

Comparative study of five different marketed Preparation (Tablets) Containing Amlodipine Besylate & Valsartan and developing novel method for simultaneous estimation of Amlodipine Besylate and valsartan using UV Visible Spectrophotometer

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Abstract

A simple, precise, accurate and economic simultaneous UV spectrophotometric method has been developed for the estimation of Amlodipine Besylate and Valsartan in combination in bulk and tablet. The estimation was based upon measurement of absorbance at absorbance maxima of (λ_{max}) 230-240 nm for Amlodipine Besylate (API) and 240-260 nm for Valsartan (API) in Ethanol : Distilled Water (1:1 ratio) as a solvent respectively in bulk mixture and tablet C. The Beer Lambert's law obeyed in the concentration range 5-25 $\mu\text{g/ml}$, 10-50 $\mu\text{g/ml}$ for Amlodipine Besylate and Valsartan, respectively. The estimation of bulk mixture and tablet was carried out by simultaneous equation, Q-analysis and area under curve method for estimation of Amlodipine Besylate & Valsartan. Method was validated with respect to specificity, linearity, range, accuracy, precision, Limit Of Detection, Limit Of Quantitation. Validation was performed as per ICH guidelines the results were found out to be for Amlodipine Besylate and Valsartan. (as per label claim). Comparative Study was done using Five Different Marketed Preparation (Tablet) Containing Amlodipine Besylate and Valsartan. (Amlopress VL (5/80): Cipla Ltd, Exforge (5/80) : Novartis Pharmaceutical Ltd, Amlosartan (5/80): Incepta Pharma Ltd, Amlovas VS (5/80) :Popular Pharma Ltd, AV (5/80) : Drug International Ltd).

Keywords: amlodipine besylate, valsartan, comparative study, simultaneous estimation

Introduction

Amlodipine: Amlodipine is a 1,4-dihydropyridine calcium channel blocker. It is used for management of hypertension and angina pectoris. Formulations of Amlodipine may contain its different salts such as besylate, mesylate, or maleate. A second proposed mechanism for the drug's vasodilatory effects involves pH-dependent inhibition of calcium influx via inhibition of smooth muscle carbonic anhydrase. Some studies have shown that amlodipine also exerts inhibitory effects on voltage-gated N-type calcium channels. N-type calcium channels located in the central nervous system may be involved in nociceptive signaling and pain sensation. Amlodipine is used to treat hypertension (Antihypertensive Drug) and chronic stable angina.

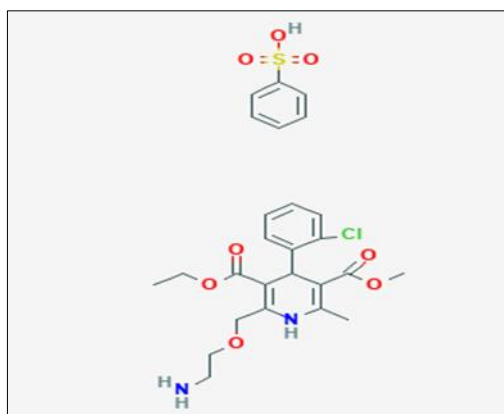


Fig 2: Structure of Amlodipine Besylate

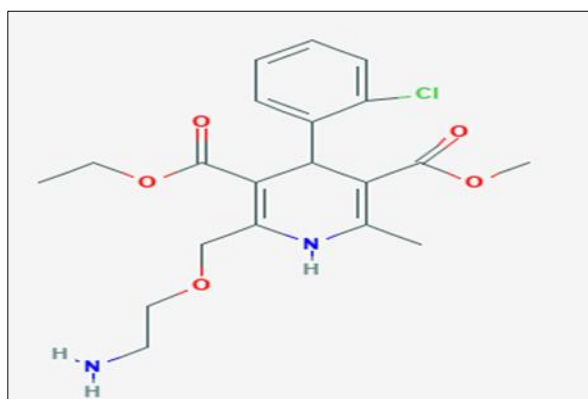


Fig 1: Structure of Amlodipine Drug

Valsartan: Valsartan, chemically is N-valeryl-N ([2-[1H-tetrazol-5-yl] biphenyl-4-yl] methyl) valine has an empirical formula of C₂₄H₂₉N₅O₃ and a molecular weight of 435.5 g/mol. Valsartan is a nonpeptide, orally active, and specific Angiotensin II Antagonist acting on the angiotensin II type 1 (AT1) receptor subtype. Valsartan is a new potent, highly selective, and orally active Antihypertensive Drug belonging to the family of AT1 receptor antagonists. Valsartan has much greater affinity (about 20,000-fold) for the AT1 receptor than for the AT2 receptor, thereby relaxing blood vessels and causing them to widen, which lowers blood pressure and improves blood flow [1]. Peak plasma

concentrations of valsartan will be reached in 2-4 h after dosing. The amount absorbed varies widely. Valsartan is a tetrazole derivative that contains acid ($pK_a=4.73$) and carboxylic ($pK_a=3.9$) groups making the compound soluble in the neutral pH range

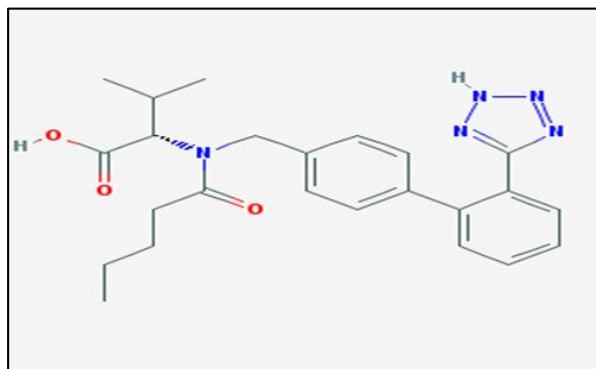


Fig 3: Structure of Valsartan

Experimental

Reagent and Materials

All the reagents in this assay along with triple distilled water were of analytical grade. Valsartan and Amlodipine Besylate were obtained as a gift sample from Lupin Ltd, Mumbai. The marketed tablets used are AMLOPRESS VL (5/80): Cipla Ltd, Exforge (5/80): Novartis Pharmaceutical Ltd, Amlosartan (5/80): Incepta Pharma Ltd, AMLOVAS VS (5/80): Popular Pharma Ltd, AV (5/80): Drug International Ltd) were purchased from local market.

Apparatus

Spectral analysis were made on a Jasco Spectrophotometer, Model- V-630 (Japan), was employed with spectral bandwidth of 1nm and wavelength accuracy of ± 0.3 nm with automatic wavelength correction with a pair of 10mm quartz cells. Glass wares used in each procedure were soaked overnight in a mixture of chromic acid and sulphuric acid rinsed thoroughly with double distilled water and dried in hot air oven.

Preparation of stock solution

Accurately weighed Valsartan and Amlodipine (10 mg each) was transfer two separate 100ml volumetric flask, dissolved in 100ml of Ethanol: Distilled Water (1:1 ratio) as a solvent and make up the volume up to the mark.

Preparation of working standard

Take required quantity of stock solution of Valsartan and Amlodipine diluted with Ethanol: Distilled Water (1:1 ratio) to obtained working standard of both solution.

Selection of Detection Wavelength

Solutions of drug were scanned over the range of 200-400nm. It was observed that both the drug showed considerable absorbance at 238nm for Amlodipine and 249nm for Valsartan was selected as the wavelength for detection.

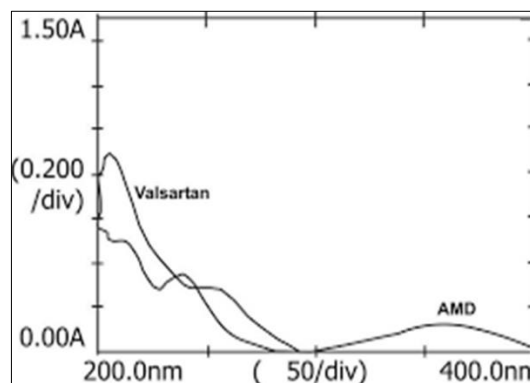


Fig 4: UV Spectra of Amlodipine and Valsartan

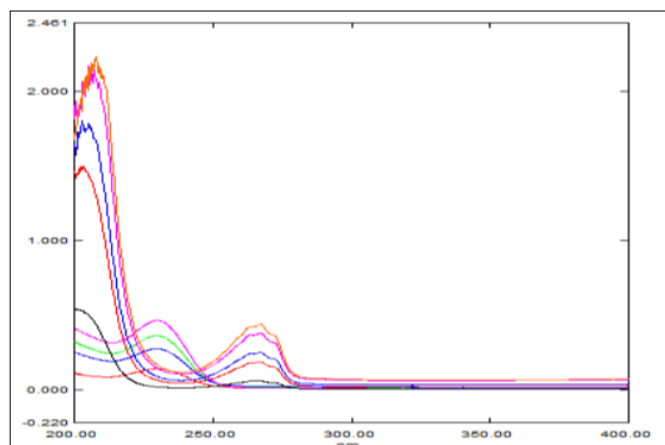


Fig 5: Calibration UV spectra of Amlodipine and Valsartan

Method Validation

Linearity

Working standard solution of Amlodipine Besylate and Valsartan was taken in different 10 ml volumetric flasks and diluted up to mark with distilled water to obtained concentrations 50, 60, 70, 80, 90 μ g/ml of Amlodipine Besylate and 2, 4, 6, 8, 10 μ g/ml of Valsartan. A calibration curve was constructed by plotting concentration versus absorbance and line equation was calculated for both the drugs.

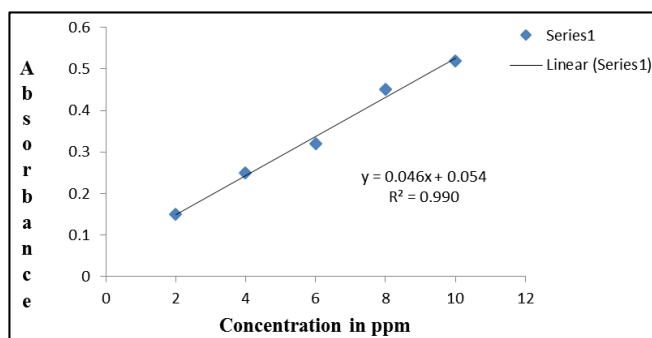


Fig 6: Calibration Curve of Amlodipine

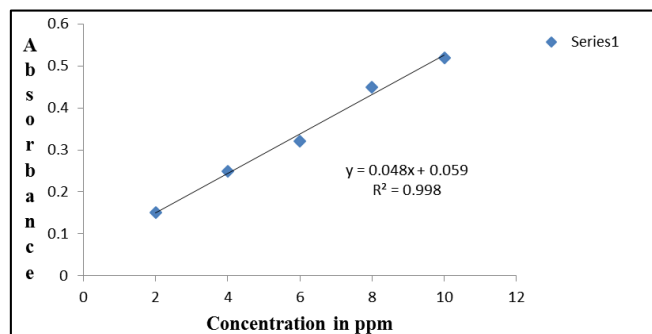


Fig 7: Calibration Curve of Valsartan

Precision

The repeatability studies were carried out by estimating

response of Amlodipine Besylate and Valsartan five times and results are reported in terms of relative standard deviation. The intermediate precision were carried out by estimating the corresponding responses 3 times on the same day and 3 different days for 3 different concentrations of Amlodipine Besylate and Valsartan and results are reported in terms of relative std. deviation.

Accuracy

Recovery studies of Amlodipine Besylate and Valsartan were performed to judge the accuracy of the method by standard additions at three different levels 80, 100, 120 %. Mean percentage recovery was determined. Recovery values were calculated shown in table 1.

Table 1: Recovery Studies (API)

Amount of drug sample used Valsartan	Obtained(µg) Valsartan (n=3)	% Recovery	Amount of drug sample used Amlodipine Besylate	Theoretical amount added (%)	Obtained (µg) Amlodipine Besylate (n=3)	% recovery
80µg	80.05	100.12	5µg	80	5.21	100.15
80µg	79.85.	99.15	5µg	100	5.99	102.30
80µg	80.01	100.01	5µg	120	5.79	101.06
	Mean % recovery	100.02			Mean % recovery	100.10

Assay of Drug Formulation (Tablet Dosage Form)



Fig 8: Five tablet brands containing Amlodipine Besylate 5mg and Valsartan 80mg

Table 2: Assay of Combined Dosage

Sr. No.	Brand Name	Drug	Label Claim (mg/Tablet)	Amount Estimated (mg/Tablet)*	Percentage Label Claim (%)
1	AMLOPRESS VL (5/80): CIPLA LTD	Amlodipine Besylate	5	5	100
		Valsartan	80	79.99	99.99
2	EXFORGE (5/80) : NOVARTIS PHARMACEUTICAL LTD,	Amlodipine Besylate	5	5	100
		Valsartan	80	80	100
3	AMLOSARTAN (5/80) : INCEPTA PHARMA LTD,	Amlodipine Besylate	5	4.99	99
		Valsartan	80	79.50	99.50
4	AMLOVAS VS (5/80) : POPULAR PHARMA LTD	Amlodipine Besylate	5	4.95	99.15
		Valsartan	80	80	100
5	AV (5/80) : DRUG INTERNATIONAL LTD)	Amlodipine Besylate	5	4.98	98.99
		Valsartan	80	79.65	99.63

*Mean of five reading

Detection Limit

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitative as an exact value.

LOD =

Where, σ = Relative std. deviation of the response, S = slope of calibration curve.

Quantitation Limit

The quantitation limit of an analytical procedure is the lowest amount of analyte in a sample, which can be quantitatively determine with suitable precision and accuracy.

LOQ =

Where, σ = Relative std. deviation of the response, S = slope of calibration curve.

Table 3: Method Validation Parameters

Parameter	Result	
	Amlodipine Besylate	Valsartan
Linearity range ($\mu\text{g/ml}$)	2-8	50-80
Sensitivity($\text{mg/cm}^2/0.001$ absorbance unit)	0.015	0.199
Correlation Coefficient (r^2)	0.991	0.989
Slope (m)	0.051	0.013
Intercept (c)	0.036	0.0415
Accuracy	99.98 %	100 %
Precision (% RSD)		
Repeatability	0.358	0.632
Intraday	0.32	0.62
Interday	0.52	0.81
LOD (μg)	1.1	6.3
LOQ (μg)	2.1	20.65

Results & Discussion

Comparative Study of Five Different Marketed Preparation (Tablets) Containing Amlodipine Besylate and Valsartan Shows that near about 100% of Label Claim. The developed UV-Visible Spectrophotometric method for the simultaneous estimation of Valsartan and Amlodipine was found to be simple and useful with high accuracy, precision, LOD, LOQ as per ICH guidelines. Sample recoveries in all formulations using the above method was in good agreement with their respective label claim or theoretical drug content, thus suggesting the validity of the method and noninterference of formulation excipients in the estimation. In the selected solvent system Ethanol: Distilled Water (1:1 ratio), drugs were stable for more than 48 hours, thus suggesting that samples need not be estimated immediately after collection. The method was successfully used for determination of drugs in their pharmaceutical formulation.

Conclusions

The developed UV-Visible Spectrophotometric method for the simultaneous estimation of Amlodipine Besylate and Valsartan in the tablet dosage form in the solvent system Ethanol: Distilled Water (1:1 ratio) give proper estimation of percentage label claim of marketed product.

Acknowledgement

Authors are sincerely thankful to Loknete Shri Dadapatil Pharate College of Pharmacy, Mandavgan Pharata, Shirur, Pune. (M.S.) for providing necessary facilities for work.

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