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Research Article

ESTIMATION OF PRAMIPEXOLEDI HYDROCHLORIDE IN BULK AND TABLET DOSAGE FORM USING AREA UNDER CURVE METHOD

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ABSTRACT

A simple, rapid, accurate and economical UV-Spectrophotometric method has been developed for estimation of pramipexole dihydrochloride from bulk and pharmaceutical formulation. The λmax of pramipexole dihydrochloride in water was found to be 261 nm. The drug follows linearity in the concentration range 10-35μg/ml with correlation coefficient value 0.989. The proposed method was applied to pharmaceutical formulation and % amount of drug estimated 98.05%–100.77%was found in good agreement with the label claim. The accuracy of the method was checked by recovery experiment performed at three different levels i.e., 80%, 100% and 120 %. The % recovery was found to be in the range 99.10% – 100.90%. The low values of % RSD are indicative of the accuracy and reproducibility of the method. The precision of the method was studied as an intra-day, inter-day variations and repeatability. The % R.S.D. value less than 2 indicate that the method was precise. Ruggedness of the proposed method was studied with the help of two analysts. The above method was a rapid and cost-effective quality-control tool for routine analysis of pramipexole dihydrochloride in bulk and in pharmaceutical dosage form.

Keywords: Pramipexoledihydrochloride, UV-Spectrophotometry, Area Under Curve, Validation.

1. INTRODUCTION

Pramipexoledi hydrochloride is chemically (s)-2-amino-4,5,6,7-tetrahydro-6-(propylamino) benzothiazole dihydrochloride[1] is a nonergot dopamine agonist recently approved for the treatment ofearly and advanced Parkinson's disease. Restless legs syndrome (RLS)[1]. It is also sometimes used off-label as a treatment for cluster headache and to counteract the problems with sexual dysfunction experienced by some users of the selective serotonin reuptake inhibitor (SSRI) antidepressantsA detailed literature survey for pramipexoledi hydrochloride revealed that the drug can be estimated by spectrophotometric method, LC method[5] and electrophoresis were developed for estimation of pramipexole dihydrochloridein bulk, combination formulation and pharmaceutical dosage form. However area under curve method have not been developed and validated for pharmaceutical dosage form. Hence, our study reports a simple, precise and economical UV- Spectrophotometric method for estimation of pramipexoledi hydrochloride in tablet formulation. The method was validated according to ICH guidelines[7].

2. Experimental Work

2.1 MaterialandMethod

Pramipexole working standard was obtained as gift sample from Sigma Aldrech The drug was used without further purification. A tablet formulation containing 0.25 mg of pramipexoledi hydrochloride was purchased from local market. Analytical grade solvents was used for the experiment.

2.3 Preparation of standard stock and working standard solution
The standard stock solution of pramipexole dihydrochloride was prepared by dissolving accurately weighed 5 mg of the drug in water and diluted to 100 mL with same solvent to obtain a final concentration of 5µg/mL.

2.4 Selection of Wavelength for analysis
Appropriate volume 2 ml of standard stock solution of pramipexole dihydrochloride was transferred into 10 ml volumetric flask, diluted to mark with water to give concentration of 5µg/ml. The resulting solution was scanned in UV range (200nm–400nm). In spectrum Pramipexole Dihydrochloride showed absorbance maximum at 261nm (Fig. 2).

3. Validation of the method
The method was validated in terms of linearity, accuracy, precision, and ruggedness.

3.1 Linearity study
Different aliquots of pramipexoledihydrochloride in range 2-4.5 ml were transferred into series of 10 ml volumetric flasks and the volume was made up to the mark with water to get concentrations 10, 15, 20, 25, 30 and 35 µg/ml, respectively. The solutions were scanned on spectrophotometer in the UV range 200-400 nm. The two wavelength **230.00 and 284.60 nm**was selected for the determination of Area Under Curve (AUC). The calibration plot was constructed as Area Under Curve vs concentration (Fig. 3).

3.2 Accuracy
To the pre analyzed sample solutions, a known amount of standard stock solution was added at different levels i.e. 80%, 100% and 120 %. The solutions were reanalyzed by proposed method.

3.3 Precision
Precision of the method was studied as intra-day and inter-day variations. Intra-day precision was determined by analyzing the 15, 20 and 25 µg/ml of pramipexole dihydrochloraide solutions for three times in the same day. Inter-day precision was determined by analyzing the 15, 20 and 25 µg/ml of Pramipexole Dihydrochloride solutions daily for three days over the period of week.

3.4 Sensitivity
The sensitivity of measurements of pramipexole dihydrochloride by the use of the proposed method was estimated in terms of the Limit of Quantification (LOQ) and Limit of Detection (LOD). The LOQ and LOD were calculated using equation LOD = 3.3 x N/B and LOQ = 10 x N/B, where, 'N' is standard deviation of the peak areas of the drugs (n = 3), taken as a measure of noise, and 'B' is the slope of the corresponding calibration curve.

3.5 Repeatability
Repeatability was determined by analyzing 20 µg/ml concentration of Pramipexole dihydrochloride solution for six times.

3.6 Ruggedness
Ruggedness of the proposed method is determined for 20 µg/ml concentration of pramipexole dihydrochloride by analysis of aliquots from homogenous slot by two analysts using same operational and environmental conditions.

4. Determination of Pramipexole Dihydrochloride in bulk
Accurately weighed 5 mg of pramipexole dihydrochloride was transferred to a 100 mL volumetric flask and 100 mL water was added. After ultrasonic vibration for 10 min, the mixture was diluted to volume with water. An appropriate aliquot was taken in such a way that the final concentration in 3 mL is 20µg/mL.The concentrations of the drug were calculated from linear regression equations.

5. Application of proposed method for Pharmaceutical formulation
For analysis of commercial formulationpramipexole dihydrochloride (0.25mg) equivalent to 5mg of drug was transferred to a 100 mL volumetric flask and 100 mL water was added. After ultrasonic vibration for 10 min, the mixture was diluted to volume with water. From this solution an appropriate aliquot was taken in such a way that the final concentration in 1 mL is 5µg/mL. The concentrations of the drug were calculated from linear regression equations.

6. RESULTS AND DISCUSSION
6.1 Method Validation
The proposed method was validated as per ICH guidelines. The solutions of the drugs were prepared as per the earlier adopted procedure given in the experiment.

6.1.1 Linearity studies
The linear regression data for the calibration curves showed good linear relationship over the concentration range 10-35µg/ml for pramipexoledi hydrochloride. Linear regression equation was found to be Y = 0.432

X + 0.037 (r^2 = 0.989). The result is expressed in (Table 1).

6.1.2 Accuracy

The solutions were reanalyzed by proposed method; results of recovery studies are reported in (Table 2) which showed that the % amount found was between 99.10% – 100% with % R.S.D. less than 2.

6.1.3 Precision

The precision of the developed method was expressed in terms of % relative standard deviation (% RSD). These result shows reproducibility of the assay. The % R.S.D. values found to be less than 2, so that indicate this method precise for the determination of the drug in formulation (Table 3).

6.1.4 Sensitivity

The linearity equation was found to be Y = 0.0396X + 0.0333. The LOQ and LOD for Pramipexole Dihydrochloride were found to be 0.02525 µg/mL and 0.0833 µg/mL respectively.

6.1.5 Repeatability

Repeatability was determined by analyzing 20µg/mL concentration of Pramipexole Dihydrochloride solution for six times and the % amount found was between 99.6% to 100.45% with % R.S.D. less than 2 (Table 4).

6.1.6 Ruggedness

Peak area was measured for same concentration solutions, six times. The results are in the acceptable range for both the drugs. The results are given in (Table 5). The result showed that the % R.S.D. was less than 2%.

7. Determination of Pramipexole dihydrochloride in bulk

The concentrations of the drug were calculated from linear regression equations. The % amount found was between 98.85% to 99.65% (Table 6).

8. Application of proposed method for pharmaceutical formulation

The concentrations of the drug were calculated from linear regression equation. The % amount was found between 98.75% to 99.05% (Table 7).

9. CONCLUSION

Method that was developed for the determination of pramipexoledihydrochoride based on different analytical techniques, UV-Spectrophotometric, AUC method. The method was validated and found to be simple, sensitive, accurate, and precise. Hence, the method can be used successfully for routine analysis of pharmaceutical dosage form of pramipexoledihydrochloride. The proposed spectrophotometric method will not replace the presently known methods available for the analysis of pramipexoledihydrochloride. However, it can serve as an alternative where advanced instruments (e.g. HPLC) are not available for routine analysis.

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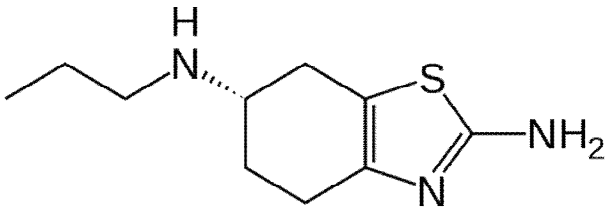

Fig. 1: Chemical structure of Pramipexoledi hydrochloride

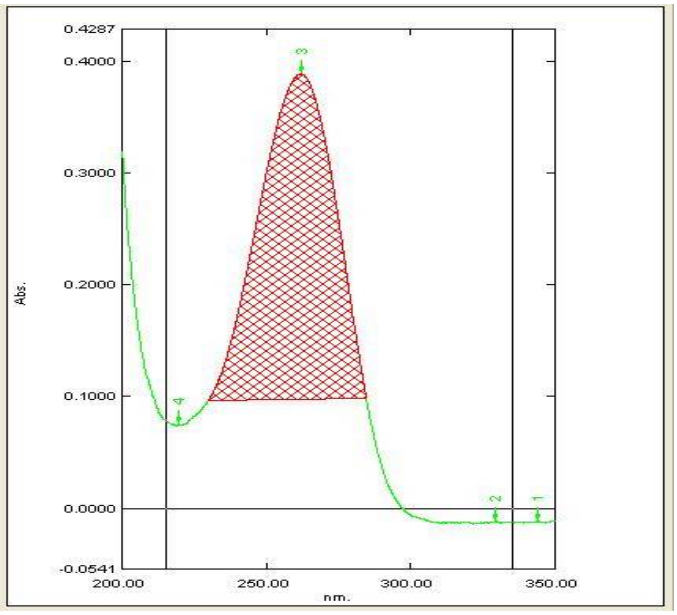

Fig. 2: Area under curve spectrum of pramipexole dihydrochloride in water

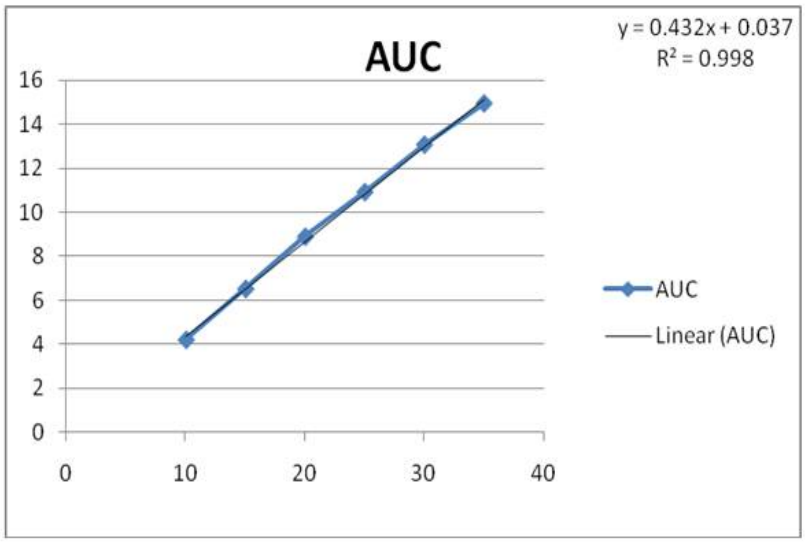

Fig. 3: Calibration Curve of pramipexole dihydrochloride; Y = 0.432 X+0.037; Where, Correlation coefficient = 0.999, Slope = 0.432±0.0005,Intercept = 0.037±0.0114

Table 1: Linearity study of pramipexole dihydrochloride

Concentration of pramipexole [µg/mL]	Area Mean ± SD	% RSD
10	4.1936±0.01	0.23
15	6.5048±0.01	0.14
20	8.8831±0.03	0.35
25	10.9121±0.03	0.32
30	13.1174±0.07	0.51
35	14.9198±0.05	0.36

n= no. of estimations

Table 2: Recovery studies

Drug	Initial amount [µg/mL]	Amount added [µg/mL]	Amount recovered [µg/mL, n=3]	% Recovered	% RSD
Pramipexole dihydrochloride	10	5	4.97	99.07	0.24
	10	10	10.00	100.00	0.76
	10	15	15.07	100.00	0.53

n= no. of estimations

Table 3: Precision studies

Drug	Concentration [µg/mL]	Intra –day [n=3]	% RSD	Inter-day [n=3]	% RSD
Pramipexole dihydrochloride	15	6.4166±0.030	0.4761	6.42±0.03	0.4651
	20	8.621±0.026	0.3076	8.6±0.026	0.3076
	25	10.68±0.0173	0.1621	10.68±0.02	0.1621

n= no. of estimations

Table 4: Repeatability studies

Drug	Amount taken [µg/mL]	Amount found [µg/mL]	% Amount found
Pramipexole dihydrochloride	20	20.04	100.2
	20	20.01	100.5
	20	19.98	99.9
	20	20.05	100.25
	20	20.09	100.45
	20	19.72	98.6
	Mean ± SD	19.98167±0.1334	99.87833±0.655604
	% RSD	0.668008	0.656403

Table 5: Ruggedness studies

Drug	Analyst - 1		Analyst - 2	
	% Amount found ± SD [n=3]	% RSD	% Amount found ± SD [n=3]	% RSD
Pramipexole Dihydrochloride	98.33±0.09073	0.09227	99.81± 0.03511	0.03512

n= no. of estimations

Table 6: Analysis of Bulk material

Drug	Amount taken [µg/mL]	Amount found [µg/mL]	(%) Amount found
Pramipexole dihydrochloride	20	19.84	99.2
	20	19.89	99.45
	20	19.93	99.65
	20	19.82	99.1
	20	19.77	98.85
	20	19.84	99.2
	Mean ± SD	19.8433±0.0556	101.58 ± 0.2710
	% RSD	0.2668	0.2668

Table 7: Analysis of pramipexoledihydrochloride Formulation

Drug	Label-claim [mg]	Amount taken [µg/mL]	Amount found [µg/mL]	% Amount found
Pramipexole dihydrochloride	0.25mg	20	19.75	98.75
		20	19.71	99.05
		20	19.84	99.02
		20	19.82	99.01
		20	19.92	99.06
		20	19.88	99.04
		Mean ± SD	19.8367±0.088	99.1833±0.2943
		% RSD	0.2968	0.2968

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