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Comparative study of five different marketed tablets containing amlodipine & valsartan

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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 µg/ml, 10-50 µg/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

1. Introduction

1.1 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 sown in Fig1 & Fig2. 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 [1].

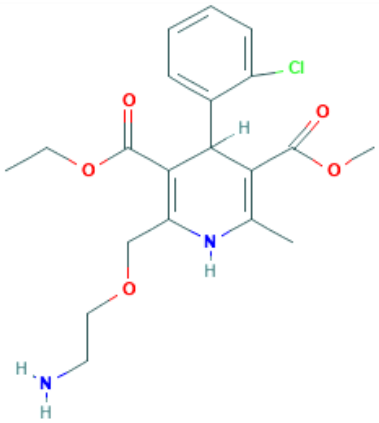

Fig 1: Structure of Amlodipine Drug

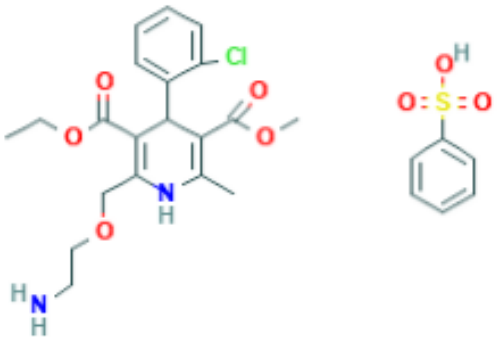

Fig 2: Structure of Amlodipine Besylate

1.2 Valsartan

Valsartan, chemically is N-valeryl-N ([2-[1Htetrazol-5-yl] biphenyl-4-yl] methyl) Valsartan has an empirical formula of C24H29N5O3 and a molecular weight of 435.5 g/mol shown in Fig3. Valsartan is a non-peptide, orally active, and specific Angiotensin II Antagonist acting on the angiotensin II type 1 (AT1) receptor sub-type. 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 [2]. 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 (pKa=4.73) and carboxylic (pKa=3.9) groups making the compound soluble in the neutral pH range.

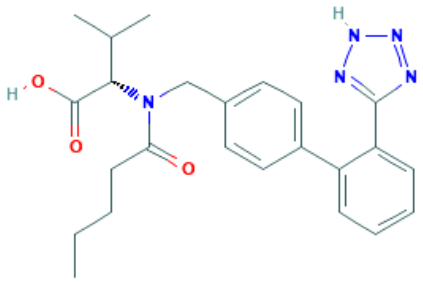

Fig 3: Structure of Valsartan

2. Experimental

2.1 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 [3]. 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.

2.2 Apparatus

Spectral analysis were made on a Jasco Spectrophotometer, Model- V-630 (Japan), was employed with spectral bandwidth of 1nm and wavelength accuracy of ±0.3nm with automatic wavelength correction with a pair of 10mm quartz cells [4]. 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.

2.3 Preparation of stock solution

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

2.4 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 solutions.

2.5 Selection of detection

Wavelength Solutions of drug were scanned over the range of 200-400nm shown in Fig4. 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.

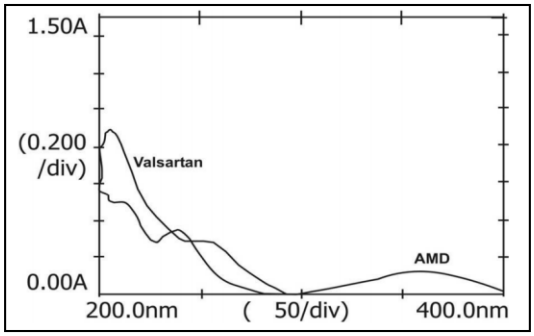

Fig 4: UV Spectra of Amlodipine and Valsartan

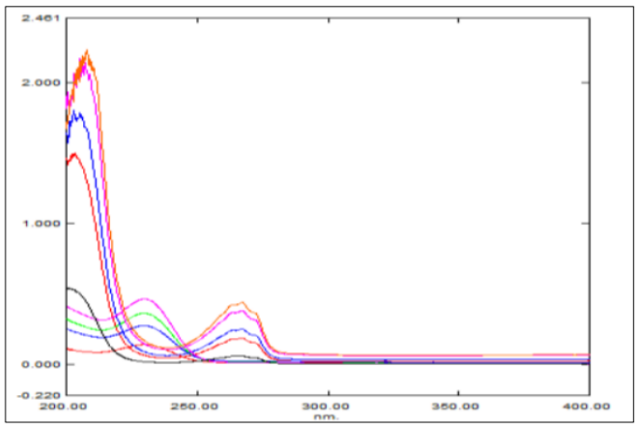

Fig 5: Calibration UV spectra of Amlodipine and Valsartan

3. Method validation

3.1 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, 90µg/ml of Amlodipine Besylate and 2, 4, 6, 8, 10µg/ml of Valsartan. A calibration curve was constructed by plotting concentration versus absorbance and line equation was calculated for both the drugs.

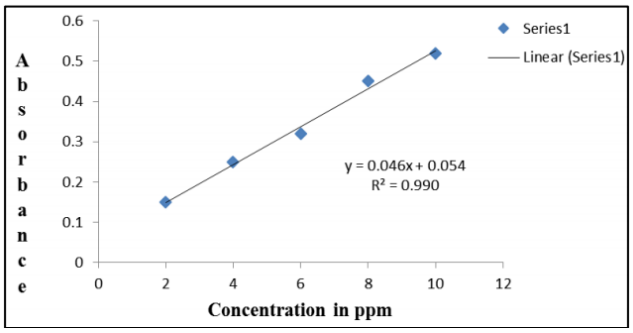

Fig 6: Calibration Curve of Amlodipine

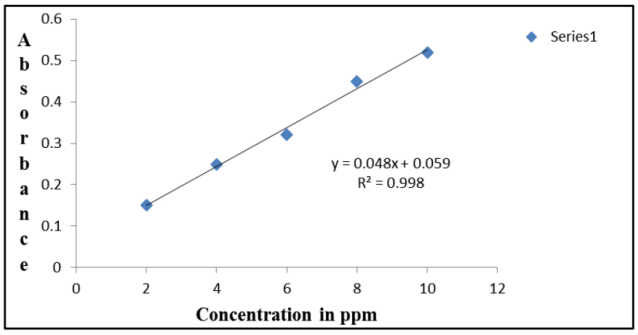

Fig 7: Calibration Curve of Valsartan

3.2 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.

3.3 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 as 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
		100.02				100.10
	Mean % recovery	100.02			Mean % recovery	100.10

3.4. Limit of detection

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.

$$LOD = \frac{3\sigma}{S} \quad (1)$$

Where,

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

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

S. 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 harmaceutical 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

3.5. Limit of quantitation

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

$$LOQ = \frac{10\sigma}{S} \quad (2)$$

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 (µg/ml)	2-8	50-80
Sensitivity(mg/cm2/.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

4. 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 were in good agreement with their respective label claims or theoretical drug content, suggesting the validity of the method and non-interference in the estimation of the formulation excipients. In the solvent system selected Ethanol: Distilled Water (1:1 ratio), drugs were more than 48 hours stable, and suggesting that samples should not be estimated immediately after collection. The method was used successfully in the pharmaceutical formulation to determine drugs.

5. Conclusion

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) gave proper estimation of percentage label claim of marketed product.

6. References

1. Gupta KR, Mahapatra AD, Wadodkar AR, Wadodkar SG. Simultaneous UV Spectrophotometric Determination of Valsartan and Amlodipine in tablet International Journal of ChemTech Research. 2010; 2(1):551-556.
2. Varsha Galande R, Baheti KG, Indraksha S, Dehghan MH. Estimation of amlodipine besylate, valsartan and hydrochlorothiazide in bulk mixture and tablet by UV spectrophotometry. Indian j pharm sci. 2012; 74(1):18-23.
3. Atana E, Altinay A. Simultaneous determination of valsartan and hydrochlorothiazide in tablets by firstderivative ultraviolet spectrophotometry and LC. J Pharm Biomed Anal. 2001; 25:1009-13.
4. Tatar S, Saglik S. Comparison of UV and second derivative spectrophotometric and LC methods for the determination of valsartanin pharmaceutical formulation. J 888ssssPharm Biomed Anal. 2002; 30:371-5.
5. Tripathi KD. Essential of Medical Pharmacology, 5th Edition, Jaypee Brothers Medical Publisher New Delhi. Pp. 515-516.
6. Patil SS, Bonde CG. Development and Validaton of an analytical method for simultaneous estimation of Glibenclamide and Metformin HCl in bulk and tablets using UV visible spectroscopy, Int JChen Tech Res. 2009; 1(4):905-909.
7. Campbell DB, Lavielle R, Nathan C. The mode of action and clinical pharmacology of gliclazide: a review. Diav Res Clin Prac. 1991; 14:S21-S36.
8. Hassasaad SM, Mahmoud WH, Elmosallamy MA, Othman AH. Determination of metformin in pharmaceutical preparation using potentiometry, spectrofluorimetry and UV visible spectrophotometry. Anal Chimic. 1999; 378(1-3):299-311.
9. ICH Harmonised Tripartite Guideline. Text on Validation of Analytical Procedures, International Conference on Harmonization, Geneva, 1994, 1-5.
10. Budavari S, Neil MJ, Smith A, Heckelman PE. The Merck Index, Mary Adele 13th ed. Published by Merck Research Lab, Division of Merck and Co., White house station, NJ, USA, 2001, 1767.
11. British Pharmacopoeia. Vol I, Controller of Her Majesty's Stationary Office, Norwish, 125. 3. Erk N. and Altuntas T.G., Spectrophotometric analysis of valsartan and hydrochlorthiazide Anal. lett., 2002-2004; 35(2):283-302
12. Sibel A, Ozakan SE, Gorger N, Altinay S, Zuhre S. Simultaneous determination of valsartan and Hydrochlorthiazide in tablets by first-derivative UV spectrophotometry and LC J. Pharm. Biomed Anal. 2001; 25(5):1009-1013.
13. Daneshtalab N, Lewanczuk RZ, Fakherddin J, High-Performance liquid Chromatographic analysis of angiotensin II receptor antagonist valsartan using a liquid extraction method. J. Chromatogr. B: Analyt. Technol. Biomed and Life sci. 2002; 766(2):345-349
14. Selvan PS, Gowda KV, Mandal U, Solomon WD, Pal TK. Simultaneous determination of fixed dose combination of nebivolol and valsartan in human plasma by liquid chromatographic-tandem mass spectrometry and its application to pharmacokinetic study Journal of Chromatography: B. 2007; 858(1-2):143-150.
15. Hao LI, Yingwu W, Yao J, Tang Y, Jiang W, Limei Z, Jingkai Gu. A liquid chromatography/tandem mass spectrophometry for the simultaneous quantification of valsartan and hydrochlorthiazide in human plasma. Journal of Chromatography. 2007; 852(2):436-442.
16. Azza Gazy AA. Determination of amlodipine besylate by adsorptive square-wave anodic stripping voltametry on glassy carbon electrode in tablets and biological fluids. Talanta. 2004; 62:575-582.
17. Raman N, Hoda MN. Validated spectrohotometri methods for the determination of amlodipine besylate in drug formulation using 2,3-dichloro 5,6-dicyano 1,4-benzoquinone and ascorbic acid J. Pharm. Biomed. Anal. 2003; 31(2):381-392.
18. Gohil K, Trivedi P, Molvi KI. Spectrophotometric analysis of amlodipine besylate in bulk and in tablet dosage forms. Ind. J. Pharm. Sci. 2005; 67(3):376-78.

19. Kasture AV, Ramteke M, Simultaneous UV. Spectrophotometric method for the estimation of atenolol and amlodipine besylate in combined dosage form. Ind. J. Pharm. Sci. 2006; 68(3):394-396.
20. Valiyare GR, Chandra A, Apte SK. HPLC determination of Amlodipine, Losartan and Ramipril in Pharmaceutical formulation, Indian Drugs. 2005; 42(5):309.
21. Zaparkar SS, Kanyawar NS. Simultaneous estimation of amlodipine and losartan potassium in tablet dosage from, Indian Drugs. 2002; 39(6):338.
22. Nathan SN, Sharma GV, Suresh B. HPLC method for simultaneous determination of benazepril and amlodipine from tablets, Eastern Pharmacist. 2003; 2:100.
23. Kamble N, Venkatchalam A. HPLC method for analysis of simultaneous determination of lisinopril and amlodipine from tablets. Indian Drugs. 2004; 41(3):179
24. Gupta KR, Wankhede SB, Tajne MR, Wadodkar SG. Simultaneous determination of amlodipine and ramipril by HPTLC, Asian J. Chem. 2007; 19(6):4177-82.
25. Mahadik KR, Kadam SS, Agrawal H, Kaul N. Simultaneous HPTLC estimation of amlodipine besylate and losartan potassium in tablets dosage forms. Int. Pharm. Feb. World Cong. 2002; 68:38.