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Analytical Method Development & Validation Protocol For Trospium Chloride In Tablet Dosage Form

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Abstract— Trospium Chloride is an antispasmodic, antimuscarinic agent. It is used in the treatment of overactive bladder with urge incontinence. It is also used as anticholinergic compound. It acts as a direct antagonist at muscarinic acetylcholine receptors in cholinergically innervated organs. It appears as white crystalline powder. It is very soluble in water, freely soluble in methanol and practically insoluble in methylene chloride. A simple spectrophotometric method was developed for the determination of Trospium Chloride in pharmaceutical tablet dosage form. Trospium Chloride exhibiting λ max at 224 nm in mobile phase (0.1 N HCl) and obeyed linearity in the concentration range of 10 – 60 mcg. The proposed method was statistically validated.

Keywords : Trospium Chloride, Analytical Method Development, Validation Protocol.

INTRODUCTION

The scope of developing and validating analytical method is to ensure a suitable method for a particular analyte more specific, accurate and precise the main objective for that is to improve the condition and parameter, which should be followed in the development and validation [1,2]. Trospium Chloride is an antispasmodic, antimuscarinic agent. It is used in the treatment of overactive bladder with urge incontinence. It is also used as anticholinergic compound. It acts as a direct antagonist at muscarinic acetylcholine receptors in cholinergically innervated organs [3]

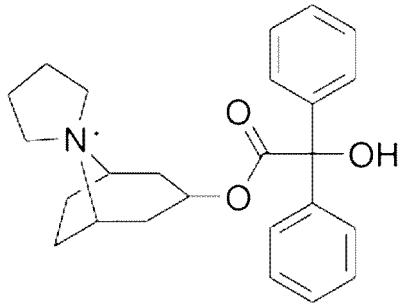

Fig.1. Spiro[8-azoniabicyclo[3,2,1]octane-8,1'-pyrrolidinium]-3- [(hydroxyldiphenyl-acetyl)-oxy]chloride(1α, 3β, 5α)-(9Cl).

Tablet formulation containing 20 mg Trospium Chloride conventional form is available in the market. Literature survey revealed that various analytical methods such as TLC, liquid chromatography, fluorimetric method, are used for estimation of Trospium Chloride [4, 5]. No simplest UV-Spectrophotometric method has been reported for estimation of Trospium Chloridein tablet dosage form. Hence, an attempt has been made to develop new spectrophotometry method for its estimation in pharmaceutical tablet dosage form with good accuracy, simplicity, and precision. In UV-Spectrophotometric method UV spectrum is set in 224 nm and blank is placed in the cuvettes, after setting zero transmittance the sample is placed in another cuvette for measuring the absorbance the sample.

MATERIALS AND METHODS

Absorbance measurements were made on LABINDIA, UV 3000^{+}Spectrophotometer. ConTECH-CA 123balance was used for weighing the sample. Commercially available tablets of the Trospium Chloride were procured from the local market and estimated.

Preparation of standard stock solution

Accurately weighed quantity of Trospium chloride 100 mg was transferred into 100 ml volumetric flask, dissolved and diluted up to mark with 0.1 N HCl to obtained 1000 µg/ml.

Preparation of working standard solution

10 µg/ml of Trospium chloride solution was prepared by diluting 10 ml of stock solution with 0.1 N HCl in 10 ml volumetric flask up to the mark.

Procedure for determination of wavelength of maximum absorbance

Working standard solution of Trospium Chloride was scanned between 200-300 nm on Shimadzu double beam UV visible spectrophotometer against 0.1 N HCl as blank. A wavelength maximum exhibited for Trospium Chloride was at 224 nm.

Construction of Calibration curve

Aliquot of the standard stock solution (0.1, 0.2, 0.3, 0.4, 0.5, 0.6 ml) was transferred into a series of volumetric flask (10 ml) and volume was adjusted up to the mark with 0.1 N HCl to get desired concentration (10 – 60 µg/ml). The absorbance of the prepared solutions was measured at 224 nm against 0.1 N HCl. [6]

VALIDATION [7, 8-12]

Assay: The assay of the proposed method was ascertained by performing assay of the standard drug with reference to the sample drug and finding out the absorbance. From the absorbance percentage purity was calculated. The readings are shown in **table 1**.

Table 1: Assay of Trospium Chloride Tablet

	Claim of tablet (mg/tablet)	*Drug found (mg/tablet)*	*%Purity*
TROZYD tab (20mg)	*20*	*20.2*	*101.00%*

RESULTS & DISCUSSION

Linearity: To establish linearity of the proposed methods, six separate series of solutions of Trospium Chloride (10-60 mcg) in mobile phase (0.1 N HCl) were prepared from the stock solutions and analyzed. Least square regression analysis was performed on the obtained data. Linearity data are shown in **table 2 & 3** as follows:

Table 2: Linearity Table of Trospium Chloride in Working Standard

Concentration (mcg)	*Absorbance*
10	*0.166*
20	*0.3182*
30	*0.436*
40	*0.5748*
50	*0.719*
60	*0.839*

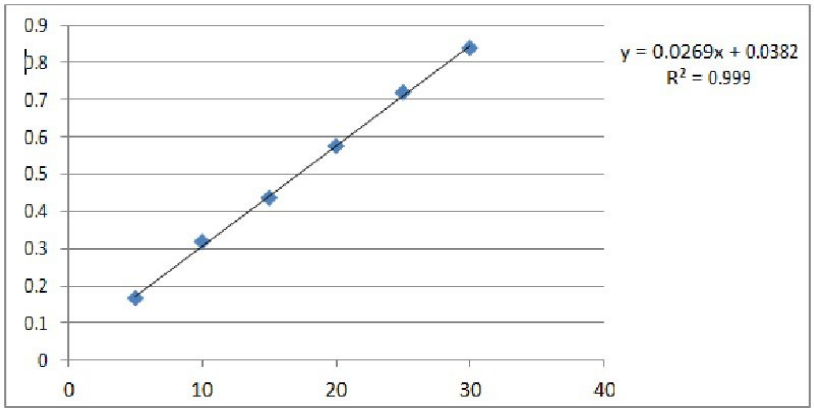

Fig. 3: Linearity Curve of Trospium Chloride in Working Standard

Table 3: Linearity Curve Data

Beer's law limit (mcg)	*10-60*
Correlation coefficient (R^2)	*0.999*
Regression equation (y⋆)	*y = 0.0269x + 0.0382*
Slope (m)	*0.029*
Y-Intercept(c)	*0.156*

PRECISION

Repeatability

Percentage R.S.D. was found between 0.3454678- 0.97524193%.

Percentage R.S.D. is less than 1 %, it proves that UV-Visible spectrophotometer gives precise results.

Table 4 : Repeatability data of Trospium Chloride

Concentration (µg/ml)	***% R.S.D.(n = 3)***
20	*0.34546788*
20	
20	
30	*0.46585937*
30	
30	
40	*0.97524193*
40	
40	

INTRADAY PRECISION

Percentage R.S.D for intraday precision was found between 0.15 - 0.36 %.

Percentage R.S.D. is less than3 %, it prooves that method is precise.

INTERDAY PRECISION

Percentage R.S.D. for interday precision was found between 0.46 – 2.02%.

Percentage R.S.D. is less than 5 %, it proves that method is precise

Table 5: Intraday and Interday precision of Trospium Chloride

Concentration (µg/ml)	*INTRADAY (n =5) % R.S.D.*	*INTERDAY (n =5) %R.S.D.*
10	*1.45*	*1.86*
20	*1.02*	*2.03*
30	*0.45*	*0.46*
40	*0.32*	*1.18*
50	*0.08*	*1.15*
60	*0.07*	*2.02*

Table 6: Accuracy data of Trospium Chloride

Amount of Trospium Chloride in sample (µg)	*Amt of std Trospium Chloride added (µg)*	*Total amount of Lornoxicam*	*Amount of Trospium Chloride found*	*% Recovery (n = 3)*	*Mean % recovery*
50	-	*50*	*50.61*	*101.22*	*100.97*
50	-	*50*	*50.24*	*100.48*	
50	-	*50*	*50.61*	*101.22*	
50	*10*	*60*	*61.14*	*101.90*	*101.38*
50	*10*	*60*	*60.77*	*101.28*	
50	*10*	*60*	*60.58*	*100.97*	
50	*30*	*80*	*80.90*	*101.25*	*101.29*
50	*30*	*80*	*80.90*	*101.25*	
50	*30*	*80*	*81.09*	*101.36*	
50	*50*	*100*	*101.22*	*101.22*	*100.91*
50	*50*	*100*	*100.66*	*100.66*	
50	*50*	*100*	*100.85*	*100.85*	

ACCURACY: To determine the accuracy of the proposed method, recovery studies were carried out by adding different amounts of standard bulk sample of Trospium Chloridewith in the linearity range were taken and added to the pre-analyzed formulation of concentration 5 mcg and percentage recovery values are calculated (**Table 6**).

Mean percentage recovery was found between 100.91 – 101.38 %.%.

Mean percentage recovery is between 98 – 102 %, it proves that method is accurate.

RUGGEDNESS

The data for ruggedness obtained from two different analysts is presented in Table 7.

Percentage R.S.D. was found between 0.48 - 1.79 %.

Percentage R.S.D. is less than2 %, it proves that method is rugged.

Table 7: Ruggedness data of Trospium Chloride

Concentration (µg/ml)	***% R.S.D. (n = 2)***
50	*0.74*
60	*1.01*
70	*0.48*
80	*1.79*
90	*1.45*
100	*1.73*

TABLE 8: Summary of validation parameter

PARAMETER	***RESULTS OFLORNOXICAM***
Linearity range (µg/ml)	*10-60*
Correlation coefficient, r	*0.999*
Precision (% R.S.D.) *Repeatability Intraday (n=5)* *Interday (n=5)*	*0.34-0.97* *0.07-1.45* *1.15 -1.86*
Ruggedness (% R.S.D.)	*0.48 – 1.79*
Mean % recovery	*100.38 – 101.48 %.*

CONCLUSION

The proposed method was simple and reliable with good precision, accuracy, linearity and ruggedness. The proposed method is specific while estimating the commercial formulations without interference of the excipients and other additives. Hence, this method can be used for the routine determination of Trospium Chloride in pure and pharmaceutical formulation.

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