INTERNATIONAL JOURNAL OF APPLIED BIOLOGY AND PHARMACEUTICAL TECHNOLOGY

Volume: 2: Issue-3: July-Sept -2011 IJABPT *ISSN 0976-4550*

SIMULTANEOUS DETERMINATION OF PERINDOPRIL ERBUMINE AND AMLODIPINE BESYLATE BY ABSORPTION FACTOR METHOD.

Jignesh P. Prajapati*[a], M.B.Patel[b], Rashmika J. Prajapati[c], Nimesh A.Prajapati[c]

[a]Researcher of Singhania University, Jhunjhunu,

[b]K.B.Raval college of pharmacy, [c]Saraswati institute of pharmacy

***Corresponding author:**Mobile:09909917614,E-mail:jignesh.rx@gmail.com

ABSTRACT: In this study, Absorption factor method have been developed and validated for the simultaneous determination of perindopril erbumine and amlodipine besylate in their combined pharmaceutical formulation dosage form. Absorption factor method was performed for perindopril erbumine and amlodipine besylate at wavelength maxima 215 nm and 237 nm respectively. Amlodipine besylate was show liner at 237 nm but Amlodipine besylate also showed absorbance at 215nm and give interference in determination of Perindopril erbumine. Quantitative estimation of Perindopril erbumine was carried out by subtracting interference of Amlodipine besylate using experimentally calculated absorption factor. Result of analysis was validated by statistically. The result of the studies showed that the proposed Spectroscopic method is simple, rapid, precise and accurate, which can be used for the routine determination of Perindopril erbumine and Amlodipine besylate in bulk and in its pharmaceutical formulation.

Keywords: Perindopril erbumine, Amlodipine besylate, Absorption factor, Spectroscopy.

INTRODUCTION

Perindopril erbumine 2-Methyl Propane-2-amine (2S, 3As, 7As)-1-[(2S)-2-2[[(1S)-1-(ethoxycarbonyl) butyl] amine] propanoyl] octahydro-1H-indol-2-carboxylate (Figure 1) is an angiotensin-converting enzyme (ACE) inhibitor. Perindopril erbumine is converted to Perindoprilat in the liver and is used to treat hypertension and heart failure, to reduce proteinuria and renal disease in patients with nephropathies, and to prevent stroke, myocardial infarction, and cardiac death in high-risk patients. The absolute oral bioavailability of Perindopril is about 75%. Following absorption, approximately 30–50% of systematically available Perindopril is hydrolyzed to its active metabolite, perindoprilat, which has a mean bioavailability of about 25%. Peak plasma concentration of perindoprilat is attained in 3–7 h after Perindopril administration. The presence of food in the gastrointestinal tract does not affect rate or extent of absorption of Perindopril but reduces bioavailability of perindoprilat by about 35%. Perindopril is extensively metabolized following oral administration with only 4–12% of the dose recovered unchanged in the urine.

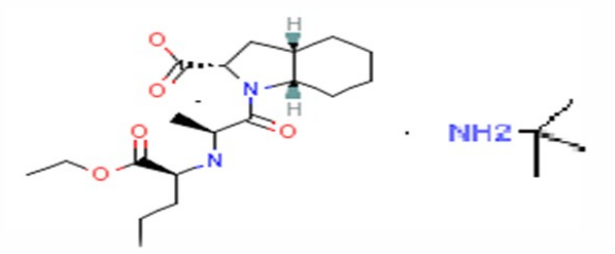

Figure: 1 Structure of Perindopril erbumine

Amlodipine besylate 2-MethylPropane-2-amine (2S, 3As, 7As)-1-[(2S)-2-2[[(1S)-1- (ethoxycarbonyl) butyl] amine] propanoyl]octahydro-1H-indol-2-carboxylate (Figure 2) is a calcium channel blocker. Amlodipine besylate is a dihydropyridine type long acting calcium channel blocker with slow onset of vasodialatory action. The use of this drug in treatment of variant and stable angina and hypertension. As an additional property, Amlodipine inhibits vascular smooth muscle cell growth through interactions with targets other than L-type calcium channels and is more selective for arterial vascular smooth muscle than cardiac tissues. It has been investigated that Amlodipine exhibits ameliorating effects on plasma and myocardial catecholamines with a significant reduction of calcium deposition and may be useful in dilated cardiomyopathy. Amlodipine is well absorbed following oral administration with peak blood concentrations occurring after 6–12 h and bioavailability is about 60–65%. Amlodipine is extensively metabolized in the liver; metabolites are mostly excreted in urine together with less than 10% of a dose as unchanged drug.

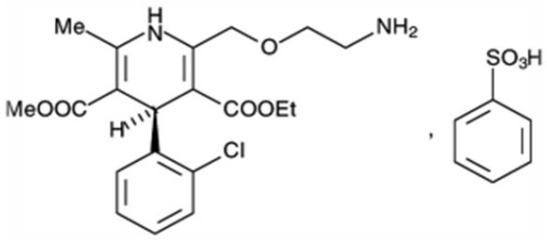

Figure:2 Structure of Amlodipine besylate

MATERIALS AND METHOD

Perindopril erbumine and Amlodipine besylate were generously given by Arti Industries Ltd and Cadila health care Ltd. Method was developed with Perkin elmer (Model-19) Ultraviolet spectroscopy, HPLC grade water, and Methanol as diluent. The tablet COVERSYL with 4 mg Perindopril erbumine and 5 mg Amlodipine Besylate which was manufactured by SERDIA Pharmaceutical Ltd. Mumbai.

Wavelength maxima selection:

4,6,8,10, and 12 µg/ml solutions of Perindopril erbumine and 5,7.5,10,12.5, and 15 µg/ml solutions of Amlodipine besylate were prepared in diluent and spectrum were recorded between 200-400 nm. Amlodipine besylate shows linier response at its λ_{max} 237 nm but Perindopril erbumine cannot shows linier response at its λ_{max} 207nm so Perindopril erbumine has been measured at 215nm.

Absorption Factor Method

Prepare standard stock solution of perindopril erbumine (A) (200 µg/ml) and amlodipine besylate (B) (350 µg/ml) in methanol, Take 1 ml of stock solution (A) and (B) into 25 ml of volumetric flask and make up the volume up to mark with methanol. Perindopril erbumine and Amlodipine besylate were prepared in concentration range 4 – 12 µg/ml and 5 – 15 µg/ml respectively in methanol and plot the calibration curves. Prepare Sample solution of perindopril erbumine and Amlodipine besylate were 8 µg/ml and 10 µg/ml respectively in the diluent.Perindopril erbumine and Amlodipine besylate solution in diluent of know concentrations were scanned against blank on spectrophotometer. The value of Absorption factor was found to be 1.2936. Quantitative estimation of the Perindopril erbumine and Amlodipine besylate was carried out using following equation.

Absorption of Perindopril erbumine at 215nm =

$$Abs_{215}\,(Peri+Amlo) - \left(\frac{Abs_{215}\,(Amlo)}{Abs_{237}\,(Amlo)}\right) X\ Abs_{237}\,(Peri+Amlo)$$

Abs: Absorption Value

Peri: Perindopril erbumine

Amlo: Amlodipine besylate

RESULT AND DISCUSSION

The proposed analytical method is simple, accurate and reproducible. Perindopril erbumine and Amlodipine besylate measured at λ_{max} at 215 nm and 237 nm respectively. As their λmax differ more than 20 nm, typical spectrum was shown in Figure: 3. Absorption factor method was tried for their simultaneous estimation in formulation. Amlodipine besylate also showed absorbance at 215nm and give interference in determination of Perindopril erbumine. Quantitative estimation of Perindopril erbumine was carried out by subtracting interference of Amlodipine besylate using experimentally calculated absorption factor.

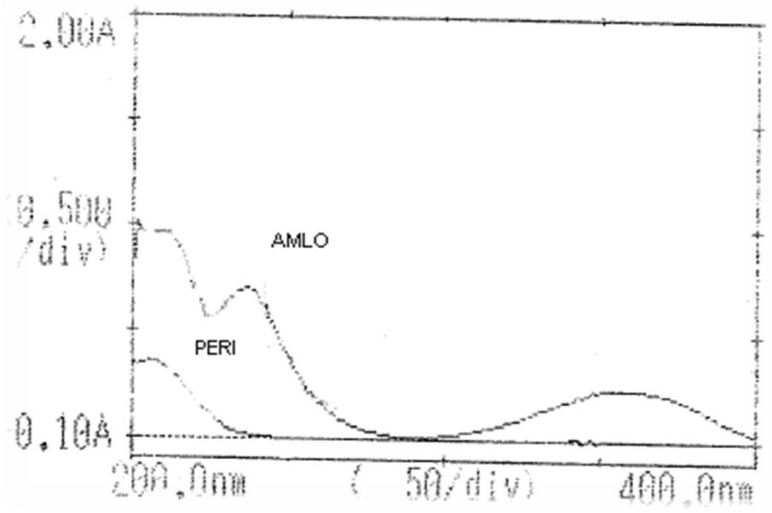

Figure: 3 Overlain spectrum of Perindopril erbumine and Amlodipine besylate in Methanol

Assay of formulation:

An accurately weighed ten intact tablets equivalent to 40 mg of Perindopril erbumine and 50 mg of Amlodipine in to a 200 ml volumetric flask. Add 150 ml of methanol and sonicate it for 30 min. filter it through 0.45 µm HVLP filter. Transfer 1.0 ml of filtrate into 25 ml volumetric flask and add diluent up to mark to get final concentration of Perindopril erbumine 8µg/ml and Amlodipine 10µg/ml.

Validation parameters:

The accuracy of the method was studied by recovery studies at three stages 50%, 100% and 150% of the assay amount. The results obtained are shown in **table.1**

Table: 1 Validation parameter

Parameter	Perindopril erbumine		Amlodipine besylate	
Linearity	4-12 µg/mL		5-15 µg/mL	
Correlation coefficient	0.998		0.999	
Precision (% RSD)	0.7		0.3	
Ruggedness (% RSD)	0.6		0.3	
Accuracy	At level	%	At level	%
	50%	99.6	50%	98.6
	100%	100.8	100%	99.2
	150%	98.8	150%	99.9

Conclusion

The Absorption factor method was developed and validated for simultaneous determination of perindopril erbumine and Amlodipine besylate in combined pharmaceutical formulation. The method was found to be simple, precise and rapid. The assay result obtained by this method is in fair agreement. This method can be used for routine determination of Perindopril erbumine and Amlodipine besylate.

REFERENCES

1. K.D.Tripathi's (2003) Essentials of medical Pharmacology, 5th Edition, Jaypee Brothers Medical Publishers (P) Ltd., p488, 496, 497.
2. O'Neil M.J., Edn (2006) The Merck Index-An Encyclopedia of Chemicals, Drug and biologicals, 14th Edn, Merck & Co., Inc, p 6836.
3. Sahu R, Patel Vandana B, Simultaneous spectrophotometric determination of Amlodipine besylate and Atorvastatin calcium in binary mixture. Indian J. Pharma. Sci.2007, 69(1): 110-111
4. Erk N, Comparison of spectrophotometric and an LC method for the determination perindopril and indapamide in pharmaceutical formulations, Journal of Pharmaceutical and Biomedical Analysis 2001; 26, p.43-52.
5. D.K.Modi, C.N.Patel, Development and validation of spectrophotometric method for simultaneous estimation of perindopril and indapamide in combined dosage form by simultaneous equation method,Eurasian Journal of Analytical Chemistry, Vol 6, No 1 (2011).
6. P.R Patil, S.U Rakesh, P.N Dhabale, K.B Burade, Simultaneous Estimation of Ramipril and Amlodipine by UV Spectrophotometric, Research J. Pharm. and Tech.2 (2),April.-June. 2009.
7. K.R.Gupta, A.D.Mahapatra,A.R.Wadodkar,S.G.Wadodkar, Simultaneous UV Spectrophotometric Determination of Valsartan and Amlodipine in tablet, International Journal of ChemTech Research, Vol.2, No.1, pp 551-556, Jan-Mar 2010.
8. Aboul-Enein H Y, Bunaciu A, Bala C, Fleischin S.Enalapril and ramipril selective membranes, Anal. Lett. 1997; 30: 1999–2008.
9. Bonazzi D, Gotti V, Andrisano V, Cavrini V. Analysis of ACE inhibitors in pharmaceutical dosage forms by derivative UV spectroscopy and liquid chromatography (HPLC). J. Pharm. Biomed. Anal. 1997, 16: 431–438.
10. ICH, Q2B. Validation of Analytical Procedure: Methodology. International Conference on Harmonization, IFPMA, Geneva. 2005.