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SIMULTANEOUS SPECTROPHOTOMETRIC DETERMINATION OF METOPROLOL TARTRATE AND RAMIPRIL

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The present investigation deals with the development of a new, simple, specific, sensitive, rapid and economical procedure for simultaneous estimation of metoprolol tartrate and ramipril in a combined dosage form. The method is based on the ultraviolet absorbance maxima of the above two drugs at 209.5 nm and 222 nm, respectively. Both the drugs obeyed Beer's law in the concentration range of 40-120 and 4-20 μg/ml, respectively. The proposed methods were successfully applied for the simultaneous determination of both drugs in commercial capsule preparations. The results of the analysis have been validated statistically and by recovery studies.

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1. Introduction

Metoprolol tartrate, (MT) is chemically a bis[(2 RS)-1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl) amino] propane-2-ol] (2R,3R)-2,3-dihydroxybutanedioate. It is a prototype β_1-antiadrenergic drug which has the potency to increase the heart rate and decrease renin release from kidney. Ramipril (RP) is (2S, 3aS, 6aS) 1[(S)1(ethoxycarbonyl)3phenylpropyl]amino] propanoyl]octahydrocyclopenta[b] pyrrole -2-carboxylic acid and it is the ACE inhibitor. Literature survey revealed that Flourimetric [1]. HPLC [2,3], LC/MS [4], GC/MS [5], methods for estimation of MT individually and in combination with other drugs. Ramipril have been reported for the estimation as individual or in combination with other drugs in various analytical methods such as Voltametric [6], Capillary electrophoresis [7], GC/MS [8], UV [9], HPLC [10], and LC/MS [11] .Only one LC/MS method was reported for the simultaneous estimation of MT and RP in a combined dosage formulation [12] , A RP-HPLC method of analysis was reported for simultaneous estimation of amlodipine and metoprolol in tablet formulation [13]. Since the reported RP-HPLC and LC/MS method is expensive and involves complicated sample preparation, the present work was undertaken for simultaneous estimation of MT and RP in capsule formulations by UV spectrophotometric method.

2. Experimental

2.1 Materials and methods

A double-beam Shimadzu UV- Visible spectrophotometer (Model 1700 Pharmaspec), with spectral bandwidth of 2 nm, wavelength accuracy ± 0.5 nm and a pair of 1-cm matched quartz

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cells was used to measure absorbance of the resulting solution. Analytical grade solvents were used in the present study. Drug samples of metoprolol tartrate (MT) and ramipril (RP) were procured from M/s Arvind Remedies Ltd, Chennai. Commercial capsules of metoprolol tartrate and ramipril in a combined dosage form were purchased from the local market

2.2 Determination of linearity range

MT and RP were accurately weighed (100mg each) and dissolved separately in 35 ml of methanol and the volume made up of 100 ml with water in a100 ml volumetric flask. One milliliter of the above solutions was diluted separately to 10 ml with methanol in volumetric flask to give 100 µg/ml working standard solutions. These working standard solutions were further diluted for 10µg/ml. These dilutions were scanned in the UV region.MT showed absorption maximum at 222 nm whereas RP showed absorption maximum at 209.5 nm. MT showed linearity range from 40 – 120 µg/ml and RP showed linearity range from 4 – 12 µg/ml at the selected wavelengths respectively. The overlain spectra for the above two drugs is represented in Fig.1.

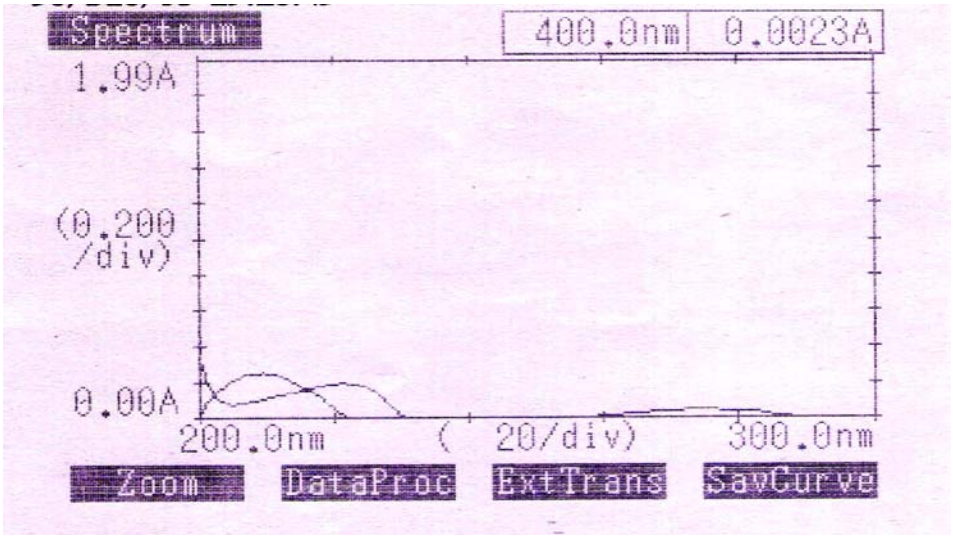

Fig 1. Overlain spectra for metoprolol tartrate and ramipril

2.3 Analysis of metoprolol tartrate and ramipril by Vierodt's method

Commercial formulation, Cap-I and Cap-II was purchased from a local pharmacy. Twenty capsules of each brand containing 25 mg of MT and 2.5 mg of RP were weighed and finely powdered in a mortar. A quantity of powder equivalent to 100 mg of MT and 10 mg of RP were weighed accurately and dissolved in 10 ml of methanol and made up to 100 ml in a volumetric flask with water (1000 µg/ml). The solution was then filtered through Whatmann filter paper to get a clear solution. From this 1 ml of solution was drawn and make up to 10 ml with water. The formulation was estimated in one concentration range by diluting stock solutions to 120 and 12 µg/ml of MT and RP. The samples containing two absorbing species MT and RP (Y & X) each of which absorbs at the λ max of the other. So the absorbance of each drugs were measured at both wavelengths λ1 & λ2 respectively.

Both the drugs were determined by simultaneous method (Vierodt's method). The absorptivity of RT (X) at λ1 (209.5) and λ2 (222.0) is ax_1 ax_2 respectively. The absorptivity of MT (Y) at λ1 (209.5) and λ2 (222.0) is ay_1 ay_2 respectively.

Absorptivity = absorbance / concentration

The absorbance of the sample (formulation) at λ1 (209.5) and λ2 (222.0) is A1 and A2 respectively. The total absorbance of the mixture is equal to the sum of individual absorbance of X and Y.

$$A_1 = ax_1bcx + ay_1bcy$$
$$A_2 = ax_2bcx + ay_2bcy$$

Cx – conc of RT

Cy – conc of MT

By using this formula both the drugs MT and RP were estimated (Table 1).

$$Cx = \frac{A_2ay_1 - A_1ay_2}{ax_2ay_1 - ax_1ay_2}$$

$$Cy = \frac{A_1ax_2 - A_2ax_1}{ax_2ay_1 - ax_1ay_2}$$

Table 1. Results of Analysis of Capsule Formulation Containing Metoprolol tartrate and Ramipril.

Capsule	Drug	Label Claim (mg/capsule)	Estimated Amount (mg/capsule)	% Label Claim	% RSD
I	Metoprolol tartrate	25.0	24.77	99.08	0.17
	Ramipril	02.5	02.48	99.20	0.59
II	Metoprolol tartrate	25.0	24.86	99.44	0.25
	Ramipril	02.5	02.49	99.60	0.35

2.4 Recovery Studies

To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method. Percent recovery for MT and RP was found in the range of 98.50% to 99.95% (Table 2).

Table 2 Recovery Study of Metoprolol tartrate and Ramipril

Drug	Label Claim (mg/capsule)	Amount added 100 %	Average % Recovery ± S.D (n = 3)	% RSD
Metoprolol tartrate	25	25	98.74 ± 0.81	0.667
Ramipril	2.5	2.5	100.95 ± 0.76	0.765

3. Results and discussion

The reproducibility of the proposed method was determined by performing assay at different time intervals on same day (Intra-day assay precision) and on three different days (Inter-day precision). Result of intra-day and interday precision is expressed in % RSD. Percent RSD for intraday assay precision was found to be 0.117 (for MT) and 0.487 (for RP) and inter-day assay precision was found to be 0.642 (for MT) and 0.498 (for RP).

The present work describes a convenient and accurate method for simultaneous analysis of MT and RP. Wavelengths selected for quantitation were 209.5 nm for MT and 222.0 nm for RP. The linearity for detector response was observed in the concentration range of 40-120 and 4-20 µg/ml for MT and RP respectively. The correlation coefficient of mixed solution at 209.5 nm and 222.0 nm were found to be 0.9991 and 0.9989 respectively. Values were calculated for both the drugs at selected wavelengths and substituted in equations for determining concentration of MT

and RP in capsule sample solution. Percent label claim for MT and RP in capsule analysis was found in the range of 99.08% to 99.60%. Standard deviation and coefficient of variance for six determinations of capsule sample was found to be less than ± 2.0 indicating the precision of both the methods. Accuracy of proposed methods was ascertained by recovery studies and the results are expressed as % recovery. Percent recovery for MT and RP was found in the range of 98.74% to 100.95%. Values of standard deviation and coefficient of variation was satisfactorily low indicating the accuracy of both the methods.

4. Conclusions

Based on the results obtained, it is found that the proposed method of analysis is accurate, precise, reproducible & economical and can be employed for routine quality control of metoprolol tartrate and ramipril in combined dosage capsule formulations.

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