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SIMULTANEOUS ESTIMATION AND VALIDATION OF TAMSULOSIN AND DEUTASTERIDE IN BULK AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

The new precise, simple, accurate RP HPLC method for the simultaneous estimation of Tamsulosin Hydrochloride and Dutasteride in pharmaceutical dosage form. Solubility determination of Tamsulosin Hydrochloride and Dutasteride in various solvents and buffers. Determine the absorption maxima of both the drugs in UV-Visible region in different solvents/buffers and selecting the solvents for HPLC method development. Optimize the mobile phase and flow rates for proper resolution and retention times. Validate the developed method as per ICH guidelines. A simple and selective LC method is described for the determination of Tamsulosin Hydrochloride and Dutasteride tablet dosage forms. Chromatographic separation was achieved on a C_{18} column using mobile phase consisting of a mixture of Phosphate buffer (KH2PO4) pH:3.5: Acetonitrile: Methanol (40:30:30v/v), with detection of 223 nm. Linearity was observed in the range 19.2-44.8 µg /ml for Tamsulosin Hydrochloride (r^2 =0.9961) and 24-56µg /ml for Dutasteride (r^2 =0.9981) for the amount of drugs estimated by the proposed methods was in good agreement with the label claim. From the above experimental results and parameters it was concluded that, this newly developed method for the simultaneous estimation of Tamsulosin Hydrochloride and Dutasteride was found to be simple, precise, accurate and high resolution and shorter retention time makes this method more acceptable and cost effective and it can be effectively applied for routine analysis.

KEYWORDS

RP-HPLC, Acetonitrile, Methanol, Ammonium acetate buffer pH3.5, C18 column and 223nm.

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INTRODUCTION

Tamsulosin is a selective antagonist at alpha-1A and alpha-1B-adrenoceptors in the prostate, prostatic capsule, prostatic urethra and bladder neck. At least three discrete alpha1-adrenoceptor subtypes have been identified: alpha-1A, alpha-1B and alpha-1D; their distribution differs between human organs and tissue. Approximately 70% of the alpha1-receptors in human prostate are of the alpha-1A subtype. Blockage of these receptors causes relaxation of

smooth muscles in the bladder neck and prostate. Dutasteride belongs to a class of drugs called 5-alpha-reductase inhibitors, which block the action of the 5-alpha-reductase enzymes that convert testosterone into dihydrotestosterone (DHT). The combination of dutasteride and tamsulosin is used to treat benign prostatic hyperplasia (BPH) in men with an enlarged prostate. A new method is developed for the simultaneous estimation and validation of tamsulosin and dutasteride[1-6].

MATERIAL AND METHOD

Instruments used

UV-spectrophotometer Nicolet evolution100, HPLC shimadzu (LC AT VP), HPLC agilent1200 series, ultrasonicator citizen digital ultrasonic cleaner, pH meter global digital, electronic balance shimadzu, syringe Hamilton, HPLC column kromosilC18 column ((250×4.6mm× 5µ).

Reagents and Materials

Water: HPLC grade, sodium hydrogen orthophosphate: AR grade, Methanol: HPLC grade, potassium dihydrogen orthophosphate: AR grade, Acetonitrile; HPLC grade, ammonium acetate; AR grade, tetra hydro furan: AR grade.

Drugs used

Tamsulosin hydrochloride and deutasteride bulk drug gift samples were obtained from Chandra labs, hyd, veltam plus (0.4+0.5) (tamsulosin 0.4mg and deutasteride 0.5mg label claims), manufactured by arron (intas pharmaceuticals ltd) India which is obtained from local pharmacy.

Mobile Phase

A mixture of 40 volumes of 20mM Ammonium acetate buffer pH 3.5: 30 volumes of Acetonitrile: 30 volumes of Methanol. The mobile phase was sonicated for 10 min to remove gases.

Preparation of Ammonium acetate buffer (20mM)

0.15416 gm of Ammonium acetate was weighed and dissolved in 100ml of water and volume was made up to 100ml with water. Adjust the pH to 3.5 using ortho phosphoric acid. The buffer was filtered through 0.45µ filters to remove all fine particles and gases.

METHOD

Weigh accurately 40 mg of Tamsulosin Hydrochloride and 32 mg of Dutasteride in 100 ml of volumetric flask and dissolve in 10ml of mobile phase and make up the volume with mobile phase. From above stock solution 40 µg/ml of Tamsulosin Hydrochloride and 32 µg/ml of Dutasteride is prepared by diluting 5ml to 50ml with mobile phase. This solution is used for recording chromatogram. And the chromatographic conditions are mobile phase as ammonium acetate buffer: acetonitrile: methanol in the ratios 40:30:30 and kromosil C18 column (250×4.6mm× 5µ) and wavelength at 223nm and the buffer pH 3.5. And the chromatogram was shown in the Figure No.1-2 and the efficiency and the retention time are satisfactory.

METHOD VALIDATION

System suitability

Standard solutions were prepared as per the test method and injected into the chromatographic system. The system suitability parameters like theoretical plates, resolution and asymmetric factor were evaluated.

Linearity and range

Standard stock solutions were prepared by dissolving 40 mg of Tamsulosin Hydrochloride and 32 mg of Dutasteride dissolved in sufficient mobile phase. After that filtered the solution using 0.45-micron syringe filter and Sonicated for 5min and dilutions were made, five injections were taken for each drug and noted down the concentrations and areas and the linearity graphs were plotted shown in Figure No.3 and 4.

Accuracy

To check the accuracy of the method, recovery studies were carried out by addition of standard drug solution to pre-analyzed sample solution at three different levels 80%, 100%, 120%. The percentage recovery and mean recovery are estimated (Table No.1).

Method precision

Prepared sample preparations of Tamsulosin Hydrochloride and Dutasteride as per test method

and injected 6 times in to the column. The % RSD is estimated (Table No.1).

Limit of Detection

$$LOD = \frac{3.3\sigma}{S}$$

Where, σ = the standard deviation of the response, S = the slope of the calibration curve. The slope S may be estimated from the calibration curve of the analyte. It is separately estimated for both the drugs.

Limit of Quantification

$$LOQ = \frac{10\sigma}{S}$$

Where, σ = the standard deviation of the response, S = the slope of the calibration curve

Robustness

Robustness of the method, prepared solution as per test method and injected at different variable conditions like using different conditions like Temperature and wavelength.

Ruggedness

Ruggedness can be defined as the difference between analyst to analyst.

RESULTS AND DISCUSSION

A simple and selective LC method is described for the determination of tamsulosin hydrochloride and dutasteride tablet dosage forms. The proposed methods were validated. The accuracy of the methods was assessed by recovery studies at three different levels. The method was found to be precise as indicated by the repeatability analysis, showing % RSD less than 2. All statistical data proves validity of the methods and can be used for routine analysis of pharmaceutical dosage form (Table No.3 and 4).

Table No.1: Accuracy, Percentage recovery and Average % recovery of Tamsulosin hydrochloride

S.No	Recovery level	Accuracy Tamsulosin Hydrochloride					Average% Recovery
		Amount taken (mcg/ml)	Area	Average area	Amount recovered (mcg/ml)	% Recovery	
1	80 %	32	1245.776	1243.999	32.11	100.34	100.23 %
		32	1242.478				
		32	1243.744				
2	100 %	38.4	1585.507	1588.772	37.88	98.65	
		38.4	1592.771				
		38.4	1588.039				
3	120 %	44.8	1806.204	1863.448	45.57	101.72	
		44.8	1891.924				
		44.8	1892.215				

Table No.2: % Recovery of Dutasteride

S.No	Recovery level	Accuracy Dutasteride				
		Amount taken (mcg/ml)	Area	Average area	Amount recovered (mcg/ml)	% Recovery
1	80%	40	1225.647	1209.380	39.29	98.23
		40	1195.931			
		40	1206.561			
2	100%	48	1534.413	1529.259	47.65	99.26
		48	1527.826			
		48	1525.537			
3	120%	56	1795.856	1802.554	56.52	100.92

Table No.3: Assay results of Tamsulosin and Dutasteride

S.No	Parameters	Standard Area	Sample Area	Standard Area	Sample Area
1	Injection-1	1218.293	1229.507	1183.851	1216.259
2	Injection-2	1248.324	1246.813	1228.600	1215.705
3	Injection-3	1289.749	1236.109	1270.837	1215.781
4	Injection-4	1222.300	1228.810	1175.298	1196.616
5	Injection-5	1221.445	1241.937	1198.939	1204.885
6	Average Area	1240.022	1236.635	1211.505	1209.849
7	Tablet average weight	3.5		3.5	
8	Standard weight	32		40	
9	Sample weight	280		280	
10	Label amount	0.4		0.5	
11	std. purity	99.2		99.3	
12	Amount found in mg	0.40		0.50	
13	Assay (% purity)	98.93		99.16	

Table No.4: Result of Tamsulosin and Dutasteride using mobile phase

S.No	Name	Rt (min)	Peak Area	Asymmetry	Efficiency	Resolution
1	Tamsulosin Hydrochloride	2.653	1223.618	1.195	2813	-
2	Dutasteride	4.693	1191.699	1.241	3021	6.925

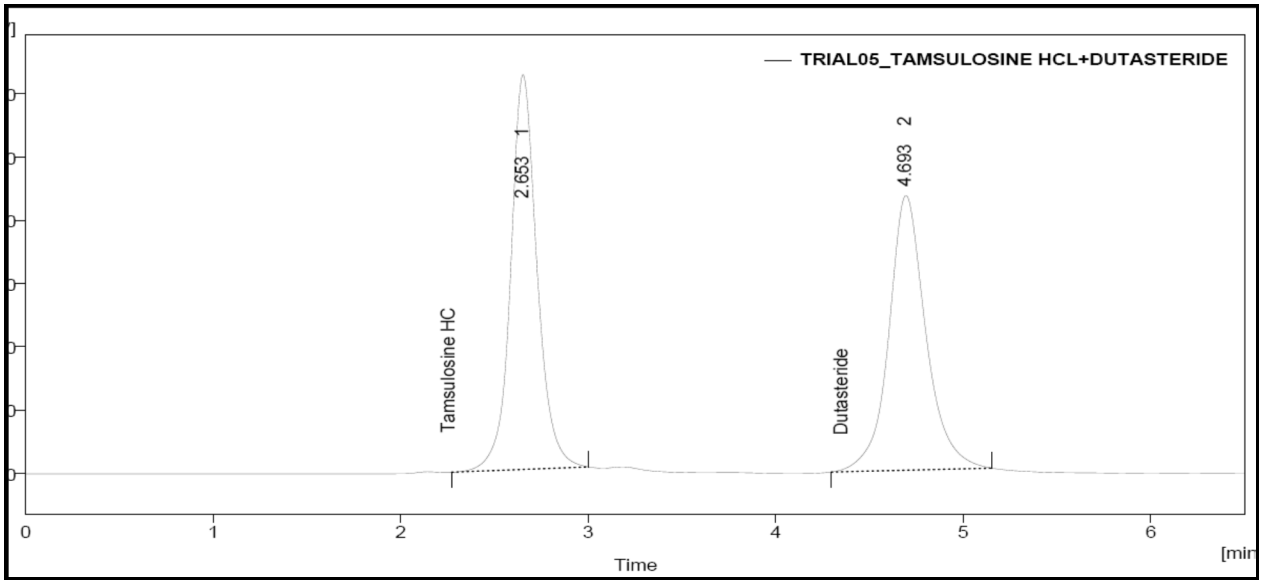

Figure No.1: Chromatogram of Tamsulosin and Dutasteride using mobile phase

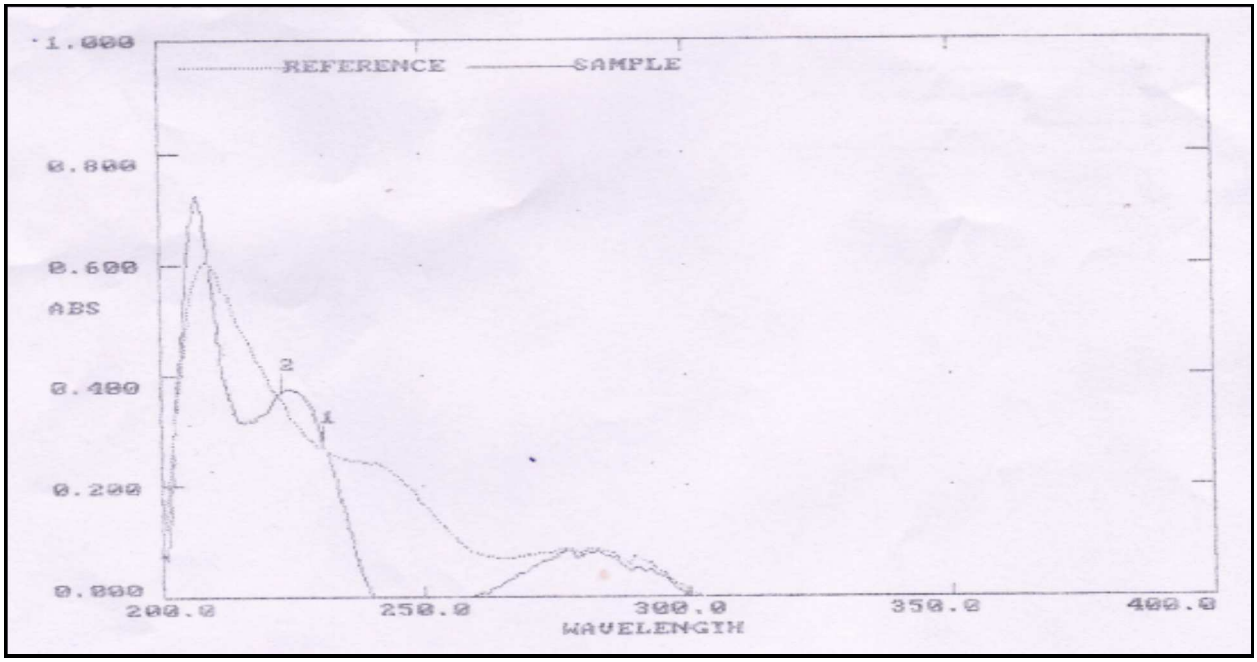

Figure No.2: UV-Visible spectrum of Tamsulosin and Dutasteride isobestic point

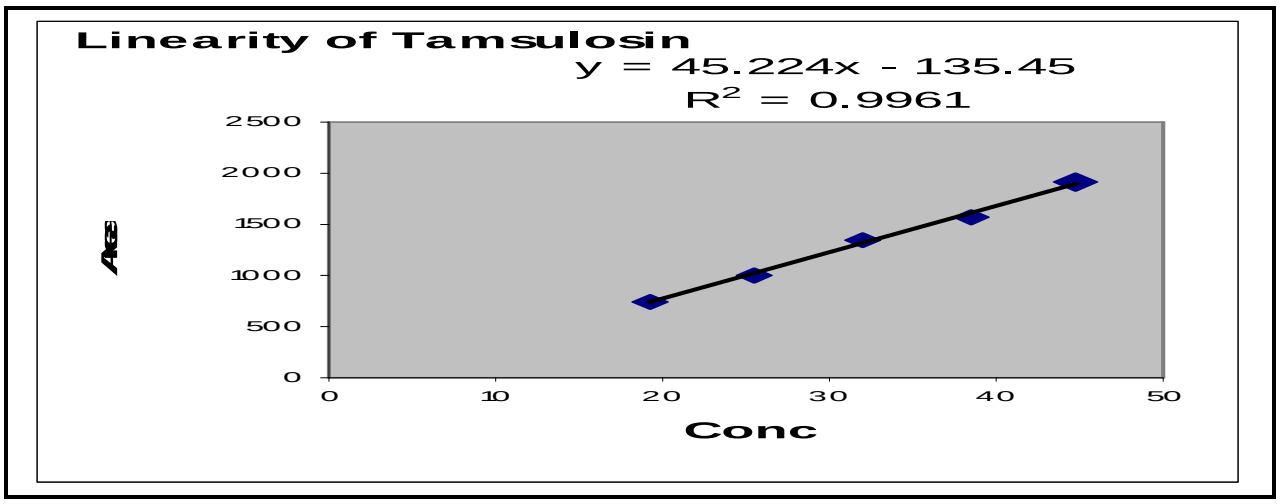

Figure No.3: Linearity of Tamsulosin

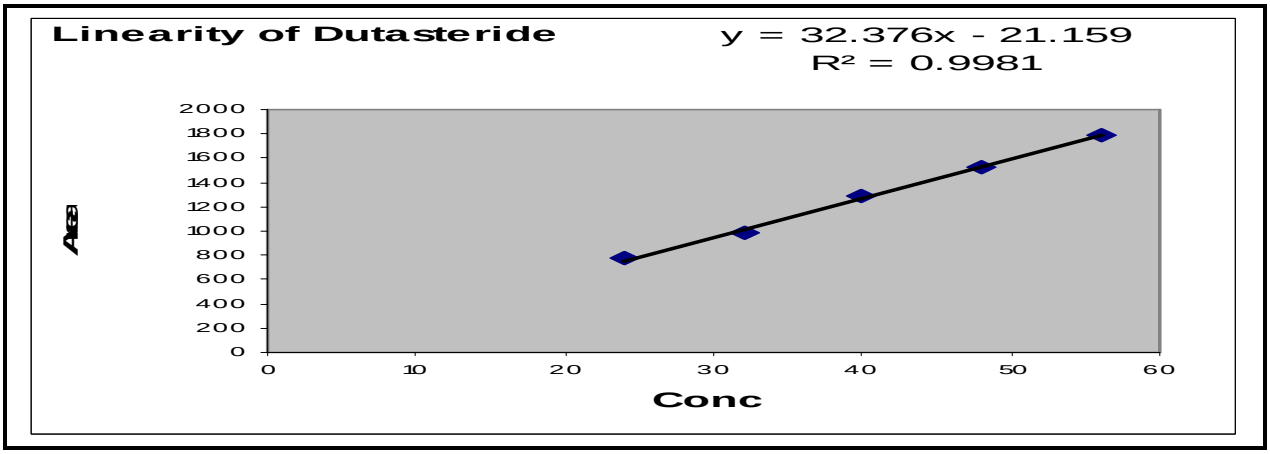

Figure No.4: Linearity of Dutasteride

CONCLUSION

From the above experimental results and parameters it was concluded that, this newly developed method for the simultaneous estimation of Tamsulosin Hydrochloride and Dutasteride was found to be simple, precise, accurate and high resolution and shorter retention time makes this method more acceptable and cost effective and it can be effectively applied for routine analysis in research institutions, quality control department in meant in industries, approved testing laboratories, bio-pharmaceutical and bio-equivalence studies and in clinical pharmacokinetic studies in near future.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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