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VALIDATED HPTLC METHOD FOR THE ESTIMATION OF ANTIHYPERTENSIVE DRUGS IN PHARMACEUTICAL COMBINED DOSAGE FORMS

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ABSTRACT

A new, rapid, precise, accurate and specific chromatographic methods for the simultaneous determination of Telmisartan and Atorvastatin in combined pharmaceutical dosage forms by utilizing silica gel 60F254 high performance thin layer chromatography and densitometric detection at 291nm using chloroform : methanol(90:10) as the mobile phase

KEYWORDS Telmisartan; Atorvastatin; high performance thin layer chromatography.

INTRODUCTION

Telmisartan, chemically it is 4[(1, 4-dimethyl-2-pyl (2, 6-bi-1H-benzimidazol]-1-yl) methyl] [1, 1-biphenyl]-2-carboxylic acid[1]. Atorvastatin is (βR,dR)-2-(4-fluorophenyl)-β,d-dihydroxy-1-methylethyl)-3-phenyl-4[(phenylamino) carbonyl]-lH-pyrrole-1-tanoic acid, calcium salt, is a synthetic cholesterol-lowering agent[2] .Telmisartan and Atorvastatin are introduced into the market in combined dosage form, which is widely used in the treatment of hypertension. Literature review reveals that the methods for Telmisartan and Atorvastatin alone or in combined dosage forms are RP-HPLC Method for Estimation of Telmisartan in Tablet dosage form [3.] Rekha Gangola, Sunil Kaushik, Paras Sharma. Spectrophotometric Simultaneous determination of Hydrochlorothiazide and Telmisartan in Combined Dosage Form [4]. RP-HPLC Method for Simultaneous Estimation of Telmisartan & Amlodipine in Tablet Dosage Forms[5]. Stability-indicating high-performance liquid chromatographic assay of atorvastatin with fluorescence detection[6].Stability-indicating reversed-phase liquid chromatographic method for simultaneous determination of atorvastatin and ezetimibe from their combination drug products[7]. Simultaneous quantitative resolution of atorvastatin calcium and fenofibrate in pharmaceutical preparation by using derivative ratio spectrophotometry and chemometric calibrations[8]. Stability indicating RP-HPLC method for simultaneous determination of atorvastatin and amlodipine from their combination drug products[9] .Development of UV Spectrophotometric method for the simultaneous estimation of olmesartan Medoxomil and atorvastatin calcium in tablet by simultaneous equation and first order derivative method[10]. RP-HPLC method for the determination of Atorvastatin Calcium and Nicotinic acid in combined tablet dosage form[11].Development and Validation of an RP-HPLC method for the determination of Atorvastatin Calcium and Aspirin in capsule dosage form[12]. Development and Validation of method for simultaneous densitometric estimation of Atorvastatin Calcium and Ezetimibe as the bulk drug and in tablet dosage form[13] .

EXPERIMENTAL

Apparatus

Samples were applied as 8 mm bands by means of a Camag Linomat V automatic samples applicator (Muttenz Switzerland) equipped with a 100 µL syringe. The distance between the bands was 11.4 mm. Silica gel 60 F_{254} HPTLC plates (20×10 cm, aluminium) were from Merck (Darmstadt, Germany). Densitometric scanning was performed at 291nm with a camag TLC scanner 3 equipped with camag Wincats software 1.42 using the deuterium light source and slit dimensions of 4.00 mm × 0.30 mm.

Chemicals

Telmisartan & Atorvastatin reference standards was supplied by M/s Microlabs limited, Bangalore**,**India. HPLC grade chlororm, methanol was purchased from Merck (Mumbai, India). All chemicals were of analytical grade. Commercially available tablets (Telday-AV of Torrent, Gujarat, India), containing 40 mg Telmisartan and 10 mg Atorvastatin per tablet, were used for analysis. Standard solutions (0.1 mg mL-1) were prepared in methanol.

Chromatographic conditions

Chromatography was performed on 20 × 10 cm aluminum HPTLC plates coated with 0.2 mm layers of silica gel 60 F_{254} (Merck). Before use plates were washed with methanol and dried in an oven at 120°C for 20 min. ascending development of the plate with a migration distance of 50 mm was performed at 23± 2°C using chloroform: methanol (90:10 v/v) as the mobile phase and a Camag twin-trough chamber previously saturated with mobile phase for 20 min. the average development time was 5 minutes.

Calibration

Mixed working standard solutions equivalent to 4, 6, 8, 10, 12, 14, 16 µL were separately stopped on the TLC plate in order to obtain final concentrations at 400, 600,800,1000,1200,1400,1600 ng $spot^{-1}$ for both drugs respectively. The plates were developed in a 20 × 10 cm twin through chamber using 20 mL freshly prepared mobile phase.

Analysis of Tablet Formulation

The tablets were weighed, triturated and the average weight was calculated. A 0.1 mg/mL solution was prepared in methanol and filtered through Whatman filter paper no. 41. The above stock was diluted in the ratio of 1:00 with methanol which was used as the working standard solution. The 8µL solution was spotted on the HPTLC plate and the concentrations were calculated from the calibration graph.

Recovery study

The accuracy of the proposed method was evaluated by the addition of a standard drug solution at three different concentration levels at 50, 100, and 150% of linearity for both drugs.

RESULTS AND DISCUSSION

A number of experimental parameters, such as mobile phase composition, scan modes and detection wavelengths, were optimized during method development in order to provide accurate, precise and reproducible results for the simultaneous determination of OML and HCT. Maximum separation was achieved (Atorvastatin Rf 0.24, Telmisartan Rf 0.64) and minimum tailing were obtained when using a mobile phase composition of chloroform: methanol (90:10 v/v) respectively (Fig. 1). Table 1 shows that correlation coefficients were 0.998 for OML and 0.998 for HCT. The LOD values were 100 ng spot -1and 50 ng spot -1, while LOQ values were 300 ng spot -1and 150 ng spot -1for both Atorvastatin and Telmisartan respectively. The proposed method was used for the determination of both drugs in tablets and results are also shown in Table 2. Good recoveries and standard deviations were observed.

CONCLUSION

A method was developed for the determination of tablets which is simple, quick, reliable, inexpensive and simple. The results indicate that the described method can be used for quantitative analysis of the compound.

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Parameter	HPTLC	
	Telmisartan	Atorvastatin
Linearity range	400-1600 ng/ml	400-1200 ng/ml
Regression equation		
Slope	3.36	4.861
Intercept	3291	1107
Coefficient of correlation	0.998	0.998
Limit of detection (LOD)	50 ng/ml	100 ng/ml
Limit of quantitation (LOQ)	300 ng/ml	150 ng/ml

Table 1.Calibration graphs of Telmisartan and Atorvastatin

Brand name	**Compound**	**% Assay**	**% recovery**
HPTLC	Telmisartan	99.90	100.5
	Atorvastatin	99.18	99.6

Table 2: Assay and Recovery studies of Olmesartan & Hydrochlorothiazide

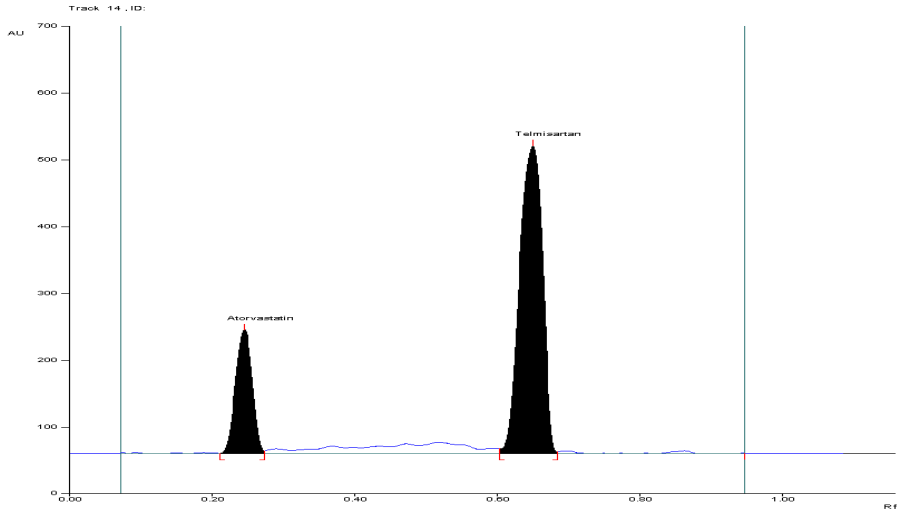

Figure 1: HPTLC Sample chromatogram for Telmisartan and Atorvastatin

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