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Research Article

Development and Validation of New Analytical Methods for the Assay of Ziprasidone Hydrochloride Monohydrate

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Abstract

Ziprasidone hydrochloride monohydrate is an atypical antipsychotic used for the treatment of schizophrenia and bipolar disorder. New spectrophotometric methods (Zero order and first order) spectrophotometric methods have been proposed for the assay of Ziprasidone in pharmaceutical dosage forms using double beam SHIMADZU Model UV-1800UV-VIS spectrophotometer for the present study. Ziprasidone has shown linearity over the concentration range 0.5-60 µg/mL in distilled water and phosphate buffer (pH 7.5) in zero order spectroscopy and 5-70 µg/mL in first order derivative spectroscopic method and the methods were validated for precision and accuracy as per ICH guidelines. The proposed methods are simple, economical and can be successfully applied for the assay of Ziprasidone hydrochloride in pharmaceutical dosage forms.

Keywords: Ziprasidone Hydrochloride; Spectrophotometric; Phosphate Buffer Methanol; First Derivative Spectroscopy; Validation

Introduction

Ziprasidone hydrochloride monohydrate (CAS No. 138982-67-9) is chemically 5- [2-[4-(1,2-Benziso thiazol-3-yl)-1-piperazinyl] ethyl]-6-chloro-1,3-dihydro-2H-indol-2-one hydrochloride monohydrate with molecular weight 467.41 gms/mole. It is used to treat schizophrenia and bipolar disorder [1]. It can effectively reduce the rate and time of relapses in schizophrenia and can be used to treat manic episodes in bipolar disorder although the mechanism of action is unknown. Although Ziprasidone (Figure 1) is classified as an atypical antipsychotic [2] it appears to have a lower incidence of metabolic adverse effects compared to other medications in the same class.

Literature survey revealed that analytical methods such as RP-HPLC [3-12], LC-MS [13,14] (Table 1) and spectrophotometry [15-26] (Table 2) were developed earlier for the estimation of Ziprasidone in pharmaceutical dosage forms and biological fluids. In the present study, the authors have proposed new spectrophotometric methods for the assay of Ziprasidone hydrochloride monohydrate and the methods were validated as per ICH guidelines [27].

Materials and Methods

Shimadzu Model No. UV-1800 double beam UV-VIS spectrophotometer with quartz cells is used for the entire study, and all the solutions were scanned 200-400 nm. The Phosphate buffer (pH 7.5) was prepared as per IP 2022.

Ziprasidone HCl stock solution was prepared by dissolving 25 mg of Ziprasidone HCl in 25mL volumetric flask in methanol (1000 µg/mL) and working standard solutions were prepared in methanol (100 µg/mL) and further dilutions were prepared by diluting the working standard solutions with distilled water and Phosphate buffer (pH 7.5) as per the proposed requirement. It is available as capsules with label claim: 20, 40, 60 and 80 mg with brand names, Zipral (Lifecare Neuro Products Ltd.); Zipsydon (Sun Pharma), Zipwell (Wellona Pharma); Geodon (Pfizer); Zeldox (Pfizer) etc. in India.

Method validation

Zero order spectroscopy (D_o)

A series of Ziprasidone HCl monohydrate solutions 0.5-60 µg/mL were prepared from working standard solution on dilution

Table 1: Review of RP-HPLC and LC-MS methods.

Liquid Chromatographic methods (RP-HPLC)			
Mobile phase (v/v)	**Column**	**Linearity (µg/ml)**	**Reference**
Buffer (pH = 3.0): Methanol (45:55)	Zorbax SB C-8	20-299	[3]
Phosphate buffer (pH-3): methanol 60:40)	YMC C18	10-50	[4]
20 mM Ammonium acetate: Methanol (30:70)	Lichrospher RP-18	1-500 g mL-1	[5]
Water: Methanol (45:55)	Hemochrom-Intertsil C18-5U	2-12	[6]
Potassium dihydrogen orthophosphate buffer: Acetonitrile: Methanol	Hibar® C18	1-10	[7]
Buffer: Acetonitrile: methanol (45: 40: 15)	ODS C18	50-150	[8]
Methanol: Phosphate buffer (55:45)	ODS C18	0.5-30	[9]
Sodium phosphate monohydrate buffer (pH-6.0): Acetonitrile (40:60)	Sunsil C18	100-300	[10]
Methanol: Acetonitrile (60:40)	Thermo C_{18}	5-25	[11]
Phosphate buffer (pH 4.5): Acetonitrile (70:30)	RP-C8	50-150	[12]
Liquid Chromatography-Mass spectrometry methods (LC-MS)			
Mobile phase (v/v)	Column	Linearity (ng/ml)	Reference
Aqueous ammonium acetate: Methanol: Acetonitrile (10: 45: 45)	C18	0.25-500	[13]
0.01M Ammonium acetate pH 5.0: Acetonitrile (60:40) (UHPLC)	Waters Acquity BEH C18	25-100	[14]

Table 2: Review of Spectrophotometric Methods.

Reagent	Linearity (µg/ml)	λ_{max} (nm)	Reference
Phthalate buffer (pH 4.0)	4-24	415	[15]
Acetate buffer pH 4.0	0.5-30	315	[16]
Phosphate buffer pH 5.0	1-120	315.4	
Water: Acetonitrile (50:50)	10-30	260	[17]
Saline buffer (pH 7.4)	2-10	318	[18]
N-(1-naphthyl) ethylene diamine di hydrochloride	2-10	540	[19]
Ferric chloride and 1,10- Phenanthroline	250-2000	509	[20]
Ferric chloride and 2, 2'- bipyridyl	500-2500	521	
1M Methanolic HCl	10-70	315	[21]
Tpooo dye in 0.1N HCl	2-10	490	[22]
Methanol, Sodium dihydrogen phosphate buffer pH 7.4, 2% SLS	10-70	318	[23]
1N Folin-ciocalteau reagent	5-250	436	[24]
Potassium ferricyanide	10-50	733	
Picric acid	4-20	400	[25]
Chloroanillic acid	16-36	520	
MBTH reagent and $FeCl_3$	8-56	640	[26]
Methyl orange	3-15	420	
Phosphate buffer (pH 7.5)	5-70	209	Present method
Distilled water	0.5-60	208.6	

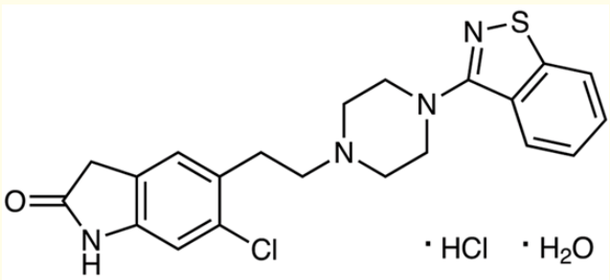

Figure 1: Chemical structure of Ziprasidone hydrochloride monohydrate.

with distilled water and phosphate buffer (pH 7.5) and scanned (200-400 nm) against their reagent blank. The zero order spectrum so obtained has shown λ_{max} at 208.6 nm with distilled water and at 209 nm with phosphate buffer (pH 7.5) respectively and a calibration curves were drawn by taking the concentration of the drug solution on the X-axis and the corresponding absorbance value on the Y-axis for both the methods.

First order derivative spectroscopy (D_1)

The individual zero-order absorption spectra of Ziprasidone HCl monohydrate so obtained were converted into their first-order derivative spectra with the help of inbuilt software of the instrument for both the methods. The resultant derivative spectrum has shown minima in both the methods and calibration curves were drawn by taking the concentration of the drug solution on the X-axis and the corresponding derivative absorbance value on the Y-axis.

Precision studies were performed by calculating the percentage relative standard deviation of independent assays of 6 determinations of the test concentration and the accuracy studies were carried out by standard addition method.

Assay of Ziprasidone HCl monohydrate capsules

Ziprasidone HCl monohydrate is available as capsules with label claim: 20, 40, 60 and 80 mg with different brand names in India. Two different brands of the marketed formulations were chosen and extracted with methanol, sonicated and diluted as per the requirement (10µg/mL) with distilled water and phosphate buffer (pH 7.5) and the and the percentage recovery was calculated as per the linear regression equations obtained.

Results and Discussion

Two different techniques – Zero-order (D_0) and First-order derivative spectroscopy (D_1) have been developed for the assay of Ziprasidone HCl monohydrate capsules using distilled water and phosphate buffer (pH 7.5). The review of earlier established analytical methods reported were summarised and compared with the present proposed methods in Table 1.

Zero order spectroscopy (D_0)

The zero order spectrum so obtained for Ziprasidone HCl monohydrate has shown λ_{max} at 208.6 nm with distilled water and at 209 nm with phosphate buffer (pH 7.5) respectively and the absorption spectra of Ziprasidone HCl monohydrate (D_0) were given in Figure 2. Ziprasidone HCl monohydrate obeys Beer-Lambert's law over the concentration range 0.5-60 µg/mL (Table 3) for distilled water and phosphate buffer (pH 7.5). The linear regression equations were found to be $y = 0.0513x + 0.0107$ ($R^2 = 0.9998$) and $y = 0.0542x + 0.0106$ ($R^2 = 0.9999$) for Phosphate buffer (pH 7.5) and distilled water (Figure 3) respectively.

Zero order spectroscopy (D_0)			First derivative spectroscopy (D_1)		
Conc. (µg/ml)	Absorbance at λ_{max}		Derivative absorbance (Minima)		
	Phosphate buffer (pH 7.5)	Distilled water	Conc.(µg/ml)	Phosphate buffer (pH 7.5)	Distilled water
0.5	0.028	0.031	5	0.012	-
1	0.053	0.059	10	0.023	0.08
2	-	0.1087	20	0.048	0.15
5	0.261	0.29	30	0.074	-
10	0.516	0.56	40	0.094	0.29
20	1.028	1.10	50	0.119	0.37
40	2.051	2.196	60	0.146	-
60	3.091	3.25	70	0.165	0.51

Table 3: Linearity of Ziprasidone HCl monohydrate.

*Mean of three replicates.

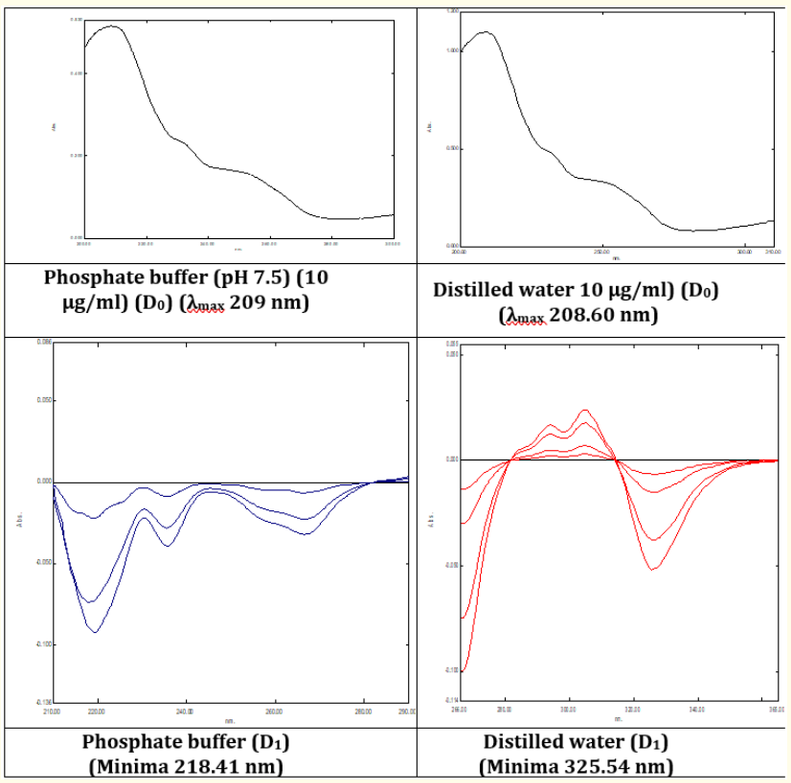

Figure 2: Absorption spectra of Ziprasidone HCl monohydrate in Zero order (D_0) & First derivative spectroscopy (D_1).

First order derivative spectroscopy (D_1)

The overlay first-order derivative spectra of Ziprasidone HCl monohydrate in distilled water and phosphate buffer (pH 7.5) were shown in Figure 2. The derivative spectrum has shown minima and therefore the minima value was taken against the concentration and calibration curves were drawn. Ziprasidone HCl monohydrate obeys Beer-Lambert's law over the concentration range 5-70 µg/mL in distilled water and respectively. The linear regression equations that are found to be y = 0.0024x + 0.0001 (R^2 = 0.9993) in phosphate buffer (pH 7.5) and y = 0.0073x + 0.0036 (R^2 = 0.9997) in distilled water respectively. The percentage RSD in accuracy and precision studies for all the methods was found to be less than 2 in indicating that the methods are precise and accurate. The assay was performed for the Ziprasidone HCl monohydrate capsules and the percentage recovery was calculated (Table 4). The optical characteristics of the method were shown in Table 4.

Table 4: Optical characteristics of Ziprasidone HCl monohydrate.

Parameters		Zero order spectroscopy (D_0)		First order derivative spectroscopy (D_1)	
		Phosphate buffer (pH 7.5)	Distilled water	Phosphate buffer (pH 7.5)	Distilled water
Linearity range (µg/mL)		0.5 – 60	0.5 – 60	0.1 – 20	0.1 – 15
λ_{max} or Minima (nm)		208.6	209	218.41	325.54
Molar extinction coefficient (litre/mole/cm^{-1})		2.3978×10^4	2.5333×10^4	0.1121×10^4	0.3412×10^4
Sandell's sensitivity (µg/cm^2/0.001 absorbance unit)		0.01938	0.01788	0.43478	0.125
Slope		0.0513	0.0542	0.0024	0.0073
Intercept		0.0107	0.0106	0.0001	0.0036
Correlation coefficient		0.9998	0.9999	0.9993	0.9997
Assay (%)	Brand I	99.91	99.57	99.63	99.81
	Brand II	99.82	99.49	99.54	99.75

Conclusion

All the spectrophotometric techniques were validated and found to be very simple, accurate, precise, and economical. These methods can be conveniently used for the routine analysis of Ziprasidone HCl monohydrate in pharmaceutical formulations.

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