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Simultaneous estimation of Ramipril and Olmesartan Medoxomil by first derivative UV Spectrophotometric method

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Abstract

In the present work a simple, precise and economical procedure for the simultaneous estimation of Ramipril and Olmesartan Medoxomil in tablet formulation has been developed using Elico SL- 160 UV spectrophotometer. Results from the present study indicate that Olmesartan Medoxomil has zero crossing point at 243.4 nm, where Ramipril zero crossing point at 237.4 nm in methanol. Both these drugs obey Beer's law in the concentration range employed (5-35 microgram/ml) for the present method. The result of analysis has been validated statistically by recovery studies. The outcome of the present study conclude that the developed method is a sensitive, accurate, precise and simple, which can be successfully employed for the routine estimation of both these drugs in bulk drugs and formulations without the interference of common excipients.

Key Words: Ramipril, Olmesartan Medoxomil, First Derivative, Simultaneous, Estimation

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1.0 Introduction

Both Ramipril (RAM) and Olmesartan Medoxomil (OLM) are antihypertensive agents belonging to category of angiotensin-converting enzyme (ACE) inhibitors. ACE inhibitors lower the production of angiotensin-II and relax arterial muscles, at the same time enlarging the arteries allowing the heart to pump blood more easily and thereby increase the blood flow. They also block the conversion of angiotensin-I to angiotensin-II and lower the arteriolar resistances and increase the venous capacity, cardiac index, stroke work and volume. Angiotensin II receptor blockers (ARBs) are agents that block the action of angiotensin II by preventing angiotensin II from binding to angiotensin II receptors on blood vessels. Due to blocking of Angiotensin II enzyme, blood vessels dilate and blood pressure is reduced which improves heart failure. ARBs have effects that are similar to ACE inhibitors, but ACE inhibitors act by preventing the formation of angiotensin II rather than by blocking the binding of angiotensin II to muscles on blood vessels .Both ACE inhibitors and ARBs are widely used in renal failure patients in the treatment of hypertension, left ventricular dysfunction, and diabetic nephropathy. Their efficacy in these conditions is well established, and generally both classes of drugs are well tolerated, with a low incidence of side effects [1]. Combination of ACE inhibitors and ARBs is proved to be a useful combination therapy for the treatment of ischemic heart diseases [2]. RAM is a pro drug belonging to the class ACE inhibitor used to treat hypertension and congestive heart failure, where as OLM is an ARB used to treat high blood pressure. Review of literature revealed that there are very few methods reported for the estimation of RAM and OLM individually and in combined dosage forms [3-27]. No derivative spectroscopic method has been so far reported for simultaneous estimation of these drugs in combined dosage form. So, the aim and objective of present study was to develop a first derivative UV-Visible spectrophotometric analytical method for the estimation of RAM and OLM in bulk and formulated dosage form in combination without prior separation and to establish a simple, sensitive, standard, reproducible method for the quality control of RAM and OLM.

2.0 Materials and Methods

Elico SL-160 double beam UV-visible spectrophotometer with 1 cm matched quartz cells was used for all the measurements. Methanol(99.5%) A.R. Grade (Qualigens, Fine chemicals) was used as the solvent.

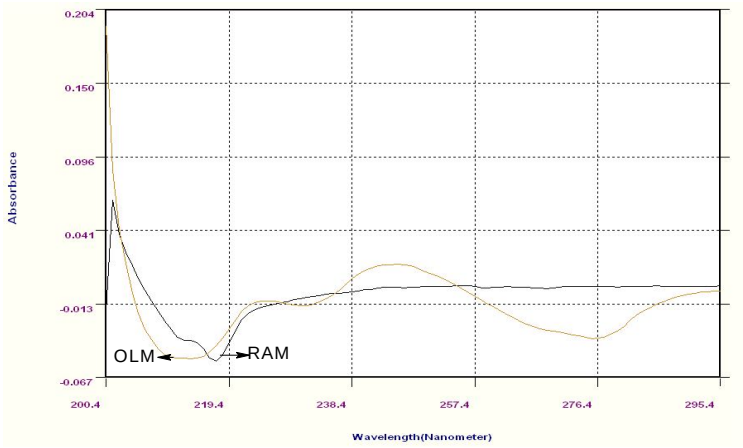


Figure-1: Overlaying spectra of RAM and OLN

2.1 Selection of Analytical Wavelength Ranges:

Standard stock solutions of 100µg/ml of RAM and OLM were prepared by dissolving separately 100 mg of each drug in 100 ml methanol. The subsequent dilutions of standard stock solution was made with methanol to get the final concentration of 10µg/ml standard solution. Thus prepared stock solution was scanned in the spectrum mode of an instrument from 300 nm to 200 nm. The first order derivatives of the spectra was processed for the selection of analytical wavelengths such that at the zero crossing of one drug and the other drug showed substantial absorbance. From the first order overlain derivative spectra of standard RAM and OLM, the wavelength was selected at 237.4 nm and 243.4 nm for the estimation of RAM and OLM respectively. Figure-1 represents the overlain derivative spectra of the two drugs.

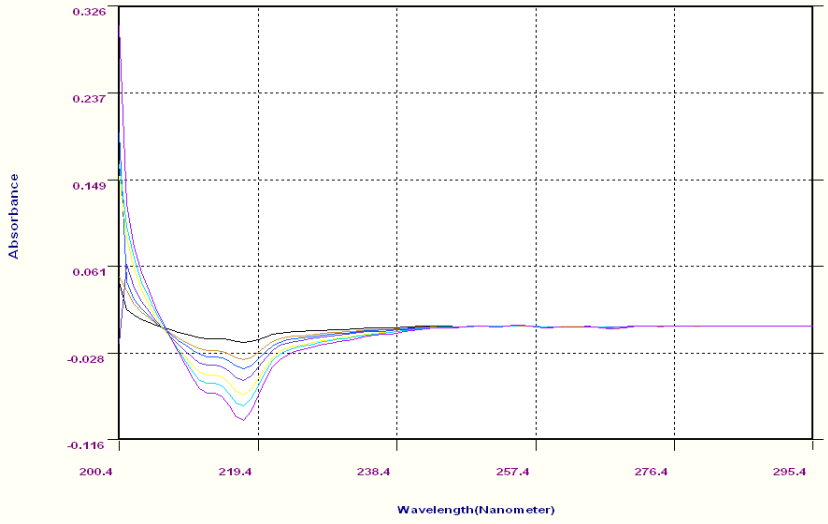


Figure-2: Overlain spectra of Ramipril showing linear range

2.3 Estimation of drug from dosage form

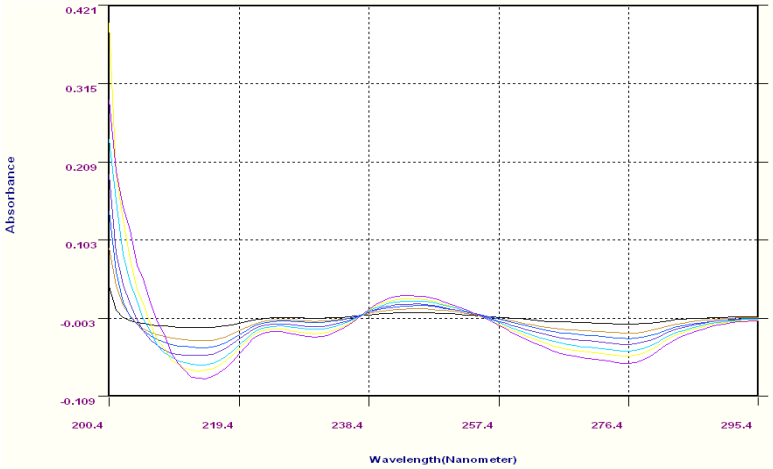
Twenty marketed tablets containing 5mg of RAM and 20mg of OLM were weighed, and finely powdered. A quantity of powder sample equivalent to 50mg of RAM and 200 mg OLM was taken in a volumetric flask and dissolved in methanol. Further dilutions were made to get a concentration of 5ug/ml of RAM and 20ug/ml of OLM. These concentrations were scanned at different wavelengths, i.e. 237.4 nm and 243.4 nm in first derivative mode. The Assay results and statistical parameters of tablet analysis are shown in Table 1.

3.0 Results and Discussion

The absorption measurements of each proposed drug in a binary mixture by zero order spectra appear to be quite impossible because of the total overlap of bands. To resolve the problem of closely overlapping spectra in derivative spectroscopy, with digital processing together with zero crossing offers the best option[28]. This technique involves the differentiation of the normal spectrum with respect to the wavelength. The average absorbance values produced when the different concentrations of RAM and OLM were scanned and these absorbance values were plotted against the respective concentrations, the curves yielded the equation y = -0.0022x-0.0006 (R^2= 0.9883) for RAM at 237.4 nm and y = 0.0075x + 0.0009 (R^2= 0.9922) for OLM at 243.4 nm, indicate the linearity of the method as shown in Figure -2. To prove the validity and applicability of the proposed method,

recovery studies were carried out on synthetic mixtures of different ratios in the concentration ranges as stated in Table-1. The results were computed against the previously constructed standard curve. Satisfactory results were obtained with a good mean recovery for RAM and OLM respectively, which prove the accuracy of the method. Similar method as above was applied to the determination of RAM and OLM in a commercial tablet preparation. The first derivative spectra of OLM shows an absorbance at 243.4 nm, where the rate of change of absorbance for RAM is zero and OLM can be specifically measured at that wavelength. RAM, on the other hand, has absorbance at 237.4 nm, where rate of change of absorbance for OLM is zero; hence RAM is specifically measured at that wavelength as shown in Figure (4)

Figure-3: Overlain spectra of Olmesartan Medoxomil showing linear range



3.1 Precision and Accuracy:

Precision of the method was determined by analyzing the marketed formulations. The results of estimation of both the drugs in tablets had been concurrent and repeatable with % R.S.D. values less than 2 % indicating the precision of the method. Satisfactory results were obtained with a mean recovery values within the required limits since the USP-acceptable limit is not less than 93.0% and not more than 107.0% stated on the labels. The data is given in Table-1.

Parameters	Ramipril	Olmesartan medoxomil
Linearity and range (µg/ml)	5-35	5-35
Correlation coefficient (r2)	0.9883	0.9922
Intercept± S.D	-0.0006±0.4472	0.0009±0.5474
Slope ± S.D	-0.0022±0.501	0.0075±0.3162
Regression equation (Y = mx +c)	0.0022x-0.0006 (R^2= 0.9883)	0.0075x + 0.0009 (R^2= 0.9922)
Accuracy and % Recovery (n = 5)	80%= 99.446±0.6605 100%=99.506±0.6238 120%=99.977±0.9118	80%= 99.808±0.2349 100%=99.902±0.0505 120%=100.036±0.0637
Precision (% R.S.D.)		
Intra-day (n = 5)	0.5035	0.3013
Inter-day (n = 5)	0.3741	0.3731

Table - 1: Results of proposed method

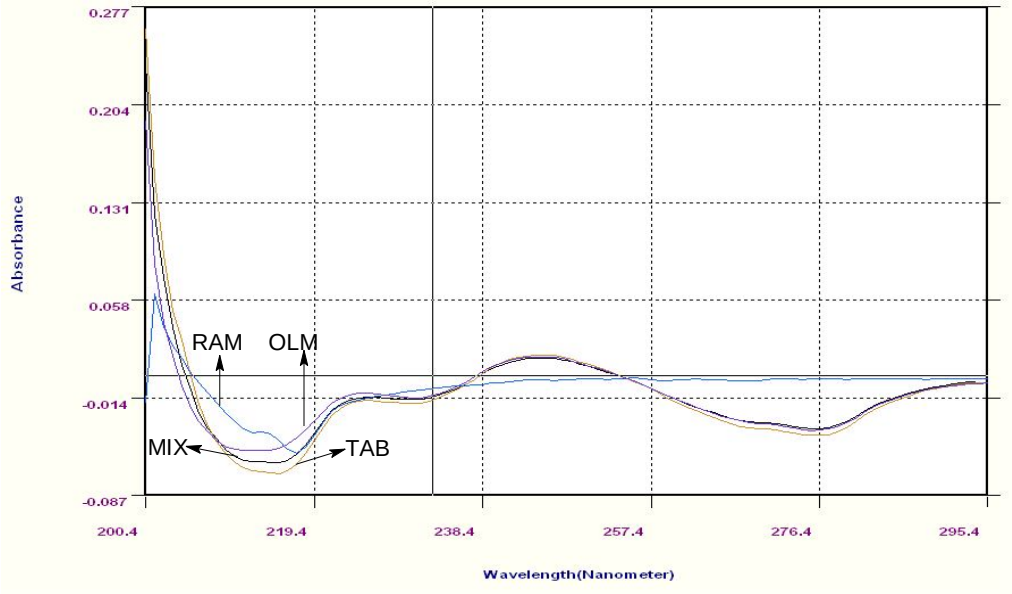


Figure 4. Overlain spectra of pure drugs, mixture, and tablets

4.0 Conclusion

The described method is an accurate and precise method for the determination of RAM and OLM mixtures in tablets without prior separation, which can be easily applied for routine analysis. The most striking feature of the derivative spectroscopic method is its simplicity and rapidity. This method also provides a simple and reproducible quantitative analysis without any interference from the excipients. The % RSD values in precision show that proposed method provide acceptable variation for RAM and OLM. The % RSD of proposed method was found to be less than 2% shows its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage. The low values of % RSD indicate that the method is precise and accurate. Results of validation parameters demonstrate that the analytical procedure is suitable for its intended purpose.

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