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Spectrophotometric Determination of Citicoline Sodium in Pure Form and Pharmaceutical Formulation

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ABSTRACT

This study proposes a simple, specific, precise and accurate spectrophotometric method for estimation of Citicoline sodium in bulk and tablet dosage form. The results presented are statistically validated in accordance with the guidelines provided by ICH (International conference on harmonization). The solvents used were 0.1N sodium hydroxide and double distilled water. With an absorption maxima of 272 nm, the drug followed a linear relationship in the range of 5-55µg/ml while the correlation coefficient was at 0.9983. The recovery was 99.90% (±0.50) and the coefficient of variance was found to be less than 5%.

Keywords: Spectrophotometric method, Citicoline sodium

INTRODUCTION

Citicoline sodium (CT) is chemically Cytidine 5‘-{trihydrogendiphosphate} p‘-[2-{trimethylammonio} ethyl] ester inner salt [1]. CT is primarily used in pharmacotherapy of brain insufficiency and other related neurological disorders viz., as stroke, brain trauma and Parkinsonism’s disease [2].

CT is a white crystalline powder, freely soluble in water but insoluble in ethanol, acetone and chloroform [3]. While few analytical methods like liquid chromatography [4], stability indicating HPLC [5], colorimetric [6] and biological assay [7] are reported, there was no mention of a method based on spectrophotometric estimation [8].

The proposed UV- Visible spectrophotometric method is a simple, specific, rapid, and accurate for quantitative estimation of CT. The results obtained have been statistically validated in accordance with the ICH guidelines [9] and therefore can be effectively used in quality control of CT for bulk as well as pharmaceutical dosage form.

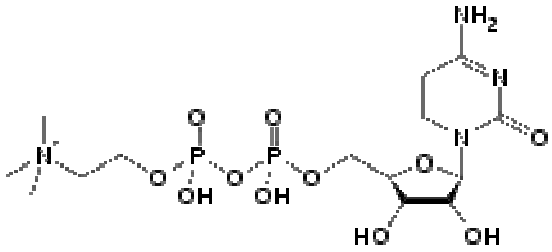

Fig. 1 Chemical structure of Citicoline sodium

MATERIALS AND METHODS

Instrumentation

A Shimadzu UV-Visible spectrophotometer model 1700 (Japan) with 1 cm matched quartz cells was used along with a Sartorius digital balance.

Chemicals and Reagents

CT was kindly supplied by M/S Strides Arcolab limited, Bangalore, India. Tablets containing CT (Citistar; Lyka Labs ltd, Thane), sodium hydroxide (AR) and double distilled water were used.

Preparation of Standard Solution

Accurately weighed 50mg of CT and transferred it to a 50ml volumetric flask. Double distilled water was used to dissolve the drug and made up to the 50ml volume mark. It was then diluted to a concentration of 100µg/ml with 0.1N sodium hydroxide and used as the stock solution for further dilutions.

Determination of Wavelength of Maximum Absorbance

The stock solution was further diluted with 0.1N sodium hydroxide to get concentration of 20µg/ml. This solution was scanned in the range 200-800 nm where 0.1N sodium hydroxide was used as blank. The wavelength of maximum absorbance of CT was found at 272 nm as shown in fig 2.

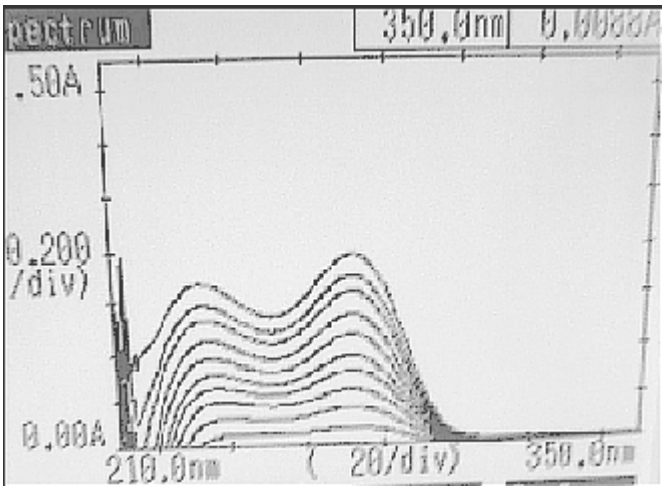

Fig. 2 Spectra of Citicoline sodium

Table 1 Absorbance of CT at Different Concentrations

Concentration (µg/ml)	Absorbance (n=9)
5	0.089
10	0.168
15	0.249
20	0.331
25	0.409
30	0.493
35	0.577
40	0.650
45	0.718
50	0.811
55	0.934

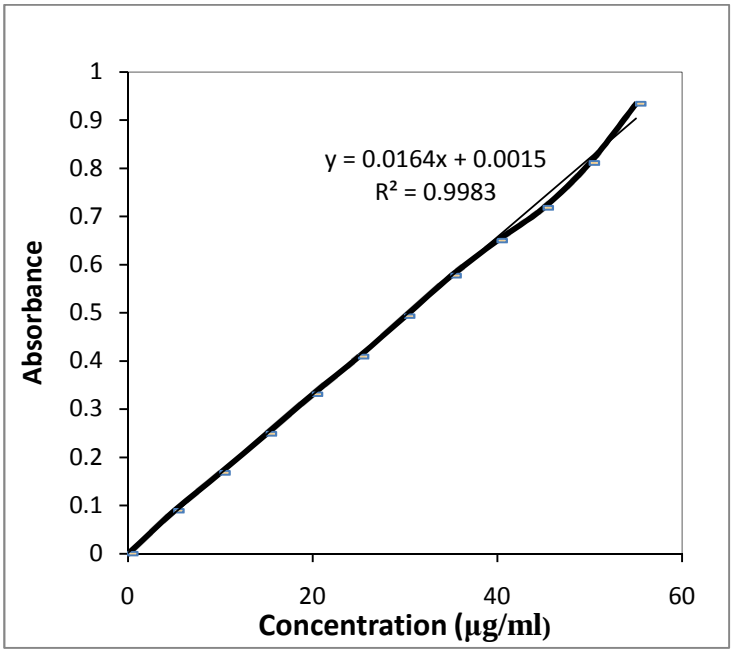

Fig. 3 Calibration Curve of CT

Preparation of Calibration Curve

The stock solution of CT was appropriately diluted to obtain concentration range of 5-55 µg/ml with 0.1N sodium hydroxide. The absorption of the solutions was measured at 272 nm. The absorbance values are shown in table1 and calibration curve is as shown in fig 3.

Assay of Marketed Formulation

Twenty tablets of CT (Citistar) were weighed and crushed to obtain fine powder. An accurately weighed tablet powder equivalent to about 100mg of CT was transferred to 100ml volumetric flask and sonicated for 15 minutes in double distilled water and made up the volume with double distilled water. The resulting solution was filtered through whatman filter paper no. 41. Filtrate was appropriately diluted to get concentration of 30µg/ml with 0.1N sodium hydroxide and the absorbance of solution was measured at 272 nm. The amount of CT present in the tablets was calculated using the standard absorptivity value and results are as given in table 2.

Table 2 Results of estimation of marketed formulation

Label claim /tablet	Percent of label claim estimated ±SD (n=6)
500mg	101.72 ± 2.72

Method Validation

Precision

Precision of the proposed method was determined by measuring the absorbance of standard solutions at different time intervals on same day (intra-day), on three different days (inter-day) and results are shown in table 3.

Table 3 Analytical Validation Parameters

PARAMETERS	OBSERVATIONS
Wavelength(nm)	272
Beer's law range(µg/ml)	5-55
Molar absorptivity (l/mol.cm)	$8.369x10^3$
Sandell's Sensitivity(µg/cm^2/0.001AU)	0.06097
Standard regression(n=9)	Y=0.0164x+0.0015
Correlation Coefficient	0.9983
Slope	0.0164
Intercept	0.0015
LOD(µg/ml)	0.28
LOQ(µg/ml)	0.85
%RSD Repeatability Reproducibility Intraday precision Interday precision	 1.9 -4.3 1.1 -3.5 0.1-3.7 0.1- 2.7
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Recovery Studies

To study the accuracy of the proposed method, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%). A known amount of CT was added to preanalysed tablet powder and percent recoveries were calculated. The results of recovery studies were satisfactory and are presented in table 4.

Table 4 Recovery Studies

Level of Recovery	Amt of drug added in the tablet powder equivalent to 100mg of CT (mg)	Percent Recovery	±SD*(n=3)
80%	80	99.93%	0.44
100%	100	99.79%	0.69
120%	120	99.79%	0.38

RESULTS AND DISCUSSION

CT being freely soluble compound in water, the stock solution of CT was prepared in double distilled water. Further dilutions were made in 0.1N sodium hydroxide, 0.1N hydrochloric acid and different buffers in the range of pH 6.8 to 10. Since hyperchromic effect was observed in 0.1N sodium hydroxide further dilutions were made in the 0.1N sodium hydroxide. It was observed that CT followed a linear relationship in the range of 5-55µg/ml with correlation coefficient of 0.9983. Precision was calculated as reproducibility, interday and intraday variations for drug. When the marketed formulation was analysed using the proposed method, the amount of CT determined in the tablets was in the range 99.0% to 104.4%. The accuracy of the method was determined at 80%, 100% and 120% level and the per cent recovery ranges from 99.1 to 100.4. The proposed method was found to be simple, accurate and rapid for the routine determination of CT in tablet formulation.

Acknowledgement

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