

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF TELMISARTAN AND HYDROCHLOROTHIAZIDE IN TABLETS USING ORTHOGONAL POLYNOMIAL FUNCTION METHOD

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ABSTRACT

A simple, accurate and reproducible spectrophotometric method, requiring no prior separation, has been developed for simultaneous estimation of Telmisartan and Hydrochlorothiazide in combined tablet dosage form. The described method was applied for the determination of these combinations in synthetic mixtures and tablet dosage form. Contents of Telmisartan and Hydrochlorothiazide in the tablets were found to be 43.43 mg and 12.38 mg respectively against label claim 40mg of telmisartan and 12.5mg of hydrochlorothiazide. The linearity was validated by least square method. The recovery was within the limit of 98% to 102%.

Keywords: Simultaneous estimation, Telmisartan, Hydrochlorothiazide, Orthogonal polynomial function.

INTRODUCTION

Orthogonal polynomial function method is a mathematical model for the elimination of irrelevant absorption proposed by Glenn [1, 2] The method involves complex calculations to select the right combination of degree of polynomial, number of points in the spectrum, interval between the points. The optimization of these parameters can be simplified by using a soft-ware. So far two methods were reported using this proposed software [3, 4]. Telmisartan is chemically designated as 4'- [(1, 4'-dimethyl-2'-propyl [2, 6'-bi-1H-benzimidazol]-1'-yl) methyl] [1, 1'-biphenyl]-2-carboxylic acid. It is an angiotensin II type I blocker and is used as an antihypertensive along with Hydrochlorothiazide. 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. Chemically Hydrochlorothiazide is 6-chloro-3, 4-dihydro-2H-1, 2, 4-benzothiazine-7sulfonamide 1, 1-dioxide. The combination of Hydrochlorothiazide and Telmisartan is useful in treatment of mild to moderate hypertension, and is well tolerated with a lower incidence of cough than ACE inhibitors. The combination of TEL and HYD is available as tablet dosage form. The Literature survey revealed that TEL is not yet official in any pharmacoopia. Several analytical methods have been reported for the determination of TEL in biological fluids [5-8] and formulations includes LCMS [5], HPLC [8,9], electrophoretic [10], polarography [11] and fluorometric methods [12]. Few analytical methods were reported for determination of TEL and HYD in combination which includes HPLC [13,14,15], HPTLC [16], TLC-densitometric [12] and derivative spectrophotometry [12]

MATERIALS AND METHODS

Telmisartan was provided by the courtesy of orchid chemicals ltd, Chennai and Hydrochlorothiazide was provided by the courtesy of Cassel Research Laboratories, Chennai as gift samples. Methanol (AR-grade) was procured from S.D. Fine Chemicals Ltd., Mumbai. The spectra were recorded in UV spectrophotometer (Shimadzu, UV 1601 PC, Japan).

25 mg of telmisartan and Hydrochlorothiazide were weighed in separate 25mL volumetric flask and made up to 25mL with methanol and further dilutions were made with distilled water to get 10 µg mL⁻¹ and UV spectra of 10 µg mL⁻¹ solution of Telmisartan and 10 µg mL⁻¹ solution of Hydrochlorothiazide were recorded from 350 to 200 nm (fig.1) and stored in ASCII format. From these spectral data, 112 convoluted graphs each for Telmisartan and Hydrochlorothiazide were obtained using the software developed in a previous study [3]. Convoluted graph of telmisartan were compared with that of corresponding hydrochlorothiazide and the optimum conditions for orthogonal polynomial function method were selected and given in (Table 1) taking following points into consideration, i) the coefficient value is negligible for one drug and as high as possible for the other and ii) as far as possible the wavelength range where there was steep rise in coefficient value of either drug was avoided.

Determination of polynomial function (P) (1 %, 1 cm)

Coefficient of polynomial is directly proportional to the concentration of analyte and it can be calculated by using equation 1 for Hydrochlorothiazide and equation 2 for Telmisartan where the factors are those of 6 point quadratic polynomials obtained from the text of numerical analysis [14].

Table 1: optimized parameters for orthogonal polynomial function method of analysis

Drug	Degree of polynomial	Number of points	Wavelength (nm)
Telmisartan	Quadratic	6	301, 303, 305, 307, 309 and 311
Hydrochlorothiazide	Quadratic	6	279.5, 281.5, 283.5, 285.5, 287.5 and 289.5

$$P_{HYD} = 5(A_{279.5}) - 1(A_{281.5}) - 4(A_{283.5}) - 4(A_{285.5}) - 1(A_{287.5}) + 5(A_{289.5}) \text{ ----- (1)}$$

$$P_{TEL} = 5(A_{301}) - 1(A_{303}) - 4(A_{305}) - 4(A_{307}) - 1(A_{309}) + 5(A_{311}) \text{ ----- (2)}$$

Where, P_{HYD} and P_{TEL} are coefficients of polynomial of telmisartan and hydrochlorothiazide, respectively and A is absorbance at respective wavelength. The P (1 %, 1 cm) is a constant which represents the coefficient corresponding to the absorbance of 1% solution kept in 1cm cell which can be used for the calculation of

concentration of sample similar to the use of A (1 %, 1 cm) in conventional spectrophotometry. Coefficient values corresponding to the absorbance values of 10 µg mL⁻¹ solution of Telmisartan or Hydrochlorothiazide were calculated as above and from this the P (1 %, 1 cm) value was calculated.

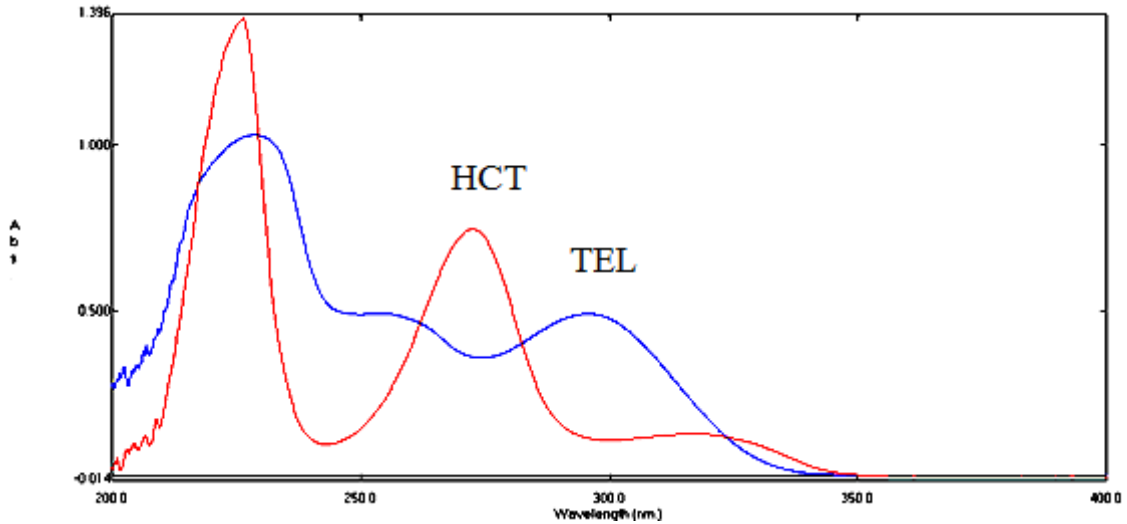


Fig. 1: Spectral character of TEL and HYD in methanol

Table 2: Shows Analysis of tablet formulation for telmisartan and hydrochlorothiazide

Telmisartan content		Hydrochlorothiazide content	
mg/tab	Label claim (%)	mg/tab	Label claim (%)
43.96	109.09	12.45	99.06
43.45	108.75	12.29	98.32
42.23	105.57	12.57	100.56
43.61	109.02	12.34	98.72
43.92	109.08	12.24	97.92
Mean	108.46	Mean	98.91
SD	± 0.7059	SD	± 0.1325
%RSD	± 1.07	%RSD	± 1.62

Label claim: Each tablet contains 40 mg of Telmisartan and 12.5 mg Hydrochlorothiazide

Analysis of tablet formulation

A total number of 20 tablets weighed and powdered by a mortar and pestle. Quantities of the powder equivalent to 40mg TEL and 12.5mg of HCT were accurately weighed and transferred to 25ml volumetric flask. Weighed tablet powder was dissolved in methanol and ultrasonicated for 5min. Then the volume made upto 25ml of methanol and mix well. Solution obtained was filtered through Whatmann filter paper no.42. Transfer 1ml of solution to 100ml volumetric flask, made up with distilled water. The concentration of TEL and HCT were calculated using simultaneous estimation method. The solution was scanned between 350 and 200 nm in UV visible spectrophotometer (Table 2).

RESULTS AND DISCUSSION

Telmisartan exhibit maximum absorbance at 306 nm in distilled water with methanol used initially to dissolve the drug. Hydrochlorothiazide exhibit maximum absorbance at 284.50 nm in distilled water with methanol used initially to dissolve the drug. These spectral characters make this an ideal combination

for orthogonal polynomial function method of analysis and estimation of both drugs without separation of each other. The optimum analytical conditions were arrived at by using the software custom developed for the purpose. When the software was executed the user will enter the UV data file name, the degree of polynomial, number of wavelengths and interval between the wavelengths. When these information's are provided, the spectral file name is opened, the wavelengths are chosen starting from the first wavelength of the spectrum and the average is calculated.

The corresponding absorbance values are substituted in the respective equations [17] to calculate the coefficient of polynomial for the selected wavelength region. The process is repeated successively to cover the entire spectra. The output can be used for construction of convoluted graph. Comparing the convoluted graph of Telmisartan with that of corresponding convoluted graph of Hydrochlorothiazide the optimum condition was arrived and given in Table 1. The convoluted graph for the optimized conditions for the estimation of Telmisartan and Hydrochlorothiazide are given in (Fig.2)

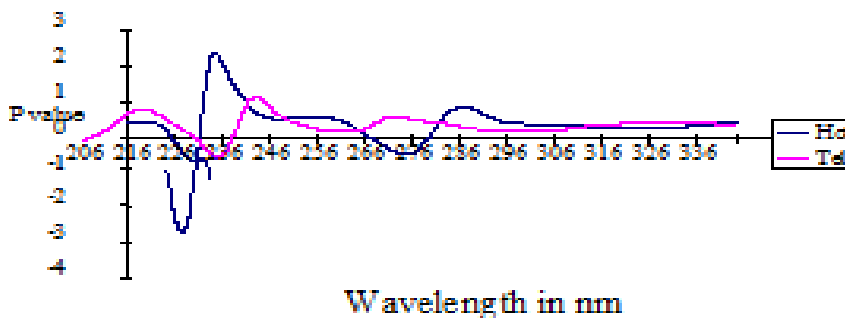


Fig. 2: Convoluted graph for HYD and TEL

CONCLUSION

Thus the proposed UV method for the simultaneous determination of telmisartan and hydrochlorothiazide in tablet dosage form was accurate, precise, linear, reliable, simple, and economic.

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