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Simultaneous Estimation of Telmisartan and Hydrochlorothiazide in Tablet Dosage Form by HPTLC Method

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A validated HPTLC method for simultaneous estimation of telmisartan and hydrochlorothiazide in tablet formulations is described. The separation was achieved on pre-coated silica gel plate 60 F_{254} using ethyl acetate:chloroform:methanol (10:3:1 v/v/v) as mobile phase. Quantification was carried out by the use of densitometer in absorbance mode at 270 nm. Linearity of detector response for telmisartan and hydrochlorothiazide estimated in the average weight of the tablet were found to be 39.58 and 12.48 mg, respectively. The percentage recovery of telmisartan and hydrochlorothiazide estimated in the average weight of the tablet were found to be 99.61 and 99.49 %, respectively. The proposed method is accurate, precise and reproducible and can be adopted for routine analysis of telmisartan and hydrochlorothiazide in tablet formulation.

Key Words: Telmisartan, Hydrochlorothiazide, HPTLC.

INTRODUCTION

Telmisartan (TELM) is chemically 4'-[(1,4'-dimethyl-2'-propyl [2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid. Hydrochlorothiazide (HCTZ) is chemically 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide-1,1-dioxide. Both the drugs are available in combination as tablet, used for treating hypertension. Literature survey reveals that telmisartan[1-3] in tablet dosage form and in biological fluids are estimated by HPLC methods. Hydrochlorothiazide[4-8] is estimated by HPLC, LC-MS and several other methods in biological fluids. No analytical method has been reported for analysis of these two drugs in combination. In the present work, a successful attempt has been made to estimate these drugs simultaneously by an accurate, precise, economical and less time consuming HPTLC method[9].

EXPERIMENTAL

Instruments used

Application mode : CAMAG Linomat IV Sample applicator
Scanner mode : CAMAG TLC Scanner III
Development mode: CAMAG Twin trough chamber

Chromatographic condition

Stationary phase : Pre-coated Silica gel plate 60 F_{254} pre-washed with methanol
Mobile phase : Ethyl acetate:chloroform:methanol (10:3:1 v/v/v)
Distance between bands : 14 mm
Injection volume : 5 µL
Separation technique : Ascending development
Scanning mode : Absorbance
Lamp : Deuterium
Wavelength : 270 nm

Label claim

TELM - 40 mg, HCTZ - 12.5 mg

Preparation of standard stock solution: An accurately weighed quantity of 125 mg of HCTZ (working standard) and 400 mg of TELM (working standard) were dissolved in diluent [methanol and chloroform (1:1)] taken in 20 mL volumetric flask. The volume is made up to 20 mL with diluent to obtain a stock solution containing 6.250 and 20 mg/mL of HCTZ and TELM, respectively.

Preparation of standard solution: Approximately 40 mg of TELM and 12.5 mg of HCTZ were weighed and transferred to 20 mL volumetric flask. Then it is made up to volume with the diluent.

Preparation of sample solution: 20 Tablets are weighed and powdered. The powder equivalent to 40 mg of TELM and 12.5 mg of HCTZ (436 mg of powdered drug that is average weight) was transferred to 20 mL volumetric flask. The contents were dissolved in diluent and the volume is made up to the mark. The contents were mixed well using ultra-sonicator and filtered through Whatman filter paper number 42.

Estimation method: The sample was spotted on the chromplate with the help of Linomat IV spotting system. The chromatograms were recorded and the peak area for TELM and HCTZ were noted down. The amount of drug present was calculated by comparing the peak area values of sample with that of standard using the formula:

$$\text{Amount of drug in each tablet} = \frac{\text{Peak area of test} \times \text{conc. of std.} \times \text{std. purity} \times (100 - \text{LOD}) \times \text{average weight}}{\text{Peak area of std.} \times \text{conc. of test} \times 100 \times 100}$$

The results were tabulated in Table-1.

Validation[10,11]: To validate the developed method parameters *viz.*, linearity, range, system repeatability test, system suitability test, accuracy in terms of recovery, precision in terms of percentage and relative standard deviation were studied.

Linearity and range: The linearity of the method was assessed by performing single measurement at several analyte concentrations. A minimum of 5 concentrations were recommended for linearity studies. Varying quantities of standard stock solution was diluted with diluent to give a concentration of 500-750 µg/mL of HCTZ and 1600-2400 µg/mL of TELM. A calibration curve was constructed for each sample by plotting peak areas against concentration.

There exists a linear relationship in the range of 1600-2400 and 500-750 µg/mL for TELM and HCTZ, respectively. From the constructed curve coefficient of variance, slope and intercept were calculated. The results were tabulated in Table-3.

System repeatability: Three replicate applications to the HPTLC plate were performed for the standard solution containing 2000 µg/mL of TELM and 625 µg/mL of HCTZ. The results obtained by repeating the estimation procedure five times were observed to be good. Precision of the method is expressed in terms of percentage relative standard deviation of the data obtained, here in this case the peak area obtained. The relative standard deviation for these areas was calculated. The results were tabulated in Table-4.

System suitability parameters: System suitability parameters like resolution of peaks, tailing factor were also determined and tabulated in Table-5.

The accuracy of the developed method can be assessed by performing recovery studies. To ensure the reliability of the present method, recovery studies were carried out by mixing a known quantity of standard drug with the pre-analyzed sample formulation and the contents were reanalyzed by the proposed method. The results were presented in Table-6.

RESULTS AND DISCUSSION

The solvent system of the mobile phase having ethyl acetate:chloroform: methanol (10:3:1 v/v/v) offered maximum resolution for the two drugs at the wavelength of 270 nm at which both the drugs had optimum absorption.

The assayed values in terms of percentage label claim were found to be within the standard acceptable limits (Table-1) and so the method can be adopted for simultaneous estimation of telmisartan and hydrochlorothiazide in tablet formulation. The statistical validation was also done for the assayed values (Table-2).

TABLE-1
QUANTITATIVE ESTIMATION

Sample	Label claim* (mg)	Label claim (%)	Deviation (%)
TELM	40.0	98.95	-1.05
HCTZ	12.5	99.84	-0.16

TABLE-2
STATISTICAL DATA

Sample	Label claim (mg)	SD	RSD (%)	SE
TELM	40.0	0.4215	1.065	0.24
HCTZ	12.5	0.0950	0.760	0.44

SD = Standard deviation, RSD = Relative standard deviation,
SE = Standard error

Linearity studies were carried out and there exists linearity in the concentration range of 1600-2400 and 500-750 µg/mL for TELM and HCTZ, respectively (Table-3).

TABLE-3
LINEARITY

Parameter	Telmisartan	Hydrochlorothiazide
Linearity range	1.6-2.4 mg/mL	0.5-0.75 mg/mL
Regression (r)	0.9998	0.9999
Slope (m)	18.204	38.19
Intercept (c)	7.14	15.91

Lower percentage relative standard deviation of measurement indicates the precision of the developed method (Table-4).

TABLE-4
SYSTEM REPEATABILITY AND PRECISION

Parameter	Telmisartan	Hydrochlorothiazide
Concentration (µg/mL)	2000	650
Peak area*	36525.1	24066.2
Standard deviation	202.87	116.66
Relative standard deviation (%)	0.555	0.485

*Mean of five individual readings.

Resolution factor and tailing factor are ensuring proper functioning of HPTLC system (Table-5) thus making the method suitable.

The good average recovery values obtained in recovery studies indicate that the proposed method is accurate for estimation of drug in tablet formulation (Table-6).

TABLE-5
SYSTEM SUITABILITY

Parameter	Telmisartan	Hydrochlorothiazide
Resolution	1.95	1.95
Tailing factor	1.90	1.25

TABLE-6
RECOVERY STUDIES

Sample	Amount of drug added (mg)	Amount of drug recovered* (mg)	Recovery* (%)
TELM	4.00	3.79	99.61
HCTZ	1.25	1.18	99.49

Thus the developed method was found to be accurate, precise, suitable and cost effective for the simultaneous estimation of telmisartan and hydrochlorothiazide in tablet formulation.

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