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Development and validation of a UV spectrophotometric method for estimation of Citicoline sodium in Bulk and Dosage Form

Jimmi A.Patel*, Bibhuranjan Panigrahi, Chhaganbhai N.Patel, Badmanaban Ramalingan, Kamal Modh

**Department of Pharmaceutical Quality Assurance,Shri Sarvajanik Pharmacy College, Near Arvind Baug, Mehsana-384 001, India*

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ABSTRACT

Development and validation of a simple UV and derivative spectrophotometric method to quantify citicoline sodium used as a single active principle in pharmaceutical dosage forms were done. Pharmacopeias have not yet provided an official method for its quantification. A study was carried out considering all the parameters established by USP XXIV to validate an analytical method i.e. linearity, accuracy, range, precision and specificity. Based on spectrophotometric characteristic of citicoline sodium, a signal at 272nm for simple UV spectrum and at 286nm for derivative spectrum ($1D_{286}$) was found adequate for quantification. The linearity signal and concentration of citicoline sodium in the range of 10-50µg/ml in aqueous solution presents a correlation coefficient (r^2) of 0.999 for simple UV and 0.9997 for 1storder derivative spectrum. The limit of detection (LOD) and limit of quantification (LOQ) was found to be 0.75µg/ml and 2.27µg/ml by simple UV and 0.69µg/ml and 2.09µg/ml by derivative spectrum respectively. The mean recovery percentage was 99.93±1.27% by simple UV and 101.08±0.5% by derivative spectrum. In addition, the proposed method is simple, easy to apply, low-cost, does not use polluting reagent and requires relatively inexpensive instruments.

Keywords: Citicoline sodium, UV spectrophotometer, Derivative spectrum

INTRODUCTION

Citicoline sodium 5'-o- [hydroxy ({ hydroxyl [2(trimethyl ammonia) ethoxy] phosphoryl } oxy}phosphroyl] cytidine, is a Psychotherapeutic agent used as psychostimulant, nootropics and neurotonics[1]. It exerts its action by activating the bio-synthesis of structural phospholipids in the neuronal membrane, increases cerebral metabolism and increases the levels of various neurotransmitters, including acetylcholine and dopamine[2]. Citicoline sodium is primarily indicated in conditions like cardiac stroke, head trauma, ischaemic heart disease, paralysis of lower extremities and can also be given in adjunctive therapy as an alternative drug of choice in Parkinson's disease[3]. Citicoline sodium is an amorphous, somewhat hygroscopic powder having molecular weight 489.332g/mol and pKa value of 4.4. It is soluble readily in water to form acidic solution, practically insoluble in most organic solvents. It is marketed in the form tablets.

Literature survey revealed HPLC method for determination of citicoline sodium in pharmaceutical preparation and in biological fluids, the active principle as well as its metabolites have been determined by HPLC through UV detection[4], proton-decoupled phosphorus magnetic resonance spectroscopy[5] and diffusion-weighted magnetic resonance imaging (DWI)[6]. As an alternative to existing methods, we propose a validated procedure to estimate Citicoline sodium when it is in a single active principle in formulation based on UV spectrophotometry. The aim of this work was to develop a cheap, less time consuming and validated method that could be useful for the individual analysis of tablets by fulfilling the requirements of analytical quality necessary for finished pharmaceutical products as per the USP XXIV[7].

MATERIALS & METHODS

Reference standard of citicoline sodium was procured as gift sample from Torrent research center, India. Distilled water was use in present study. Strolin (Torrent) purchased from the market. Simandzu UV-1700 uv/vis spectrophotometer with 10 mm matched quartz cells: - Shimadzu, Japan, Electrical Balance: -ALC-210.4, Acculab and Sonicator: - 2K503002, Eneritech were used for experiment. Absorption and overlay spectra were recorded over the wavelength range of 200-400 nm, using 1cm quartz cells at a scan speed medium and fixed slit width of 1.0 nm.

***Corresponding author.**

Jimmi A.Patel
Department of Pharmaceutical Quality Assurance
Shri Sarvajanik Pharmacy College,
Near Arvind Baug, Mehsana-384 001, India
Tel.: 919033414874
E-mail:patel_jim2005@yahoo.co.in

Preparation of standard and test solutions

Citicoline sodium standard stock solution:
10 mg citicoline sodium was accurately weighed and transferred to a 100 ml volumetric flask, dissolved the sample with distill water and finally volume was made up to the mark to make 100µg/ml stock solution.

Preparation of test solution:
Twenty tablets (strolin) were weighed and its average weight was determined. An accurately weighed tablet powder equivalent to 100 mg of citicoline sodium was transferred to a 100 ml volumetric flask, dissolved in 50ml distilled water, sonicated for 10 minutes and then volume was made up to the mark. Solution was then filtered using whatman filter paper (No 41). 3 ml of this filtrate was then taken and diluted suitably with distilled water to obtain 30 µg/ml working solution.

Determination of λmax and A(1%,1cm) value:
Working standard solution of citicoline sodium was scanned in entire UV range of 200-400 nm. Data were recorded in the interval of 1nm. The λmax of citicoline sodium were found to be 272 nm (for simple UV) and 286 nm (for 1st derivative UV) while A (1%,1cm) were found 198 (for simple UV) and 9.14 (for 1st derivative UV) respectively.

Preparation of calibration curve:
Standard stock solution was suitably diluted with distilled water to obtain concentration ranging from 10-50 µg/ml. Absorbance of these solutions was measured at 272 nm(using simple UV) and 286 nm (using 1st derivative UV). Absorbance was plotted versus concentration to obtain the calibration curve. LOD and LOQ values were calculated using the relation,

$$LOD = 3.3\sigma / S$$
$$LOQ = 10\sigma / S$$

Where, σ= standard deviation of residuals from the curve; S=slope of the curve
Analysis of the marketed formulation

Determination of accuracy:
To determine the accuracy of the method recovery study was performed by standard addition method. To the preanalyzed tablet powder equivalent to 500mg (labeled claim of a tablet), know quantities of standard drug (80,100,120% of labeled claim of a tablet) were spiked separately and the total drug contents was found out. The % recovery was determined and results are given in table 5.

Figure 1: Overlay spectrum of standard citicoline sodium using simple UV spectroscopy

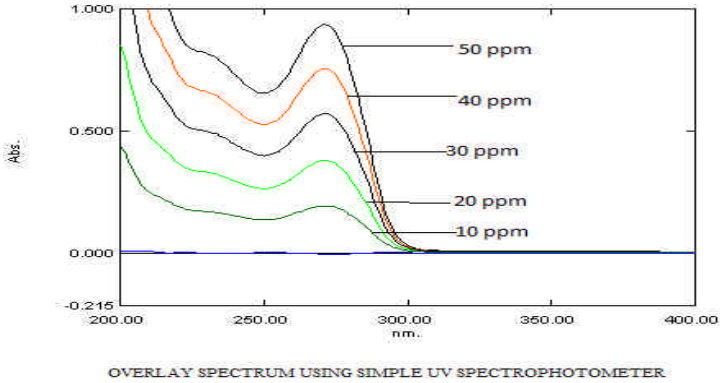
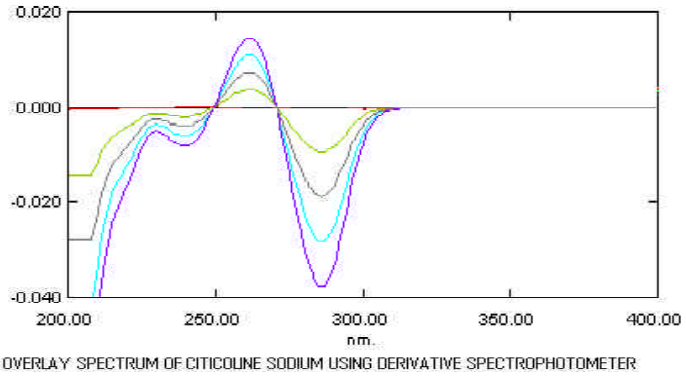


Figure 2: Overlay spectrum of standard citicoline sodium using simple 1st Derivative spectrum



Tabel 1: Calibration data for analysis of citicoline sodium at 272 nm and 1D$_{286}$nm.

Concentration (µg/ml)	Using simple UV(272nm) Absorbance Mean ±S.D	Using 1st Derivative UV(286nm) Absorbance Mean ±S.D
10	0.201±0.006	0.009±0.0004
20	0.398±0.006	0.019±0.0004
30	0.580±0.005	0.028±0.0003
40	0.776±0.004	0.038±0.0004
50	0.977±0.005	0.047±0.0005

Mean ± S.D. (n=3)

Figure 3: Result of linearity graph

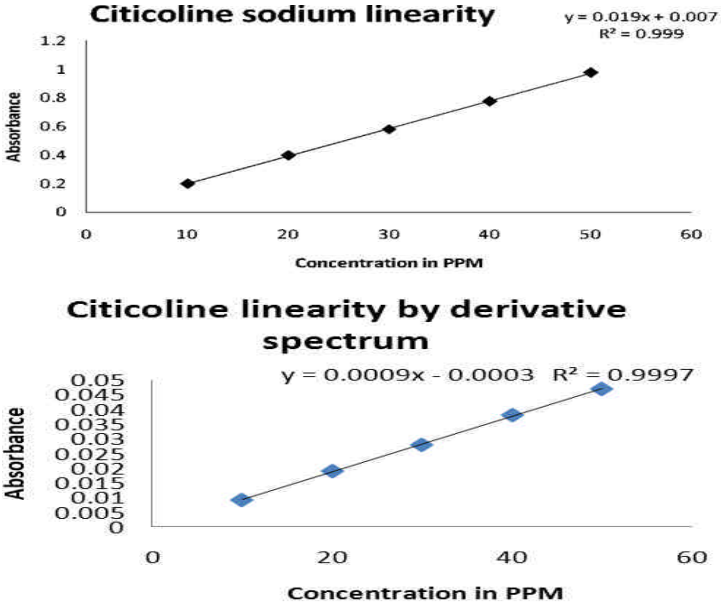


Table 2: Optical characteristic and validation parameter

Parameter	Value for simple UV	Value for 1st Derivative UV
λmax(nm)	272	286
Beer's low limit (µg/ml)	5-50	5-50
A(1%,1cm)	198	9.14
Correlation coefficient (r^2)	0.999	0.9997
Regression equation (Y=mx+c)	Y=0.019x+0.007	Y=0.0009X-0.0003
Intercept (a)	0.007	0.0003
Slope (c)	0.019	0.0009
Limit of detection (µg/ml)	0.75	0.69
Limit of quantification (µg/ml)	2.27	2.09

Table 3: Repeatability data for analysis of Citicoline sodium

Concentration (µg/ml)	Intraday simple UV Absorbance (Mean ± S.D)	Derivative UV Absorbance (Mean ± S.D)	Interday simple UV Absorbance (Mean ± S.D)	Derivative UV Absorbance (Mean ± S.D)
10	0.203±0.005	0.009±0.0004	0.201±0.006	0.008±0.0003
30	0.584±0.004	0.028±0.0003	0.580±0.005	0.026±0.0004
50	0.981±0.005	0.047±0.0005	0.977±0.005	0.044±0.0004

Mean ± S.D. (n=3)

Table 4: Reproducibility data for analysis of citicoline sodium

Concentration (µg/ml)	Absorbance (simple UV) UV 1700 (Mean ± S.D)	UV 1800 (Mean ± S.D)	Absorbance (1st Derivative UV) UV 1700 (Mean ± S.D)	UV 1800 (Mean ± S.D)
10	0.201±0.005	0.199±0.004	0.009±0.0004	0.008±0.0003
30	0.580±0.005	0.576±0.005	0.028±0.0003	0.027±0.0004
50	0.977±0.005	0.972±0.006	0.047±0.0005	0.045±0.0005

Mean ± S.D. (n=3)

Table 5: Accuracy data for analysis of standard citicoline sodium (Recovery studies)

Amount of sample taken(µg/ml)	Amount of standard added (µg/ml)	Total Amount (µg/ml)	Total amount found (µg/ml)±S.D Simple UV	Derivative UV	% Recovery Simple UV	Derivative UV
10	8	18	17.685±0.32	18.129±0.12	98.25	100.72
10	10	20	19.737±0.41	20.316±0.09	98.68	101.58
10	12	22	22.119±0.28	22.211±0.15	100.54	100.96

Mean ± S.D. (n=3)

Table 6: Analysis of marketed formulations

Formulation	%Amount Found ± SD Using simple UV	Using 1st derivative UV
Strolin	98.86±0.62	99.64±0.53

Mean ± S.D. (n=3)

RESULT AND DISCUSSION

The λ_{max} of citicoline sodium was found to be 272 nm (simple UV) and 286 nm (1st derivative UV) from its spectrum. The A (1%,1cm) value was found to be 198(simple UV) and 9.14(1st derivative UV). Citicoline sodium showed linear absorption in the range of 10-50 µg/ml. The correlation coefficient (r^2) was found to be 0.999(simple UV) and 0.9997(1st derivative UV) . The LOD and LOQ values were determined from the slope of linearity plot and standard deviation of the response and were found to be 0.75 µg/ml(simple UV), 0.69 µg/ml (1st derivative UV) and 2.27 µg/ml (simple UV), 2.09 µg/ml (1st derivative UV) respectively. The stability of solution of formulation was determined by measuring the absorbance at 272 nm at periodic intervals. There was no considerable change in the absorbance at this wavelength up to 3 hours indicating that the solution was stable for at least 3 hours.

Overlay spectra of different concentration range of standard citicoline sodium was recorded (Figure 1 & 2). Absorbance at different concentration showed in (Table 1). Linearity graph was showed in (Figure 3). Optical characteristics and other validation parameters were showed in (Table 2), Repeatability and reproducibility data for analysis of citicoline sodium were showed in (Table 3 & 4). Com-

mercial formulations containing citicoline sodium were analyzed by proposed method. Three replicate analysis of the formulation were carried out and the mean assay values in tablet formulation strolin were found to be 98.88±0.62 (simple UV) and 99.64±0.53 (1st derivative UV) and were showed in (Table 6). The corresponding RSD values were found to be 0.63 and 0.53 indicating that method has required precision. The accuracy of the method was determined by recovery studies. Pure citicoline sodium was spiked to the preanalyzed tablet powder at three different levels viz 80,100,120% of labeled claim as per the ICH guidelines. The mean recovery for strolin was found to be 99.15 indicating that the method has required accuracy and was showed in (Table 5).

CONCLUSION

The developed method is an alternative to determine citicoline sodium in pharmaceutical dosage forms that contain it as unique active principle with quite satisfactory results for the specific purpose of its design. Its advantages over other existing methods are its simplicity, fastness, low-cost and non-polluting conditions.

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