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Validated spectrophotometric methods for simultaneous estimation of telmisartan and indapamide in pharmaceutical dosage form

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ABSTRACT

Two simple, sensitive, and validated spectrophotometric methods are developed for quantitative estimation of telmisartan and indapamide in tablet dosage form. Method I is based on the simultaneous equation whereas Method II on the multicomponent analysis. The absorption maxima were found to be at 296 nm and 242 nm in methanol for telmisartan and indapamide respectively. Beer's law is obeyed in the concentration range of 5-25 µg/ml for telmisartan and 10-30 µg/ml for indapamide with correlation coefficient within range of 0.996 - 0.998 for both the drugs. The simultaneous equation method is based on the additivity of absorbances and multicomponent analysis involves recording absorbance of standard solutions at 296 nm and 242 nm. Both the methods are tested and validated for various parameters according to ICH guidelines and can be used for routine analysis of both the drugs in quality control laboratories.

Keywords: Simultaneous equation method, multicomponent analysis, telmisartan, indapamide.

INTRODUCTION

Telmisartan [TEL] chemically is 2-(4-{[4-methyl-6-(1- methyl-1H-1, 3-benzodiazol-2-yl)-2-propyl-1H-1,3-benzodiazol-1-yl]methyl}phenyl)benzoic acid [1]. It is an angiotensin II type I blocker and is used as an antihypertensive along with hydrochlorothiazide [2]. It is a thiazide diuretic which reduces the reabsorption of electrolytes from the renal tubules, thereby increasing the excretion of sodium and chloride ions and consequently of water. TEL blocks the vasoconstrictor and aldosterone secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT_1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Literature survey reveals that few spectrophotometric methods [3], HPLC [4, 5] and HPTLC [6, 7] have been reported for estimation of TEL in pharmaceutical dosage form as a single drug or in combination with other drugs. The molecular structure of TEL is shown in Figure 1.

Indapamide [IND] is a benzamide sulphonamide indole. It is an antihypertensive agent administered to individuals with mild to moderate hypertension [8]. Indapamide is chemically 3-(aminosulfonyl)-4-chloro-N-(2, 3-dihydro-2-methyl- 1H-indol-1-yl) benzamide [9] and the structural formula is as shown in Figure 2. It is official in United States Pharmacopoeia 2005[10] and British Pharmacopoeia 1995[11]. IND is an orally administered diuretic and antihypertensive drug. Its diuretic and natriuretic effects are mainly due to the presence of o-chlorobenzenesulfonamide, a molecule present in various diuretics. However, a varied side chain gives the drug characteristic properties. IND represents an indolinyl ring which uniquely exhibits free-radical scavenging activity as well as a direct vasodilator action. Literature survey reveals that a spectrophotometric [12-14], colorimetric [15], HPLC [16, 17] and LC-MS [18] method have been employed for the quantitative estimation of IND in bulk and pharmaceutical formulations.

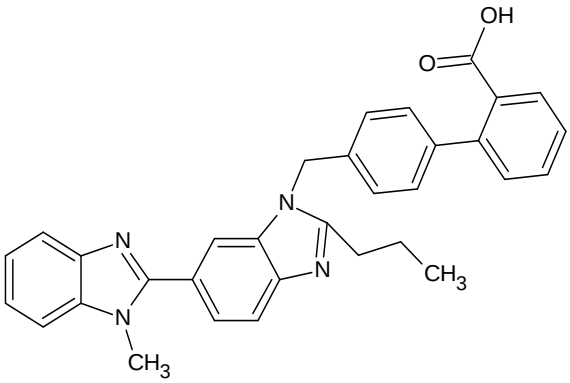

Figure 1: Chemical structure of telmisartan

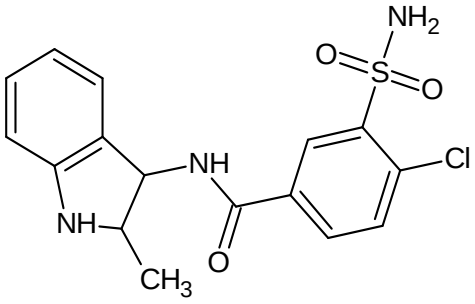

Figure 2: Chemical structure of indapamide

Literature study also reveals that only RP-HPLC [19] method is available for estimation of TEL and IND in tablet dosage form.

Since the reported RP-HPLC method is expensive and involves complicated sample preparation, the present work was undertaken for simultaneous estimation of TEL and IND in tablet formulations by UV spectrophotometric method. We have developed simultaneous equation and multicomponent analysis methods to determine the concentration of each drug in the mixture. Mixtures of known composition were used as standards to minimize errors due to the presence of other components in the solution.

MATERIALS AND METHODS

Chemicals and reagents

Analytical grade methanol used as a solvent was purchased from Qualigens. Commercially available formulations were procured from local market.

Instrumentation

A UV–Visible double beam spectrophotometer of Jasco Model: V-630, with a fixed bandwidth 2nm and a pair of 1cm matched quartz cell was used for all spectrophotometric measurements.

Selection of common solvent

After assessing the solubility of both drugs in different solvents methanol was selected as a common solvent for developing spectral characteristics.

Preparation of standard solution:

The standard stock solutions of TEL and IND were prepared by dissolving 10 mg of each drug in 40 ml of methanol and final volume was adjusted with methanol to get a solution containing 100 µg/ml of each drug.

For the selection of analytical wavelength, standard solution of TEL (20 µg/ml) and IND (20µg/ml) were prepared separately by appropriate dilution of standard stock solution with methanol and scanned in the entire UV range to determine λmax of both the drugs. The λmax of TEL and IND were found to be 296 nm and 242 nm, respectively. A series of standard solutions were prepared having concentration range of 5-25 µg/ml for TEL and 10-30 µg/ml for IND. The absorbance of resulting solutions was measured at 296 nm and 242 nm. Then calibration curves were

plotted. Both the drugs obeyed linearity in the concentration range under study. The standard calibration curve of TEL and IND are shown in Figure 3 and 4.

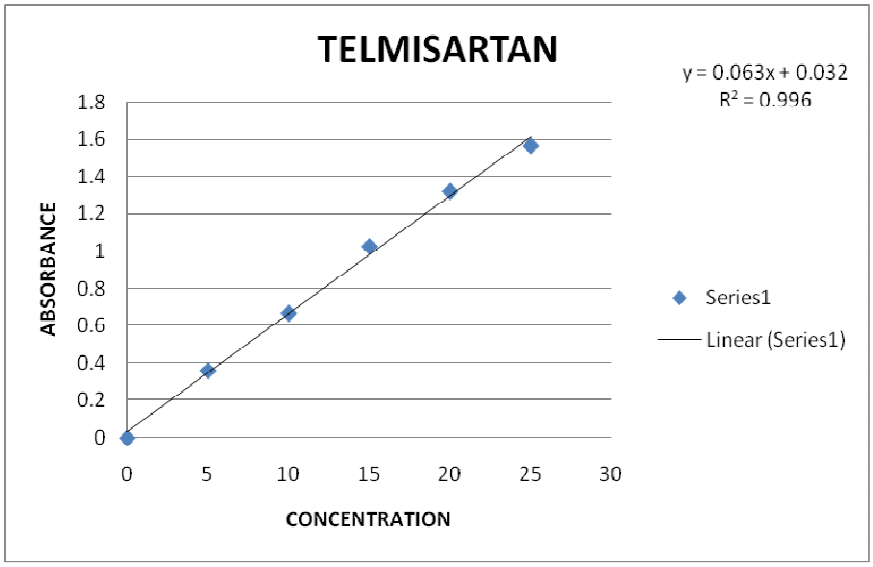

Figure 3: Standard calibration curve of TEL

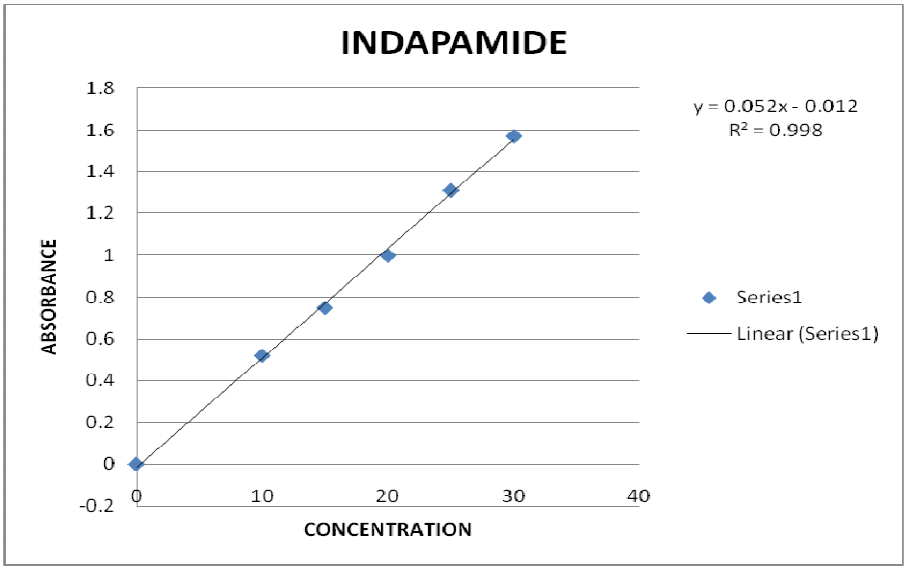

Figure 4: Standard calibration curve of IND

Method I: Simultaneous equation method

This method of analysis was based on the absorption of TEL and IND at the wavelength maximum of each other. Two wavelengths selected for the development of simultaneous equations were 296 nm and 242 nm which were λmax of TEL and IND respectively. The absorbances of TEL and IND were measured at the selected wavelengths. The absorptivity values E (1%, 1cm) were determined for both drugs at the selected wavelengths [20]. These values were mean of five estimations.Overlain spectra of TEL and IND are shown in Figure 5.

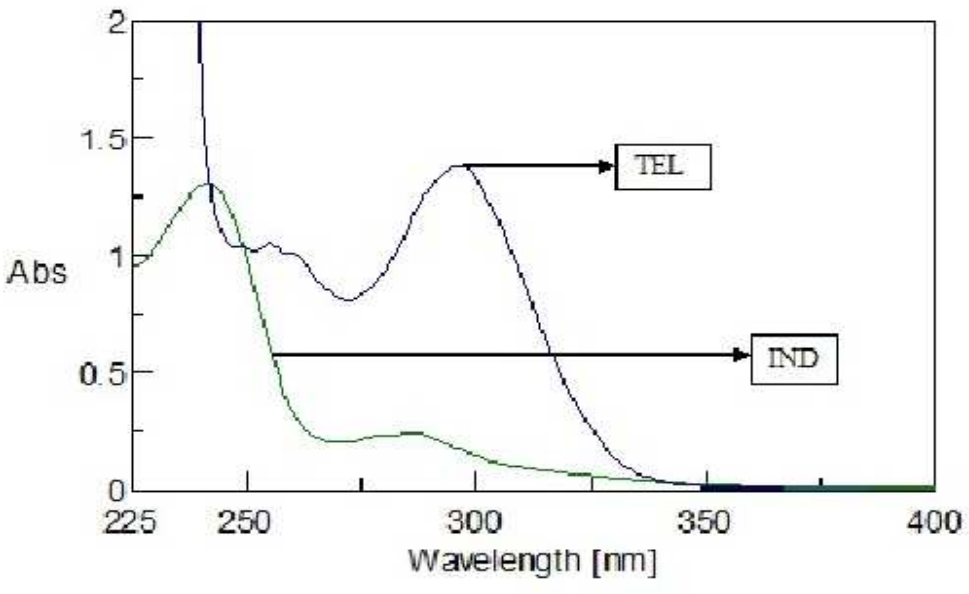

Figure 5: Overlain spectra of TEL and IND

The concentration of both drugs in mixture can be calculated by using following equations-

$$C_x = \frac{A_1ay_2 - A_2ay_1}{ax_1ay_2 - ax_2ay_1} \quad \text{.....Eq (1)}$$

$$C_y = \frac{A_1ax_2 - A_2ax_1}{ay_1ax_2.ay_2ax_1} \quad \text{.....Eq.(2)}$$

Where, A_1 and A_2 are absorbances of mixture at 296 and 242 nm respectively
ax_1 and ax_2 are absorptivities of TEL at 296 and 242 nm respectively
ay_1 and ay_2 are the absorptivities of IND at 296 and 242 nm respectively
Cx and Cy are the concentrations of TEL and IND respectively

Analysis of marketed formulation

Twenty tablets were accurately weighed; average weight was determined and finely powdered. An accurately weighed quantity of tablet powder equivalent to 20 mg of TEL was transferred to 100 ml volumetric flask and dissolved by sonication with sufficient quantity of methanol and then volume was made to the mark with methanol. The solution was then filtered through Whatmann filter paper no. 41. The filtrate 1 ml was taken in 10 ml volumetric flask and volume made to the mark with methanol. The above mixture was analyzed at 296 and 242 nm wavelengths and values of the absorbance were substituted in respective equations (Eqn. 1 and 2) to obtain the content of TEL and IND respectively. The data of analysis is mentioned in Table 1.

Table 1. The data of tablet analysis

Drug	Label Claim (mg/tablet)	Amount of drug estimated* (mg/tablet)		% Label claim estimated ± S.D.*	
		Method A	Method B	Method A	Method B
TEL	40	39.99	40.36	99.99± 0.57	100.91± 0.79
IND	1.5	1.476	1.51	98.45± 0.27	100.66± 0.19

** Mean of six determinations, where A is simultaneous equation method and B is multicomponent analysis method*

Method II: Multicomponent mode of analysis:

The use of five mixed standards and two sampling wavelength 296 nm and 242 nm were found to serve the purpose of the experiment. The overlain spectrum TEL and IND is shown in Figure 6.

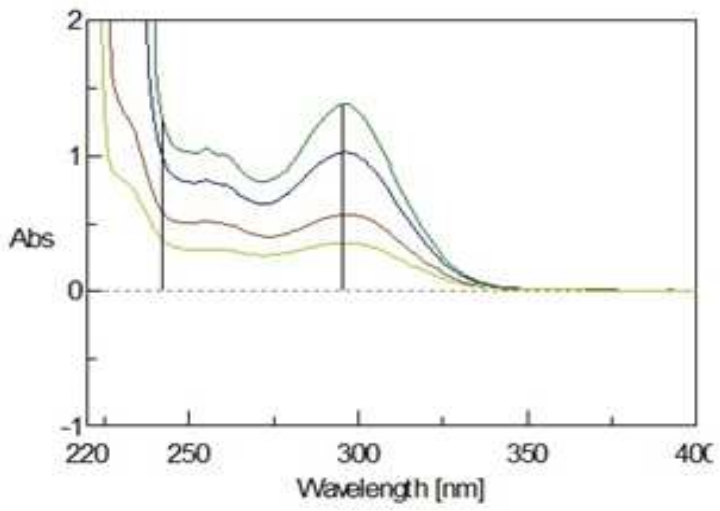

Figure 6: Overlain spectra of TEL and IND (Multicomponent mode of analysis)

In this method, five mixed standards of TEL and IND in the ratio of 40:1.5 were prepared by appropriate dilution of the standard stock solutions and scanned in the region of 400 nm to 200 nm in the multi-component mode using the two sampling wavelengths as mentioned above. Recording absorbance of the mixed standard solutions was processed by the instrument by means of matrix equations and was then corrected to determine concentrations of both the drugs in the tablet sample solutions. Tablet sample solution was prepared as described under method I. Then the sample stock solution 1 ml was taken in a 10 ml volumetric flask and final volume was made up with solvent used. Spectrophotometric analysis of the resulting solution was carried out using the multi-component mode of the instrument. The result of analysis is mentioned in Table 1.

RESULTS AND DISCUSSION

The developed methods for simultaneous estimation of TEL and IND were validated as per ICH guidelines.

Accuracy

To check the accuracy of the developed methods and to study the interference of formulation additives, recovery studies were carried out by standard addition method at three different levels (80%, 100% & 120%). The results of recovery studies expressed as percent recovery were satisfactory and are presented in Table 2.

Table 2. Result of recovery studies

Method	Level of Recovery (%)	% Recovery ± S.D. #	
		TEL	IND
A	80	99.99 ±0.0456	98.77±0.6045
	100	99.85 ± 0.0345	98.69±0.7567
	120	99.50±0.2321	98.99±0.1578
B	80	100.40±0.2341	99.60±0.567
	100	101.10±0.1679	99.60±0.6784
	120	99.50±0.2451	100.1±0.3452

#mean of three determinations, SD: Standard Deviation, TEL: Telmisartan; IND: Indapamide

Intermediate precision (inter-day and intra-day precision)

The reproducibility of the proposed methods was determined by analyzing tablets at different time intervals on same day (Intra-day assay precision) and on three different days (Inter-day assay precision). The results are presented in Table 3. Coefficient of variance for intra-day assay precision was found to be 0.1705 (for telmisartan) and 0.5816 (for indapamide) in simultaneous equation method, 0.2647 (for telmisartan) and 0.1612 (for indapamide) in multicomponent mode of analysis. Inter-day assay precision coefficient of variance was found to be 0.1507 (for telmisartan) and 0.0572 (for indapamide) in simultaneous equation method, 0.2641 (for telmisartan) and 0.0834 (for indapamide) in multicomponent mode of analysis.

Limit of detection (LOD) and Limit of quantitation (LOQ)

The LOD and LOQ were separately determined based on the standard deviation of y-intercept of the calibration curve. The limit of detection (LOD) and limit of quantification (LOQ) were determined by visual methods as suggested in ICH guidelines, which were found to be as per given in Table 3.

Table 3. Optical characteristics and validation parameters

Statistical parameter	Method A		Method B	
	TEL	IND	TEL	IND
λ max (nm)	296	242	296	242
Concentration range (µg/ml)	5-25	10-30	5-25	10-30
Regression Equation (y= a + bc)				
Slope (b)	0.063	0.052	0.0133	0.0267
Intercept (a)	0.032	0.012	0.1463	0.1903
Correlation Coefficient (r^2)	0.9968	0.9986	0.9992	0.9988
LOD (µg/ml)	0.054	0.062	0.12	0.15
LOQ (µg/ml)	0.34	0.37	0.18	0.21
Precision (COV*): Interday (n=3)	0.1507	0.0572	0.2641	0.0834
Intraday (n=3)	0.1705	0.5816	0.2647	0.1612

** COV is Coefficient of variance*

CONCLUSION

The proposed UV spectrophotometric methods are tested and validated for various parameters according to ICH guidelines and can be used for routine analysis of telmisartan and indapamide in pharmaceutical dosage forms as a quality control tool.

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