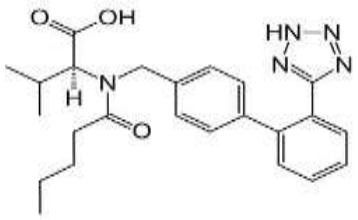

Fig no-2 Valsartan

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Valsartan is chemically know as (2S)-3-methyl-2-[N-({4-[2H-1234-tetrazol-5-yl) phenyl] phenyl} methyl) pentanamido] butanoic acid. Valsartan is ARB that selectively inhibits the binding of Angiotensin II .To AT1; this is found in many tissues such as vascular smooth muscle and the adrenal glands. This effectively inhibits the AT1-mediated vasoconstrictive and aldosterone one-secreting effective of angiotensine2and result in a decrease in vascular resistance and blood pressure.

Materials and Methods

Materials:-

Cilnidipine was obtained from J.B.Chemicals and Pharmaceutical Valsartan was kindly gifted by Lupin Laboratories Ltd. SHIMADZU UV-1800 UV/VISIBLE Spectrophotometer with UV probe 2.10 softwares and 1 cm matched quartz cells were used for the absorbance measurement. Analytical balance used for weighing standard and sample was SHIMADZU AUX 220Uni Bloc PAT 1987.

Preparation of Standard Stock Solution:-

For Cilnidipine:

10mg of Cilnidipine was accurately weighed and transferred to a 10ml volumetric flask and volume was made upto10ml with methanol (Stock solutionA-1000µg/ml).Form Stock solution A 1ml was taken into a 10ml volumetric flask and volume was made up to 10ml with Methanol (Stock solution B-100 µg/ml).

For Valsartan:

10mg of Cilnidipine was accurately weighed and transferred to a 10ml volumetric flask and volume was made upto10ml with Methanol (Stock solutionA-1000µg/ml).Form Stock solution A 1ml was taken into a 10ml volumetric flask and volume was made up to 10ml with Methanol (Stock solution B-100 µg/ml).

Procedure for analysis of tablet formulation:

Twenty tablets were weighed accurately and powdered. A quantity of tablet powder equivalent to 10mg CILNI and 80mg VAL was accurately weighted and transferred into a10ml of volumetric flask,7ml of Diluent was added .The content was ultrasonicated for 15min .The volume was then diluted to the mark and mixed well. A small portion was with-drawn and filtered through a 0.25µm filter to ensure the absence of particulate matter.

Procedure for Calibration curve:

Standard solution of Cilnidipine in concentration range of 2 µg/mL to 10 µg/mL obtained by transferring (0.2, 0.4, 0.6, 0.8, 1.0 mL) of Cilnidipine stock solution (100 µg/mL)to the series of 10ml volumetric flask and Standard solution of Valsartan in the concentration range of 8 µg/mLto 40 µg/mL were obtain by transferring (0.8,1.6,2.4,3.2,4.0 mL) of Valsartan stock solution (100 µg/mL) to the series of 10mL.All dilution scanned in wavelength range 200nmto 400nm. The absorbance were plotted against the respective concentrations to obtain the calibration curve. A Representative overlain spectrum of Cilnidipine and Valsartan in Methanol shows in Fig no 3.

Formation of Simultaneous Equation:

Set of two Simultaneous equation were Cx = (A2 ay1 - A1 ay2)/ (ax2 ay1 - ax1 ay2) and Cy = (A1 ax2 - A2ax1)/ (ax2 ay1 - ax1 ay2).Where A1and A2 are the absorbance of sample solutions at 240.20nm and 250nm respectively. Cx and Cy are concentration of Cilnidipine and Valsartan in mg /ml in sample solution. By substituting the values of A1and A2 the values of Cx and Cy can be calculated by solving the two equations simultaneously .Here ax_1 and ax2are the absorptivity coefficient of Cilnidipine at 240.20nm and 250nm respectively ay1 and ay2 are the absorptivity coefficient of Valsartan at 240.20nm and 250nm respectively. The optical parameter s & regression characteristic for Cilnidipine and Valsartan are shown in Table no-1.

Method Validation: The method was validation for System suitability, linearity, Accuracy, precision and robustness in accordance with ICH guidelines.

Linearity and Range: Linearity of the proposed method was verified by analyzing five combined different concentration in range of 8-40µg mL for valsartan, and 2-10µg mL for Cilnidipine. Each concentration was

made six time .The calibration curve of peak area vs. respective concentration was plotted and regression line equation for Valsartan and Cilnidipine was calculated.

Precision: Precision of the method was verified by repeatability and intermediate precision studies. The repeatability was evaluated by combined standard solution of six concentrations of Valsartan and Cilnidipine. The intraday precision of the developed method was evaluated by analyzing combined samples of different concentration of Valsartan and Cilnidipine on the same day and %RSD was calculated. The interday precision was evaluated form the combined concentration of Valsartan and Cilnidipine on two different days and %RSD was calculated.

Accuracy: The accuracy of the method was performed by conducting the recovery studies (80%, 100%, and 120%) of pure form and tablet formulation, by standard addition method .The actual and measured concentration were then compared with recommended limit**.**

Limit of detection LOD and limit of Quantitation LOQ:

They were calculated as **3.3 (S)/s and 10(S)/s**respectively .where (S) =standard deviation .s=Slope of the line.

Result and Discussion:

Selection of Wavelength:

The Cilnidipine Shows maximum absorption at 240nm.and Valsartan at 250.20nm.UV scan of this combination shows maximum absorption at 245nm .therefore 245nm wavelength was selected for simultaneous determination of Cilnidipine and Valsartan.

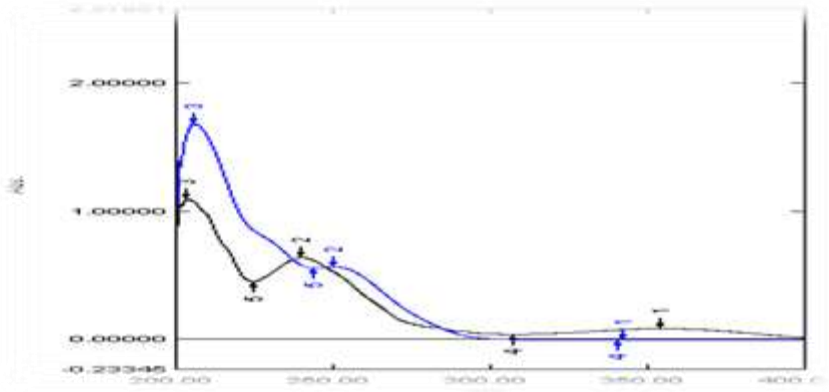

Fig no.1: Overlain spectrum of Cilnidipine and Valsartan in Methanol

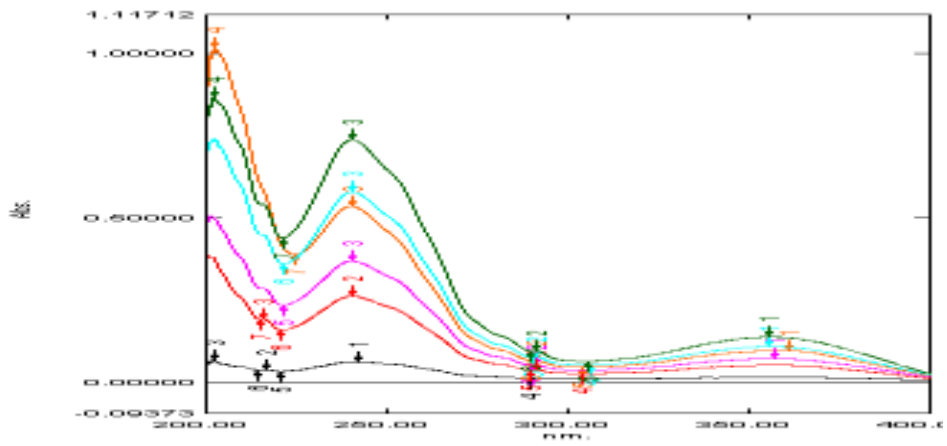

Fig no.2: Spectra of standard Cilnidipine(2µg mL-10 µg mL).

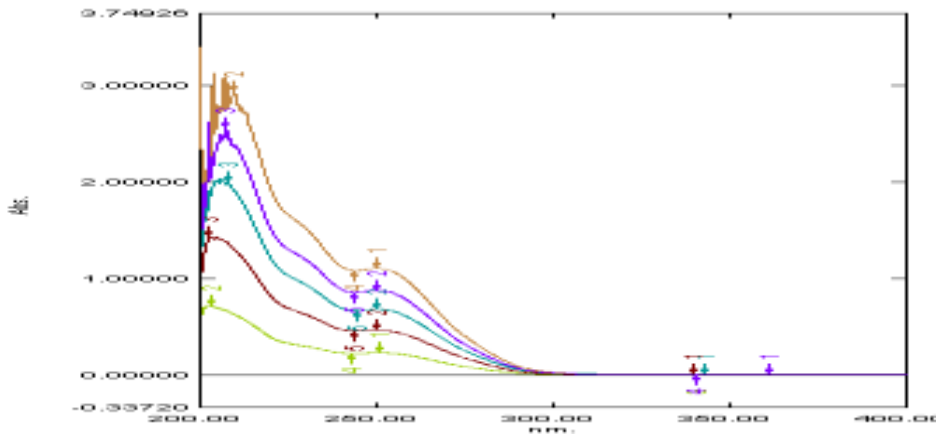

Fig no.3:Spectra of standard Valsartan (8µg mL-40µg mL).

Analytical Method Validation:

A. Linearity

Table No.1: Linearity Data of Cilnidipine and Valsartan

Parameter	Cilnidipine		Valsartan	
Wavelength	**240.20nm**	**250nm**	**240.20nm**	**250nm**
Linearityrange µg/mL	**2-10**	**8-40**	**2-10**	**8-40**
Regression equation(Y)	Y=0.062x0.004	Y=0.054x0.013	Y=0.027x0.006	Y=0.027x0.008
Slop (m)	0.062	0.055	0.027	0.027
Intercept (c)	0.004	0.009	-0.006	0.008
Correlation coefficient	0.999	0.998	0.998	0.999

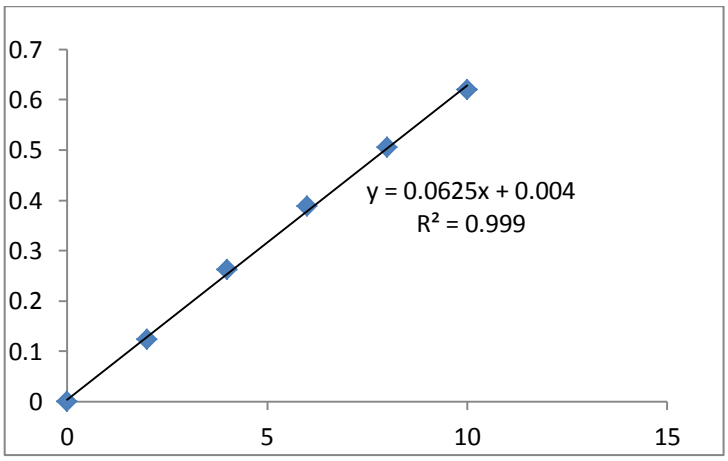

Fig no.4: Calibration Curve of Cilnidipine

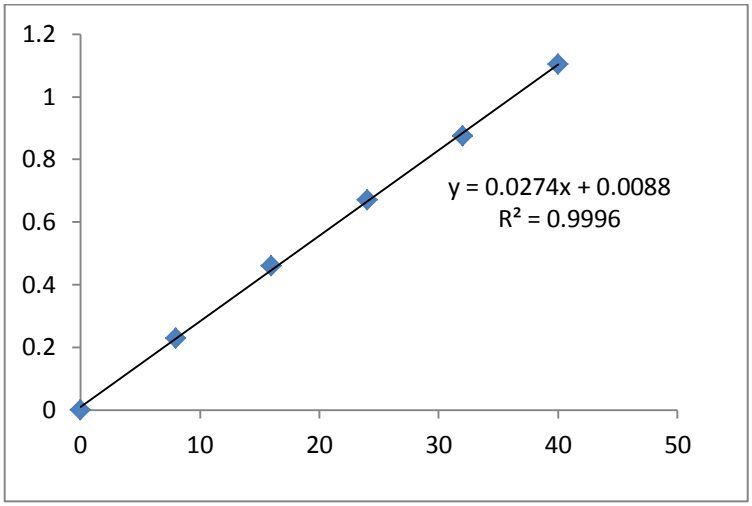

Fig no.5: Calibration Curve of Valsartan

B.Recovery study of Cilnidipine and Valsartan

Table no 2: Recovery study of Cilnidipine and Valsartan.

Recovery level (%)	Drug name	Std. Drug added	Tab Conc	Absorbance	Total Amt.of Drug found	% Recovery	SD
80	Cilnidipine	3.2	4	0.4508	3.25	101	1.17
100		4	4	0.494	3.967	99.19	
120	Cilnidipine	4.8	4	0.542	4.74	98.79	
80	Valsartan	12.8	16	0.7776	12.8	100	0.471
100		16	16	0.8637	15.98	99.93	
120	Valsartan	19.2	16	0.946	19.03	99.15	

Average of three determinations*

C.Precision

Repeatability

Table no: 3.Repeatability of Cilnidipine

Sr.no	Conc.(µg/ml)	Absorbance	Conc.found	% found Conc.
1	2	0.124	2	100
2	4	0.248	4	100
3	8	0.494	7.98	99.75

Average of three determinations*

Table no: 4. Repeatability of Valsartan

Sr.no	Conc.(µg/ml)	Absorbance	Conc.found	% found Conc.
1	8	0.215	7.97	99.627
2	16	0.431	15.9910	99.94
3	24	0.6469	23.962	99.84

Average of three determinations*

Interday Precision:-

Table no .5: dayto day Precision Cilnidipine

Sample concentration(µg/ml)	Absorbance				
	Day 1	Day2	Day3	Mean	% conc. found
4	0.248	0.248	0.249	0.2483	99.5
6	0.372	0.375	0.375	0.374	99.45
8	0.496	0.497	0.4972	0.496	99.22

***Mean of three determinations**

Interday Precision:-

Table no .6:day to day Precision Valsartan

Sample concentration(µg/ml)	Absorbance				
	Day 1	Day2	Day3	Mean	% conc found
16	0.432	0.432	0.433	0.4323	100.06
24	0.648	0.656	0.657	0.6536	100.83
32	0.864	0.865	0.865	0.8646	100.68

***Mean of three determinations**

Table .7: Result of Analyst to Analyst PrecisionCilnidipine

Method wavelength (nm)	Condition	Std conc.	Found conc.	% Assay*	% RSD
240.20nm	Analyst - 1	6	5.98	99.66	0.01153
	Analyst - 2	6	5.97	99.33	0.00416

***Mean of three determinations**

Table No.8:Result of Analyst to Analyst Precision Valsartan

Method wavelength (nm)	Condition	Std conc.	Found conc.	% Assay*	% RSD
250nm	Analyst - 1	24	23.986	99.93	0.0058
	Analyst - 2	24	23.99	99.946	0.00577

***Mean of three determinations**

D.Assay

Table No.9:Assay of tablet formulations

Cilnidipine	Valsartan	Cilnidipine	Valsartan
10mg	80mg	98.7	99.375

***Mean of three determinations**

Conclusion

The proposed method is rapid accurate and sensitive. It makes use of fewer amounts of solvents and change of set of condition required a short time.This method can be suitable analyzed for the routine analysis of Cilnidipine and Valsartan in bulk and its tablet dosage form. It does not suffer from any interference due to

common excipients present in pharmaceutical preparation and can be conveniently adopted for quality control analysis.

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