able to increase the urea level (19.9 mg/dl) significantly. Similarly the normal cholesterol level, 100 mg/dl which significantly increases up to 133 mg/dl due to paracetamol, has been decreased to 124 mg/dl. Thus *Tridax* seems to reduce the hepatotoxicity produced by the paracetamol. This needs further confirmation with the enzyme and histopathological studies.

ACKNOWLEDGEMENTS

The authors wish to acknowledge Mr. S. Sheik Abdulla., Lecturer., P.G. Dept of Biochemisty., M.I.E.T Arts Collage., Trichy-7, Mrs. S. Karpagam Kumarasundari, Head, Department of Pharmacology and Mrs. R. Florence Rajarathinam, Head, Department of Laboratory Technology, Periyar College of Pharmaceutical Sciences for Girls, Thiruchirappalli - 620 021 for their valuable suggestions.

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Simultaneous Spectrophotometric Estimation of Losartan Potassium and Hydrochlorothiazide from Combined Dosage Form

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Accepted 21 October 2000
Revised 3 October 2000
Received 24 April 2000

Two simple, accurate and economical procedures for simultaneous estimation of losartan potassium and hydrochlorothiazide in two component tablet formulations have been developed. The methods employ program in the multicomponent mode of analysis of the instrument used and simultaneous equations using area under curve. In all glass double distilled water losartan potassium has an absorbance maxima at 205 nm, hydrochlorothiazide has three absorbance maxima at 225, 272 and 315 nm. Both the drugs obey the Beer's Law in the concentration ranges employed for these methods. The results of analysis have been validated statistically and by recovery studies.

The literature describes HPLC[1-3], electrophoresis and supercritical fluid chromatography[4] methods for the analysis of losartan potassium where as HPLC[5-7], HPTLC[8], spectrophotometric[9,10] and non-aqueous potentiometric titration[11] methods for the analysis of hydrochlorothiazide. Only RP-HPLC[12] method has been established for their simultaneous determination, but no spectrophotometric method is available for estimation of these drugs in combined dosage form. The objective of this investigation was to devise two simple, accurate and economical spec-

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trophotometric methods for the simultaneous estimation of losartan potassium and hydrochlorothiazide from marketed combined pharmaceutical dosage form.

A PC based JASCO V-530 UV-VIS recording spectrophotometer was used for the experimental purpose. All glass double distilled water was used as a solvent. Gift sample of losartan potassium and hydrochlorothiazide were obtained from M/s Torrent Pharmaceuticals Ltd., Gujarat. Tablets of two different brands containing losartan potassium and hydrochlorothiazide were procured from market. (Repace-H, Sun Pharmaceutical Industries Ltd., Losar-H, Unisearch Ltd.)

TABLE 1: COMPOSITION OF MIXED STANDARDS

Standard Number	losartan potassium (µg/ml)	hydrochlorothiazide (µg/ml)
1	4.0	1.0
2	8.0	2.0
3	12.0	3.0
4	16.0	4.0
5	20.0	5.0

Concentration of losartan potassium and hydrochlorothiazide in five mixed standard solutions.

Five mixed standard solutions with different concentrations of the two drugs were prepared in all glass double distilled water. The concentrations of the two components in the mixed standard solutions are given in Table 1. All the mixed standard solutions were scanned over the range of 400 nm to 200 nm in the multicomponent mode using two sampling points 205 nm and 272 nm. The spectral data from these scans is used to determine the concentration of two drugs in the tablet sample solutions.

Twenty tablets were weighed and average weight was calculated. They were crushed to a fine powder. Tablet powder equivalent to 10 mg of losartan potassium was transferred to a 100 ml volumetric flask. The powder was dissolved in 75 ml of all glass double distilled water by intermittent shaking and volume was made up to the mark with the same solvent. The solution was then filtered through Whatman filter paper No. 41. The solution was diluted with all glass double distilled water to obtain 20 µg/ml of losartan potassium and 5 µg/ml of hydrochlorothiazide. This sample was scanned over range of 400 nm to 200 nm in the multicomponent mode and the concentration of each component were obtained by the spectral data of the sample solutions with reference to that of the mixed standards. The analysis procedure was repeated five times with tablet formulations of two different manufacturers. The results of analysis of tablet formulations, statistical validation[13] and recovery studies are shown in Table 2,3 and 4 respectively.

The 'X' values of each of the two drugs were determined at the selected wavelength range, 203 to 215 nm and 260 to 280 nm. The 'X' values were determined as,

$$X = \frac{\text{Area under curve of component between selected wavelength range}}{\text{Concentration of the component in g/l.}} \quad ...(1)$$

A set of two simultaneous equations framed using these 'X' values are given below,

$$A_1 = 1069.73 \times C_1 + 650.62 \times C_2 \quad .....(2)$$

$$A_2 = 284.50 \times C_1 + 1060.22 \times C_2 \quad .....(3)$$

TABLE 2: ANALYSIS DATA OF TABLET FORMULATIONS

Method	Tablet Sample	Label Claim (mg/tab)		Amount Found (mg/tab)		% of Label Claim*	
		LST	HCTZ	LST	HCTZ	LST	HCTZ
1	T1	50	12.5	50.70	12.38	101.40	99.08
	T2	50	12.5	50.78	12.40	101.76	99.24
2	T1	50	12.5	50.80	12.46	101.61	99.68
	T2	50	12.5	51.09	12.39	102.18	99.15

Asterisk (*) denotes average of five estimations. LST and HCTZ denote losartan potassium and hydrochlorothiazide, respectively, while T1 and T2 are brands of tablet formulation.

TABLE 3: STATISTICAL VALIDATION

Method	Tablet Sample	Standard Deviation		Coefficient of Variation		Standard Error	
		LST	HCTZ	LST	HCTZ	LST	HCTZ
1	T1	0.9974	0.7886	0.9836	0.7959	0.4460	0.3526
	T2	0.4277	0.7924	0.4203	0.7984	0.1912	0.3543
2	T1	0.9864	0.9884	0.9707	0.9915	0.4411	0.4420
	T2	0.4604	0.9502	0.4643	0.9572	0.2059	0.4249

LST and HCTZ denote losartan potassium and hydrochlorothiazide, respectively. T1 and T2 are brands of tablet formulation.

TABLE 4: RECOVERY STUDY DATA

Method	Tablet Sample	Amount added (µg/ml)		% Recovery*	
		LST	HCTZ	LST	HCTZ
1	T1	10	2.5	101.06	99.71
	T2	10	2.5	100.37	99.28
2	T1	10	2.5	101.14	99.08
	T2	10	2.5	101.85	100.56

Asterisk (*) denotes average of five estimations. LST and HCTZ denote losartan potassium and hydrochlorothiazide, respectively, while T1 and T2 are brands of tablet formulation.

Where, C_1 and C_2 are concentrations of losartan potassium and hydrochlorothiazide respectively in grams per litre in the sample solution. A_1 and A_2 are the area under curve of sample solution at the wavelength range 203 to 215 nm and 260 to 280 nm, respectively, 1069.73 and 650.62 are the 'X' values at 203 to 215 nm and 260 to 280 nm, respectively, 1069.73 and 650.62 are the 'X' values at 203 to 215 nm of losartan potassium and hydrochlorothiazide, respectively, while, 284.50 and 1060.22 are the 'X' values at 260 to 280 nm of losartan potassium and hydrochlorothiazide, respectively. The 'X' values reported are the mean of five independent determinations. By applying the Cramer's rule and Matrices to equations (2) and (3), concentrations C_1 and C_2 can be obtained as,

$$C_1 = \frac{A_1 \times 1060.22 - A_2 \times 650.62}{949047.71} \quad \ldots\ldots (4)$$

$$C_2 = \frac{A_2 \times 1069.73 - A_1 \times 284.50}{949047.71} \quad \ldots\ldots (5)$$

Tablet sample solutions were made as mentioned in first method. Area under curve of these solutions i.e. A_1 and A_2 were recorded 203 to 215 nm and 260 to 280 nm respectively and concentrations of two drugs in the sample were determined by substituting A_1 and A_2 values of sample solution in equation (4) and (5). The results of analysis of tablet formulations, statistical validation and recovery studies are shown in Tables 2, 3 and 4 respectively.

The proposed methods were found to be simple, accurate, economical and rapid for routine simultaneous estimation of two drugs. Both the methods were found to be economical, as they require only all glass double distilled water as solvent. The values of standard deviation, coefficient of variation, standard error were satisfactorily low and recovery studies lying between 100-102% (for losartan potassium) and 99-101% (for hydrochlorothiazide) were indicative of the accuracy of both the methods.

The first method is specific for this instrument. The method requires no manual calculations and gives marginally better results than other methods. The second method employing simultaneous equations using area

under curve is a very simple method and can be employed for routine analysis of these two drugs in combined dosage forms. Once the 'X' values are determined then it requires only determination of area under curve of the sample solution at the selected wavelength range and few simple calculations.

ACKNOWLEDGEMENTS

The authors thank M/s Torrent Pharmaceuticals Ltd. (Gujarat) for providing gift samples of drugs to carry out this work.

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Visible Spectrophotometric and HPLC Methods for Estimation of Rimapril from Capsule Formulation

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Accepted 21 October 2000

Revised 9 October 2000

Received 10 March 2000

Two visible spectrophotometric and one HPLC method have been developed for estimation of rimapril from its capsule formulation.The developed visible spectrophotometric methods were based on formation of chloroform extractable coloured complexes of drug with nitrosonaphthol and with bromophenol blue.The formed coloured complex with nitrosonaphthol showed absorbance maximum at 445.5 nm and Beer's law was obeyed in the concentration range of 50-300 µg/ml of drug while the formed coloured complex with bromophenol blue showed absorbance maximum at 414 nm and Beer's law was obeyed in the concentration range of 20-100 µg/ml of rimapril. Developed HPLC method was a reverse phase chromatographic method using Inertsil C_{18} column and methanol:acetate buffer::80:20 as mobile phase with detection at 230 nm. Loratidine was used as internal standard for the HPLC method. Linearity was observed in concentration range of 10-300 µg/ml of rimapril. Results of analysis for all the methods were validated statistically and by recovery studies.

Rimapril, chemically [2s-[R*(R*), 2α, 3αβ, 6αβ]-1-[2-[(1-ethoxycarbonyl)-3-phenyl]-amino]-1-oxopropyl]-octahydrocyclopenta[b]pyrrole-2-carboxilic acid, is an antihypertensive agent[1]. Few HPLC[2-4] methods are reported for estimation of rimapril from its solution matrix

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