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A sensitive spectrophotometric determination of cyanide content in Citalopram Hydrobromide API in parts per million levels

S. M. Ramdharane [1], K. B. Vyas [2], K. S. Nimavat [3]*

1 Pacific Academy of Higher Education & Research University, Udaipur, Rajasthan, India.
2 Sheth L. H. Science College, Mansa, Gujarat, India.
3 Govt. Science College, Gandhinagar, Gujarat, India.

ABSTRACT:

Citalopram hydrobromide is used as an antidepressant drug. It is manufactured by 1-(4'-fluoropheny1)-phthalane -5-carbonitrile (5- Cyanophthalane) is Alkylated with 3-N,N-dimethylaminopropylchloride in presence of strong base to get Citalopram hydrobromide. Trace level of Cyanide as residual cyanide may remain in the product. Because during manufacturing process of 5- Cyanophthalane reaction with Cyanide salt in cyanation step. The residual Cyanide content in Citalopram hydrobromide API is determined by colorimetric procedure. The method is based on principle that in In the colorimetric measurement the cyanide is converted to cyanogen chloride, CNCl, by reaction with chloramine-T at a pH less than 8 without hydrolyzing to the cyanate. After the reaction is complete, color is formed on the addition pyridine-barbituric acid reagent. This colored compound, which is a complex of Quinquevalent Cyanide ,and determined spectrophotometrically. Beer's law was obeyed in the concentration ranges 3.0 to 15 ppm .The sensitivity of the method surpasses that of the reported spectrophotometric methods. The method was successfully applied for the determination of Cyanide in Citalopram Hydrobromide API as residual Cyanide in Parts per Million Level.

KEY WORDS: Spectrophotometry, Citalopram Hydrobromide, API,Validation, Cynide, Beer law.

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***For Correspondence:**
Ramdharane SM
Research Scholar Pacific Academy of Higher Education & Research University, Udaipur, Rajasthan, India.

(www.jpsbr.org)

INTRODUCTION:

A Sensitive Spectrophotometric method is based on principle that in In the colorimetric measurement the cyanide is converted to cyanogen chloride, CNCl, by reaction with chloramine-T at a pH less than 8 without hydrolyzing to the cyanate.1 After the reaction is complete, color is formed on the addition pyridine-barbituric acid reagent. This colored compound, which is a complex of Quinquevalent Cyanide ,and determined spectrophotometrically.1 Beer's law2 was obeyed in the concentration ranges 3.0 to 15 ppm .The sensitivity of the method surpasses that of the reported spectrophotometric methods. The method was successfully applied for the determination of Cyanide in Citalopram Hydrobromide API as residual Cyanide in Parts per Million Level

A Sensitive Spectrophotometric method for determination of Cyanide as Residual in Citalopram hydrobromide, API. Cyanide salt is used as in reaction in manufacturing of Cyanophthalane.3 We Succeeded in developing a simple, rapid and accurate spectrophotometric procedure for the determination of Cyanide as residual in Citalopram hydrobromide, API in Parts per Million Level.

Experimental

Instrumentation

UV-Visible Spectrophotometer	**Shimadzu**
Balance	Sartorius
pH meter	Lab India

Reagents

Cyanide Standard Solution (1000mg/L) Certipur®Product Code 1.19533.0500	**Merck**
Chloramine-T Solution AR grade	Sigma –Aldrich
Water HPLC grade	Merck
Pyridine AR grade	Merck
Hydrochloric Acid AR grade	Merck
Barbutiric acid AR grade	Merck

General procedure

Reagents and solution preparation:

a. Chloramine-T solution:

Dissolve 1.0g in 100mL of HPLC grade water.

b. Pyridine-Barbutiric acid Reagent solution :

Transfer 6.0-7.0 g of Barbutiric acid into 100mL of volumetric flask containing 10-15mL of HPLC grade water, Add slowly 30mL of Pyridine (portion wise 10mL) to the same volumetric flask and cool the mixture in ice bath then Slowly add portion wise 6to7mLof concentrate hydrochloric acid in ice bath shake well and dissolved solid with sonication, and make up to volume up to the mark with HPLC grade water.

Standard Solution Stock (10 ppm Cyanide solution)

Take accurately 1.0 mL of Cyanide Standard Solution1000 ppm (Merck) into 100.0 mL volumetric flask. Dissolve in 50 mL HPLC grade water. Makeup to mark with same and mix well. This solution is having concentration of about 10.0ppm

Operational Conditions

Instruments: UV –Spectrophotometer

Wavelength: 578 nm

Sample preparation

Transfer 125 mg of Citalopram hydrobromide sample into 25 mL volumetric flask add 10 mL chilled HPLC grade water and mix well.Add 0.2 mL Chloramine T solution and slowly add 2.5 mL Pyridine-Barbutiric acid Reagent solution and shake for 5 min and make upto the mark with chilled water.

Standard Solution

Transfer 5.0 mL of Standard Solution Stock into 100mL volumetric Flask and mix well. Add 0.2 mL 0.2 mL Chloramine T solution and slowly add 2.5 mL Pyridine-Barbutiric acid Reagent solution and shake for 5 min and make upto the mark with chilled water. (0.5 ppm Cyanide)

Blank Solution :

Prepare same as Standard solution without cyanide solution.

Preparation of calibration curves

Solution-A: (cyanide 0.0150ppm):

Transfer 0.3ml of Standard solution into 10 mL volumetric flask, add 0.2mL of chloramine-T solution and add slowly 2.5mL of pyridine barbutiric acid and shake for 5min and make up to the mark with chilled HPLC grade water .

Solution-B: (cyanide 0.025ppm):

Transfer 0.5ml of Standard solution into 10 mL volumetric flask, add 0.2mL of chloramine-T solution and add slowly 2.5mL of pyridine barbutiric acid and and shake for 5min and make up to the mark with chilled HPLC grade water .

Solution-C: (cyanide 0.05ppm):

Transfer 1.0ml of Standard solution into 10 mL volumetric flask, add 0.2mL of chloramine-T solution and add slowly 2.5mL of pyridine barbutiric acid and shake 5min and make up to the mark with chilled HPLC grade water .

Solution-D: (cyanide 0.065ppm):

Transfer 1.3ml of Standard solution into 10 mL volumetric flask, add 0.2mL of chloramine-T solution

and add slowly 2.5mL of pyridine barbutiric acid and shake 5min and make up to the mark with chilled HPLC grade water .

Solution-E: (cyanide 0.075ppm):

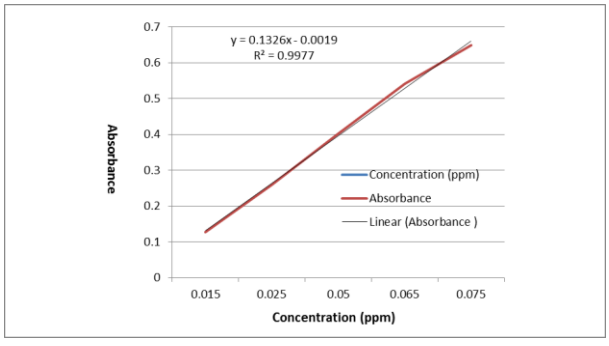
Transfer 1.5ml of Standard solution into 10 mL volumetric flask, add 0.2mL of chloramine-T solution and add slowly 2.5mL of pyridine barbutiric acid and shake 5min and make up to the mark with chilled HPLC grade water .

Procedure:

Check the absorbance of Solution-A to Solution-E . Plot the absorbance of the solutions against corresponding concentration of Cyanide Standard solution.

Table -1 Acceptance criteria: The regression coefficient should not be less than 0.98

Name of Cyanide standard solution	Concentration (ppm)	Absorbance (Reading)
Solution A	**0.0150ppm**	**0.1265**
Solution B	**0.025ppm**	**0.2599**
Solution C	**0.050ppm**	**0.4024**
Solution D	**0.065 ppm**	**0.5416**
Solution E	**0.075ppm**	**0.6484**



Graph-1

Calculation : ppm of cyanide**,** can be calculated by using following formula,

$$\text{Cyanide Content (ppm)} = \frac{\text{Absorbance of sample preparation x Concentration of standard preparation}}{\text{Absorbance of standard preparation}}$$

Results and discussion

The Method described here in very rapid , versatile and selective This system is readily available and easy to operate, and reproduces the results with less than 1 % Relative

Method Validation

As per the ICH guidelines, accuracy, precision, LOD, LOQ and linearity of the calibration curve were determined [4-10].

Linearity Study.

The linearity regression analysis was demonstrated to check the acceptability of the method for quantitative determination range of LOQ to 150% of the specification limit. The regression coefficient R^2 = 0.99 is also well within limit. The limit of quantitation (LOQ) was determined by taking the ratio of the standard deviation of the blank with respect to water and the slope of the calibration curve multiplied by the factor 10. This means that LOQ is approximately 3.3 times greater than LOD.

Precision Study

Table -2: Solution C (0.05 ppm) solution examine for six times the results are as below.

Name of solution (0.05ppm)	Absorbance Set-1	Absorbance Set -2
Solution C	0.4024	0.4056
Solution C	0.4027	0.4034
Solution C	0.4015	0.4022
Solution C	0.4020	0.4033
Solution C	0.4029	0.4053
Solution C	0.4019	0.4018

Set -1 the method precision and set -2 is intermediate precision. % RSD of Six reading is 0.13% for set -1 and for set-2 is 0.39 which is well within limit. The results

presented under table 2, which confirm good precision of the method.

Accuracy :

The percent recovery for cyanide at 30,50,100 and 150% of the specification level (Table -3) . recovery we were found to be 95 to 105% indicating the accuracy of the method.

Table-3: recovery

Specification level %	% Recovery *
30	92
50	96
100	102
150	98

* Average of three determination

Table 4 Validation Summery

Parameter	Conclusion	Limit
Linearity	The regression coefficient R^2 = 0.99	Min. 0.98
Precision	% RSD of Six reading is 0.13%	Not more than 2%
Intermediate Precision	% RSD of Six reading is 0.39%	Not more than 2%
Accuracy	95 to 105%	90 to 110 %
LOD and LOQ	LOQ is approximately 3.3 times greater than LOD.	In line with ICH

Applicability of the method

The applicability of the proposed spectrophotometric procedure for the determination of Cyanide as residual cyanide in Citalopram Hydrobromide API.

CONCLUSION

The method is simple reproducible fast and accurate for determination of residual cyanide in Citalopram hydrobromide API..

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