RESEARCH ARTICLE

Spectrophotometric Determination of Ziprasidonehydrochloride (ZPN), 5-[2-(4-Benzo [D] Isothiazol-3-YL-Piperazin-1-YL)-Ethyl]-6-Chloro-1, 3-Dihydro-Indol-2-One Hydrochloride Using Gold (III)

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Citation: A. Mohamed Sikkander (2020). Spectrophotometric Determination of Ziprasidonehydrochloride (ZPN), 5-[2-(4-Benzo [D] Isothiazol-3-YL-Piperazin-1-YL)-Ethyl]-6-Chloro-1, 3-Dihydro-Indol-2-One Hydrochloride Using Gold (III). *Chemical Engineering*. v01i01, 25-28. http://dx.doi.org/10.53709/CHE.2020.v01i01.004

DOI: http://dx.doi.org/10.53709/CHE.2020.v01i01.004

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Received on: August 11, 2020
Revised on: November 24, 2020
Accepted on: December 5, 2020

ABSTRACT

Ziprasidone hydrochloride (ZPN) forms a pink-coloured complex among gold (III) in an aqueous solution at pH 5.0. The ZPN complex show the absorption utmost at 600 nm and the BeerLambert's law is obeyed in the range of 5.0-60.0 µg/ml. The pragmatic formula and molecular mass of Ziprasidone hydrochloride (ZPN), 5-[2-(4-Benzo[d]isothiazol-3-yl-piperazin-1-yl)-ethyl]-6-chloro-1,3-dihydro-indol-2-one hydrochloride are C21H22Cl2N4OS and 448.94 correspondingly. In the present work, it was in employment for the receptive spectrophotometric determination of ZPN. The molar absorptivity and sandal's sensitivity were found to be 7.48 x 103 mol-1 cm-1 and 0.0604 µg/cm2 correspondingly. The complex shows 1:1 [ZPN: Au (III)] stoichiometry with a steadiness constant of 2.54 x 104. The effect of interference of various amounts of excipients has been studied. In addition to zero- order, first derivative spectrophotometric technique was also developed for the determination of ZPN in trace amount which was more responsive than the zero-order method. The results were in exceptional agreement with certified values. The developed method is very competent for the determination of ZPN in various kinds of pharmaceutical formulations.

Keywords: *ziprasidone hydrochloride (ZPN), Spectrophotometry, Spectrophotometric, Molar absorptivity, sandal's sensitivity, zero-order method*

INTRODUCTION

ZPN is a white to some extent pink powder. ZPN is a typical antipsychotic with a exclusive pharmacological profile. It is chemically distinct to the phenothiazine's and the atypical antipsychotics currently available. ZPN is not representative in IP, BP, USP, and EP. ZPN capsules (GEODON capsules, Pfizer, Inc., USA) are permitted for use by USFDA in February 2001. ZPN is accessible commercially as capsules existing for oral administration in 20 mg, 40 mg, 60 mg and 80 mg. ZPN capsules are full of ziprasidone hydrochloride, lactose, pregelatinized starch, and magnesium stearate. For the most part commonly observed adverse events associated with the use of ziprasidone hydrochloride and not observed at an equivalent incidence among placebo-treated patients are somnolence, respiratory tract infection, dizziness, akathisia, abnormal vision and vomiting.

ZPN exhibits a effective and highly discriminatory antagonistic activity on the D_2 and 5-HT_{2A} receptors [6]. It also has a far above the ground affinity for the 5-HT_{1A}, 5-HT_{1D} and 5-HT_{2C} receptor subtypes that could contribute to the overall therapeutic effect (Seegar, 1995). Embarrassed research trials have shown that a archetypal antipsychotics have significant advantages over standard antipsychotics, including a broad spectrum of efficacy and

improved tolerability profile, particularly with regard to neurological adverse events such as extra pyramidal symptoms (EPS) [7]. The assimilation of ZPN is rapid and C_{max} for ZPN and metabolites occurred at 2 to 6 h post dose [2].

A number of methods have been reported using liquid chromatography with UV detection liquid hromatography with fluorescence detection (Sachse, 2005) and LC-MS for the resolve of ZPN in human plasma [1]. Up to now, to our present knowledge, no visible spectrophotometric method is available for the determination of ZPN in bulk and in pharmaceutical dosage forms in literature (Usha Rani, 2011). Hence, there is a need to develop sensitive, accurate and flexible visible spectrophotometric methods, which prompted the author to choose ZPN for the investigation [10]. Reagent Ziprasidone hydrochloride is one of the important classes of reagent it contains good chelating agents and form complexes with various metal ions. Only less work has been done on the spectophotometric methods for the determination of Ziprasidone hydrochloride by using gold (III) [9]. The present work reports the simple, sensitive, selective and nonextracrive spectrophotometric fortitude 5-[2-(4-Benzo[d] isothiazol-3-yl-piperazin-1-yl)-ethyl]-6-chloro-1, 3-dihydro-indol-2-one hydrochloride Reagent by using gold (III). The developed method has been worn for the determination of ZPN in various kinds of pharmaceutical formulations (Figure: 1).

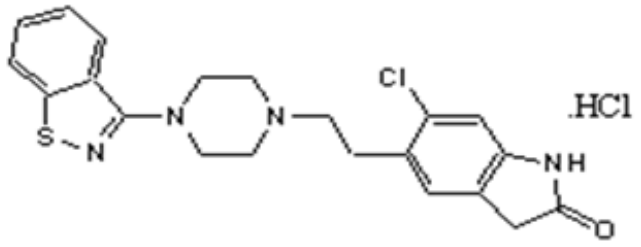

Figure: 1. Structure of the Ziprasidone Hydrochloride

MATERIALS AND METHODOLOGY

The absorbance and pH measurements were prepared on a shimadzu UV – visible spectrophotometer (model UV – 160) built-in with 1-cm quartz cells and Philips digital pH meter (model L1 613), correspondingly. The pH meter has temperature compensation planning and has reproducibility of dimensions with in ± 0.01pH [3]. The 5-[2-(4-Benzo[d]isothiazol-3-yl-piperazin-1-yl)-ethyl]-6-chloro-1,3-dihydro-indol-2-one hydrochloride (ZPN) was purchased as of SD fine chemicals, India. Gold (III) chloride trihydrate ($HAuCl_4.3H_2O$) was obtained from Alchemy Laboratories, India. Each and every one chemical and solvents used were of analytical reagent grade. Twice distilled water was used for the preparation of all solutions.

100mg of Ziprasidone hydrochloride is weighed precisely and transferred in to a 100ml standard flask and made up to the mark with methanol. This solution is diluted as obligatory. A stock solution of 0.1 gold (III) was prepared by dissolving precise amount of $HAuCl_4.3H_2O$ in 1M hydrochloric acid and standardized. The buffer solution was prepared by incorporation in 0.2M sodium acetate with +1M hydrochloric acid (pH 2.5 – 3.5) 0.2M sodium acetate and + 0.2M acetic acid (pH 3.0 -6.0). The SDS surfactant was prepared by dissolving 2gm of sodium dodecyl sulphate (SRL Chemicals) in 100ml of twice distilled water. The working solutions were prepared daily by diluting the stock solution to an appropriate volume. The solutions of the studied meddlesome ions of suitable concentrations were prepared using analytical grade reagents.

Direct spectrophotometry

10ml standard flasks were taken and 5ml buffer solution (pH 5.0), altering volumes of 2.22 X 10^{-3}MZPN solution, and 0.5 ml of gold (III) (5.0 x 10^{-3}M) solution were added and then added1.5 ml of 2% Triton X-100 surfactant solution and was made up to the mark with double distilled water. This solution heated 60minutes at 65^0C for pink colure complex structure, after cooling to room temperature. The absorbance was measured at 600nm against the buffer blank. The calibration curve was constructed by plotting the absorbance against the amount of ZPN.

Derivative Methods

For the above solutions, first derivative spectra were recorded with a scan speed of nearly 2400nm $min^{-1}$and a slit width of 1nm with one degree of freedom. The derivative peak height was measured by the peak-zero method at respective wavelengths. The peak height was plotted against the amount of ZPN to obtain the calibration.

Zero-order Method

The ZPN (Ziprasidone Hydrochloride) reacts with gold (III) forming a pink – coloured soluble complex in the acidic medium in the presence of 2% Triton x-100 surfactant. The absorbance spectra of the ZPN and its gold (III) complex under most advantageous conditions are presented in (Figure 2).

a. Au(III) Vs buffer blank, b. ZPN – Au(III) Vs buffer blank (Au(III) excess),c. ZPN – Au(III) Vs buffer blank (ZPN excess).[ZPN] = 2.22 x 10^{-3}M;[Au(III)] = 5.0 x 10^{-3}M

The ZPN complex has an absorption maximum at

http://dx.doi.org/10.53709/CHE.2020.v01i01.004

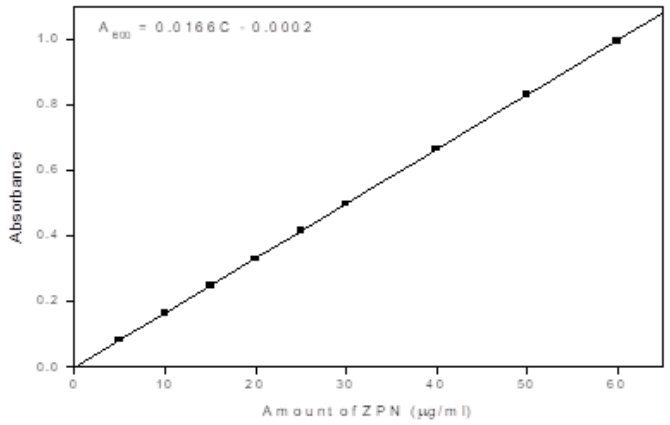

Figure-2: Absorption spectra of ZPN – Au (III) system

600nm, and at this wavelength the reagent has especially small absorbance hence, further analytical studies were carried out at 600m.Preliminary studies have indicated that ZPN reacts with Au(III) in aqueous acidic middling to form pink colour variety after heating the experimental solution at 65^0C for 60 minutes and cooling it to room temperature. The absorbance of the complex was found to be constant for further than 85 hours. The effect of pH on the intensity of colour formation was studied to optimize the pH of the ZPN complex. The grades indicate that absorbance was maximum and constant in the pH range of 4.5 – 5.5. Hence pH 5.0 was selected for further studies. A 10-fold molar surplus of gold (III) was necessary for complex and constant colour development. Excess of the metal ion has no effect on the compassion and absorbance of the complex. To determine the amount of ZPN at micro levels, beer's law was confirmed for [ZPN-Au (III)] complex by measuring the absorbance of the solutions containing dissimilar amounts of ZPN. A linear plot between the absorbance and the amount of ZPN gives the straight line obeying the beer' slaw equation (Figure 3).

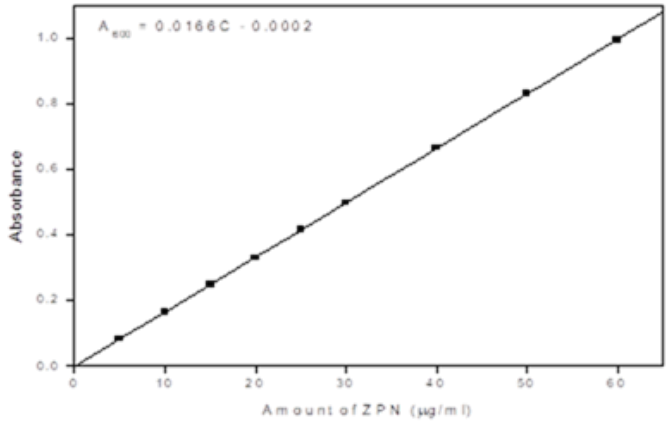

Figure-3: Absorbance Vs amount of ZPN (µg/ml);[Au(III)] = 5.0 X 10^{-3}M ; pH = 5.0; λ = 600 nm

The association coefficient ( ) of the calibration curve for experimental data was 0.9998. From the calibration plot, it is experiential that Beer's law was obeyed in the range of 5.0-60.0 µg/ml. The molar absorptivity and Sandal's compassion were 7.48 X 10^3 mol^{-1} cm^{-1} and 0.0604 µg cm^{-2}, respectively. The relative standard deviation at a attentiveness level of 10.00 µg/ml of ZPN was found to be 0.0010% (10 determinations).

RESULTS AND DISCUSSION

The result of various amounts of excipients that are generally associated with the ziprasidone hydrochloride in its pharmaceutical formulations are additional to a fixed amount of ziprasidone hydrochloride (10 µg/ml) solution and the absorbance measurements are carried out beneath optimal conditions and the results present in table 1. It was found the variety of ions do not cause an error of more than ± 4% in the absorbance is taken as the tolerance limit.it indicates that the excipients that are connected with ziprasidone hydrochloride do not interfere even in large quantities in the determination of ziprasidone hydrochloride building the method highly selective and direct (Table 1).

Table: 1. Forbearance limit of excipients; Amount of ZPN = 10 µg/ml; pH = 5.0

Excipient	Forbearance limit (µg/ml)
Fructose	1429
Glucose	1025
Sucrose	1558
Lactose	1937
Gelatin	2060
Starch	1619
Sodium Alginate	1506
Boric acid	2152
Magnesium stearate	1793

The work of art of complex was determined by jobs (Figure 4(a)) and molar ratio methods (Figure 4(b)). Both methods showed that a molar ratio of ZPN and Au (III) was 1:1. The firmness constant determined by job's method was being 2.54 x 10^4.

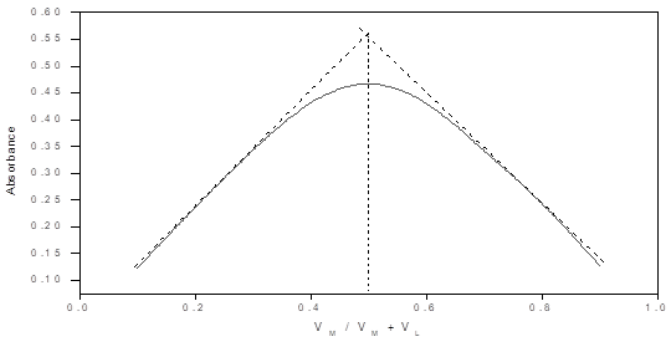

Figure 4 (a): Job's curve; Au(III)] = [ZPN] = 5.0 x 10^{-3}M ; pH 5.0 ; λ = 600 nm

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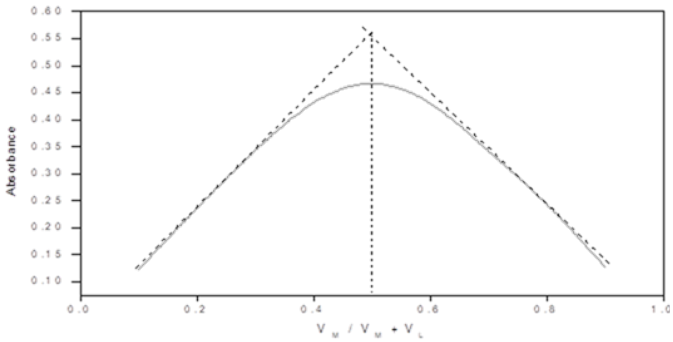

Figure 4(b): Mole ratio plot: [Au (III)] = [ZPN] = 5.0 x 10^{-3}M ; pH = 5.0 ; λ = 600 nm

Derivative methods

The first imitative spectra of experimental solutions containing different amounts of ZPN were recorded in the wavelength region. The first imitative spectra (Figure 4) showed maximum amplitude at 530nm. The derivative amplitudes at 530nm were found to be comparative to the concentrations of ZPN.The effect of various amounts of excipients on the derivative methods was also investigated. It was noticed that each and every one the excipients that did not obstruct in the zero-order determinations of ZPN (Table-1) also did not hinder in all the derivative spectrophotometric methods.

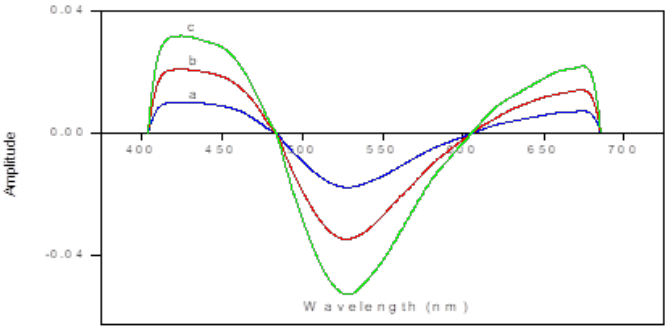

Figure 5: First derivative spectra of ZPN – Au (III) Vs Au (III) blank [ZPN] = a. 2.2 x 10^{-5}M; b. 4.4 x 10^{-5}M; c. 6.6 x 10^{-5}M

The projected method was applied for the determination of ziprasidone hydrochloride in pharmaceutical formulations and endorsed. The results of the determinations are given in below table 2.

Table 2: Statistical analysis of the determination of ziprasidone hydrochloride with gold (III)

Methods of analysis	Y-inter-cept	Correla-tion co-ef-ficient	Vari-ance	Detection limit (µg/ml)
First derivative spectro-photometer	-0.0002	0.99995	4.97 x 10^{-7}	1.168

CONCLUSIONS

The present work gives a fast, easy, responsive, and discerning method for the spectrophotometric resolve of ziprasidone hydrochloride. The process required the use of a surfactant. Further, derivative spectrophotometric methods also have been urbanized and are additional sensitive than zero-order method. The for the most part excipients do not obstruct with the determination. The process was used for the determination of ziprasidone hydrochloride in pharmaceutical formulations and certifies.

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