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Colorimetric determination of Ziprasidone hydrochloride in pharmaceutical formulations

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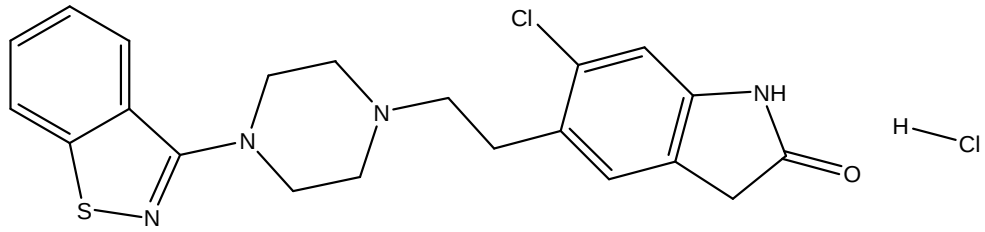
ABSTRACT

A simple and reproducible visible spectrophotometric method has been developed for the determination of Ziprasidone hydrochloride monohydrate (ZPN) in bulk and in dosage forms. The method is based on the reaction of ZPN with gold (III) chloride in the pH range 4.5 – 5.5 forming pink colour complex solution, showing absorption maxima at 600 nm. The linear plot indicates that Beer's law is obeyed in the range of 5.0 – 60.0 µg/ml of ziprasidone hydrochloride. The molar absorptivity and Sandell's sensitivity are 7.48 x 10^3 mol^{-1} cm^{-1} and 0.0604 µg/ cm^2 respectively. The standard deviation of the method for ten determinations of 10 µg/ml of ziprasidone hydrochloride is 0.0010. The correlation coefficient (γ) of the experimental data of the calibration plot is 0.9998. The effective range of concentration for accurate determination of ziprasidone hydrochloride as ascertained from Ringbom's plot and it is 10.0 - 50.0 µg/ml.

Key words: Ziprasidone, spectrophotometric method, correlation coefficient, Ringbom's plot.

INTRODUCTION

Chemically ziprasidone hydrochloride (ZPN), is 5-[2-(4-Benzo[d]isothiazol-3-yl-piperazin-1-yl)-ethyl]-6-chloro-1, 3-dihydro-indol-2-one hydrochloride. Its emperical formula and molecular weight are $C_{21}H_{22}Cl_2N_4OS$ and 448.94 respectively. Its structural formula is:



It is a white to slightly pink powder. ZPN is a typical antipsychotic with a unique pharmacological profile. It is chemically unrelated to the phenothiazines and the atypical antipsychotics currently available. The most 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[1,2].

ZPN exhibits a potent and highly selective antagonistic activity on the D_2 and 5-HT_{2A} receptors[3]. It also has a high affinity for the 5-HT_{1A}, 5-HT_{1D} and 5-HT_{2C} receptor subtypes that could contribute to the overall therapeutic effect[4]. Controlled research trials have shown that atypical antipsychotics have important 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)[5]The absorption of ZPN is rapid and C_{max} for ZPN and metabolites occurred at 2 to 6 h post dose[6].

Several methods have been reported using liquid chromatography with UV detection[7, 8], liquid chromatography with fluorescence detectio[9] and LC-MS[6] for the determination of ZPN in human plasma. So far, to our present knowledge, no visible spectrophotometric method is available for the determination of ZPN in bulk and in pharmaceutical dosage forms in literature. Hence, there is a need to develop sensitive, accurate and flexible visible spectrophotometric methods, which prompted the author to choose ZPN for the investigation.

The author has developed sensitive visible spectrophotometric method for the assay of ZPN based on its colour reaction with gold (III). It forms a pink colour complex with gold (III) in the pH range 4.5 – 5.5.

EXPERIMENTAL SECTION

Apparatus:

All spectral and absorbance measurements were made on Shimadzu digital UV-Visible spectrophotometer (UV-160A) with 10mm matched quartz cells.

Materials and reagents

All chemicals used were of analytical reagent grade and double distilled water was used for preparing the reagent solutions.

Preparation of Ziprasidone hydrochloride solution
100 mg of ziprasidone hydrochloride is weighed accurately and transferred into a 100ml standard flask, dissolved and made up to the mark with dimethyl formamide (DMF). This solution is diluted as required.

Preparation of Gold (III) solution
1gm of chloroauric acid (Johnson Mathews, materials technology, U.K.) is dissolved in distilled water after adding few drops dilute HCl. The solution is made upto the mark in 100 ml volumetric flask. The gold content of the solution is determined by rhodamine B method[10]. The working solutions are prepared by diluting the stock solution.

Determination of ziprasidone hydrochloride:
To explore the possibility of employing the colour reaction for the determination of ziprasidone hydrochloride, the absorbance of the experimental solution containing different amounts of ZPN, keeping the Au (III) concentration constant is measured

A plot of absorbance Vs amount of ziprasidone hydrochloride is presented in fig. 1 the straight line plot obtained obeys the equation A = 0.0166 – 0.0002. The linear plot indicates that Beer's law is obeyed in the range of 5.0 – 60.0 µg/ml of ziprasidone hydrochloride.

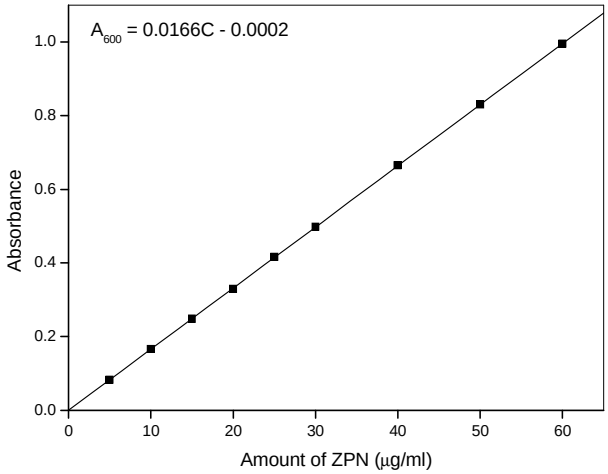


Fig. 1 Absorbance Vs amount of ZPN (µg/ml), [Au(III)] = 5.0 X 10^{-3}M ; pH = 5.0 ; λ = 600 nm

The molar absorptivity and Sandell's sensitivity are 7.48 x 10^3 mol^{-1} cm^{-1} and 0.0604 µg/cm^2 respectively. The standard deviation of the method for ten determinations of 10 µg/ml of ziprasidone hydrochloride is 0.0010. The correlation coefficient (γ) of the experimental data of the calibration plot is 0.9998. The effective range of concentration for accurate determination of ziprasidone hydrochloride as ascertained from Ringbom's plot and it is 10.0 - 50.0 µg/ml.

2. Determination of gold (III)
To explore the possibility of employing the colour reaction for the determination of gold (III) in trace level, the absorbance of the experimental solutions containing different amounts of gold (III), keeping the ziprasidone hydrochloride concentration in excess, is measured at 550 nm

The results are presented in the form of a plot of absorbance Vs amount of Au (III) and shown in fig. 2. The linear plot between the absorbance and the amount of Au (III) [fig. 2] obeys the equation A = 0.0103C – 0.0001 and indicates that Beer's law is obeyed in the range of 4.92 – 78.76 µg/ml.

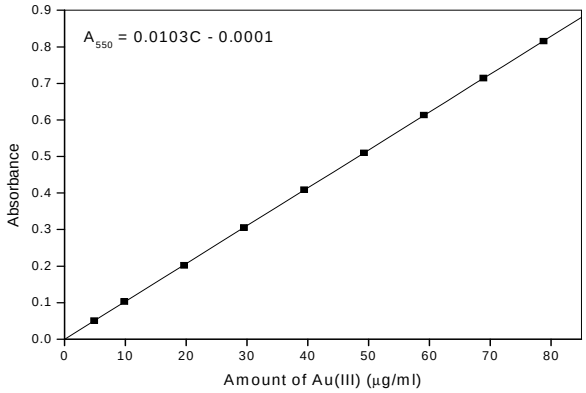


Fig. 2 Absorbance Vs amount of ZPN (µg/ml), [ZPN] = 2.22 X 10^{-3}M ; pH = 5.0 ; λ = 550 nm

The molar absorptivity and Sandell's sensitivity are 2.04 x 10^3 l mol^{-1} cm^{-1} and 0.0965 µg/cm^2 respectively. The standard deviation of the method for ten determinations of 19.69 µg/ml of Au (III) is 0.0011. The correlation coefficient (γ) of the calibration equation of the experimental data is 0.9999. The effective range of concentration of accurate determination of Au (III) as ascertained from Rigbom's plot is 9.84 – 68.91 µg/ml.

Assay of Pharmaceutical dosage form of ziprasidone hydrochloride

The present method for the determination ziprasidone hydrochloride is applied for its determination in a pharmaceutical sample.

Procedure

A known aliquot of pharmaceutical sample solution of ziprasidone hydrochloride is added to a 10 ml volumetric flask containing 5ml of buffer solution of pH 5.0 and 0.5 ml of gold (III) (5.0 x 10^{-3}M) solution 1.5 ml of 2% Triton X-100 solution. The contents are made upto the mark with distilled water. After heating for 60 minutes at 65^0C and cooling the solution to room temperature, the absorbance of the resulting solution is measured at 600 nm against the buffer blank. Figure 3 shows the Absorption spectra of ZPN – Au (III) system. The amount of ziprasidone hydrochloride is computed from the predetermined calibration plot at 600 nm. The results are presented in table 1.

Table 1: Assay of ziprasidone hydrochloride in pharmaceutical formulation

Sample (manufacturer formulation)	Label claim (mg)	Amount found * (mg)	Error (%)
GEODON capsules, Pfizer, Inc, USA	20.00	18.99	-0.55

** Average of seven determinations*

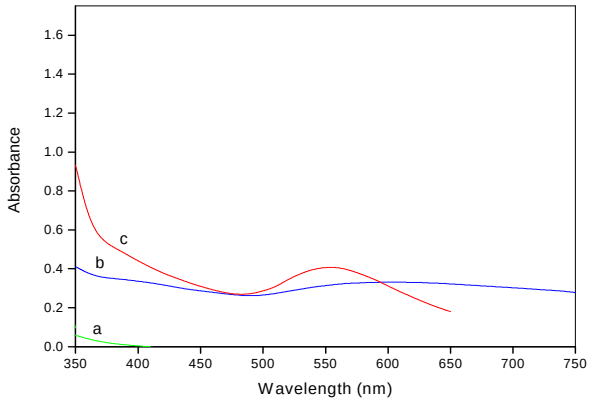


Fig. 3 Absorption spectra of ZPN – Au (III) system
a. Au(III) Vs buffer blank
b. ZPN – Au(III) Vs buffer blank (Au(III) excess)
c. ZPN – Au(III) Vs buffer blank (ZPN excess)
[Au(III)] = 5.0 x 10^{-3}M; [ZPN] = 2.22 x 10^{-3}M

Table 2: Optical and regression characteristics, precession and accuracy of the proposed method for ziprasidone hydrochloride and gold (III)

[ZPN] = 2.22 x 10^{-3}M ; pH = 5.0
[Au(III)] = 5.0 x 10^{-3}M ; λ = 600 nm

Parameter	ziprasidone hydrochloride	Gold(III)
Analytical wavelength (nm)	600	550
Beer's law limits (µg/ml)	5.0-60.0	4.92 - 78.76
Limits of detection (µg/ml)	0.1879	0.3764
Limits of quantization (µg/ml)	0.6265	1.2548
Molar absorptivity ($lmol^{-1}$ cm^{-1})	7.48 x 10^3	2.04 x 10^3
Sandell's sensitivity (µg cm^{-2})	0.0604	0.0965
Regression equation (y = a + bx)		
Slope (b)	0.0166	0.0103
Intercept (a)	-0.0002	-0.0001
Correlation coefficient (γ)	0.9998	0.9999
Standard Deviation (SD)	0.0010	0.0011

RESULTS AND DISCUSSION

Optical characteristics, accuracy and precession, data of the determinations of ziprasidone hydrochloride and gold (III) are presented in table. 2.

Interference studies

1. Effect of excipients

Various amounts of excipients that are generally associated with the ziprasidone hydrochloride in its pharmaceutical formulations are added to a fixed amount of ziprasidone hydrochloride (10 µg/ml) solution and the absorbance measurements are carried out under optimal conditions. The concentration (µg/ml) at which various ions do not cause an error of more than ± 4% in the absorbance is taken as the tolerance limit and the results are given in table 3

Table 3 Tolerance limit of excipients

Amount of ZPN = 10 µg/ml; pH = 5.0

Excipient	Tolerance 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 data in table 3 indicate that the excipients that are associated with ziprasidone hydrochloride do not interfere even in large quantities in the determination of ziprasidone hydrochloride making the method highly selective and direct.

CONCLUSION

Thus the proposed method was simple, sensitive, accurate and reproducible and can be used for the routine analysis of Ziprasidone hydrochloride monohydrate in bulk and in pharmaceutical dosage forms. The statistical parameters and recovery study data clearly indicate the reproducibility and accuracy of the methods. Analysis of the authentic sample containing ZPN showed no interference from the common excipients. Hence this method could be considered for the determination of ZPN in the quality control laboratories.

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