

Development and Validation of Second Order Spectrophotometric Method for Quantitative estimation of Flupentixol dihydrochloride in Bulk and Pharmaceutical dosage form

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Abstract: A simple, specific, accurate and precise Second order derivative Spectroscopy method was developed and validated for the estimation of Flupentixol dihydrochloride in pharmaceutical dosage forms. Flupentixol dihydrochloride has the absorbance maxima at 214 nm. Beer's law was found to be obeyed in the concentration range of 3-15 µg/ml. The Correlation coefficient was 0.9998. The regression equation was found to be $Y = 0.0036 C + 0.0001$. The method was validated for linearity, accuracy, precision, limit of detection, limit of quantitation and ruggedness. The limit of detection and limit of quantitation for estimation of Flupentixol dihydrochloride was found to be 0.36 (mcg / ml) and 1.11 (mcg / ml), respectively. The % RSD values were less than 2. Recovery of Flupentixol dihydrochloride was found to be in the range of 99.18 – 99.87 %.

Keywords: Flupentixol dihydrochloride, UV Spectrophotometry, Second order Derivative Spectroscopy.

Introduction:

Flupentixol dihydrochloride, Chemically (EZ)-2-[4-[3-[2-(trifluoromethyl) thioxanthen-9-ylidene] propyl] piperazin-1-yl] ethanol. Dihydrochloride [1]. Flupentixol dihydrochloride is an antipsychotic neuroleptic drug. It is a thioxanthene and therefore closely related to the phenothiazines. It is a powerful antagonist of both D₁ and D₂ dopamine receptors.

Flupentixol dihydrochloride previously determined by spectrometry [2], (HPLC) [3, 4, 5, 6] and high performance thin layer chromatography (HPTLC) [7, 8]. No Zero order derivative Spectroscopy method was reported for the quantitative determination of Flupentixol dihydrochloride in bulk and pharmaceutical dosage forms.

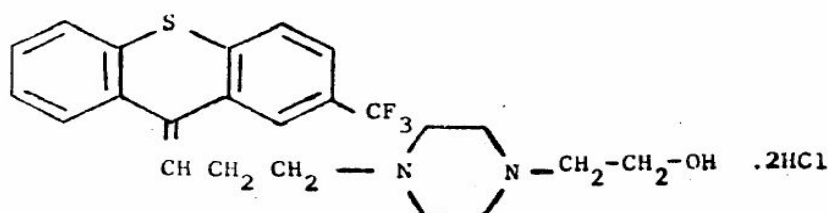


Figure 1: Chemical Structure of Flupentixol dihydrochloride

2. Experimental

2.1 Instruments and reagents

An analytically pure sample of Flupentixol dihydrochloride was procured as gift sample from Micro laboratories (Hosur, Chennai and India). Tablet formulation [fluaxol] was procured from a local pharmacy with labeled amount 3 mg per tablet. A Shimadzu UV-1800 UV/VIS spectrophotometer was used with 1 cm matched quartz cell. Distilled water was used as solvent.

2.2 Preparation of working standard drug solution

Standard Flupentixol dihydrochloride 100 mg was weighed and transferred to a 100 ml volumetric flask and dissolved in distilled water. The flask was shaken and volume was made up to the mark with distilled water to give a solution containing 1000 μg / ml. From this stock solution, pipetted out 10 ml and placed into

100 ml volumetric flask. The volume was made up to mark with distilled water to give a solution containing 100 μg / ml.

2.3 Analysis of marketed formulations

Twenty tablets were weighed and finely powdered. The powder equivalent to 50 mg of Flupentixol dihydrochloride was accurately weighed and transferred to volumetric flask of 50 ml capacity containing 25 ml of the distilled water and sonicated for 5 min. The flask was shaken and volume was made up to the mark with distilled water to give a solution of 1000 μg / ml. The above solution was centrifuged at 2000 rpm for 10 minutes and carefully filtered through Whatmann filter paper (No. 41). From this solution, 10ml was taken and diluted to 100 ml distilled water to give a solution of 100 μg / ml and used for the estimation of Flupentixol dihydrochloride.

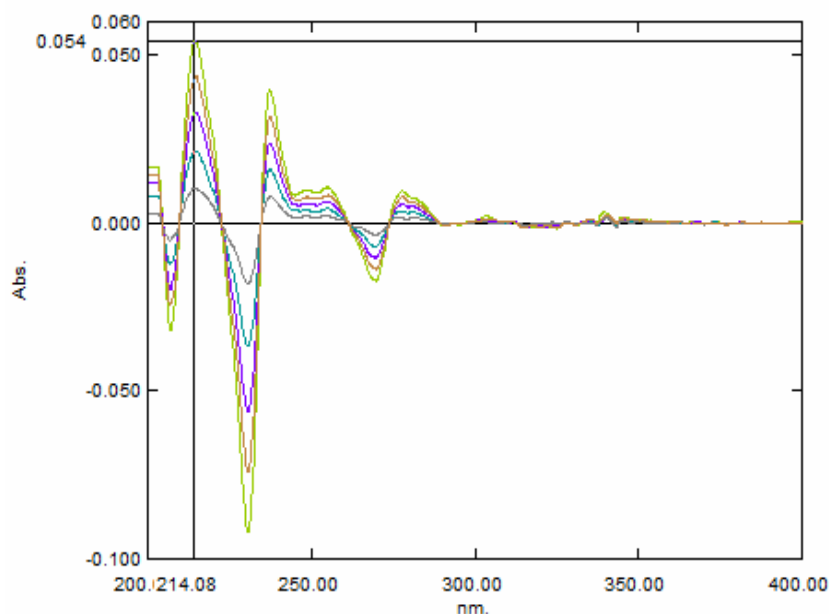


Fig: 1. Second order spectra of Flupentixol dihydrochloride at 214 nm

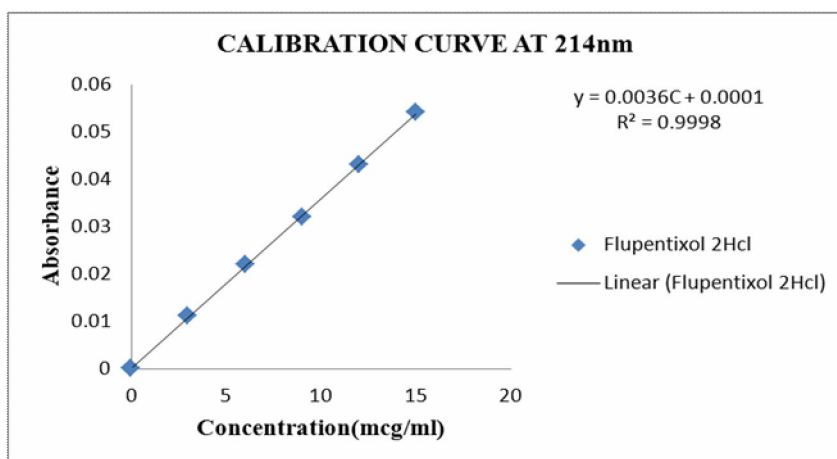


Fig: 2. Calibration curve for Flupentixol dihydrochloride at 214 nm by Second order derivative spectroscopy

Table 1: Optical characteristics and Other Parameters

Parameters	Second order Derivative Method
λ_{\max} (nm)	214
Beer's law limits (mcg / ml)	3-15
Molar extinction coefficient ($L \cdot mol^{-1} \cdot cm^{-1}$)	0.000533×10^4
Sandell's sensitivity (mcg/cm ² -0.001 absorbance units)	1.875
Regression equation (Y*)	$Y = 0.0036C + 0.0001$
Slope (b)	0.0036
Intercept (a)	0.0001
Correlation coefficient(r^2)	0.9998
Intraday Precision (% RSD**)	1.78
Inter day Precision (% RSD**)	1.76
Limit of detection (mcg / ml)	0.36
Limit of quantitation (mcg / ml)	1.11

*Y= b C + a where C is the concentration of Flupentixol dihydrochloride in mcg / ml and Y is the absorbance at the respective λ_{\max} .

**Average of six determinations.

Table 2: Determination of Accuracy results for Flupentixol dihydrochloride by Second order derivative spectroscopy

Tablet	Amount of sample (mcg / ml)	Amount of drug added (mcg / ml)	Amount Recovered (mcg / ml)	% Recovery \pm SD**
Sample	9	4.5	13.44	99.43 ± 0.51
	9	9	17.94	99.18 ± 0.27
	9	13.5	22.49	99.87 ± 0.42

**Average of six determinations.

Table 3: Determination of Precision for Flupentixol dihydrochloride at 214 nm by Second order derivative spectroscopy

Conc. mcg / ml	Intra-day Absorbance Mean \pm SD**	% CV	Inter-day Absorbance Mean \pm SD**	% CV
3	0.010 ± 0.000577	5.587261	$0.011 \pm 2.12E-18$	1.93E-14
6	0.021 ± 0.000577	2.706329	0.021 ± 0.000577	2.664694
9	0.032 ± 0.000577	1.785619	0.032 ± 0.000577	1.767399
12	0.043 ± 0.000577	1.332347	0.043 ± 0.000577	1.332347
15	0.054 ± 0.000577	1.062608	0.054 ± 0.000577	1.056129

**Average of six determinations.

Table 4: Analysis of tablet formulation

Tablet	Label claim (mg)	Analyst I		Analyst II	
		Amount found (mg)	Recovery \pm SD** (%)	Amount found (mg)	Recovery \pm SD** (%)
Sample	3	2.988	99.75 ± 0.11	2.979	99.28 ± 0.08

**Average of six determinations.

3. Result and Discussion

The method was validated according to the ICH guidelines with respect to linearity, accuracy, precision and ruggedness. [9, 10, 11]

Appropriate dilutions were prepared for drug from the standard stock solution and the solutions were scanned in the wavelength range of 200-400 nm. The Flupentixol dihydrochloride shows absorption maxima at 214 nm. The linearity was found in the concentration range of 3-15 mcg / ml was shown in Fig: 1. The Correlation coefficient was 0.9998. The regression equation was found to be $Y = 0.0036 C + 0.0001$ were shown in Fig: 2. The method was validated for accuracy and precision. All the Characteristic parameters were shown in Table: 1.

Determination of method accuracy by the standard addition method at three concentration levels returned a mean recovery of 98.58 - 101.4 was given in Table: 2.

6. References

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The results of Precision were shown in Table: 3.

The results of marketed formulation were shown in Table: 4.

4. Conclusion

The proposed method is validated and found to be simple, sensitive, accurate, precise, reproducible, rugged and relatively inexpensive. The developed method can be easily applied for the routine Quality Control analysis of Flupentixol dihydrochloride in bulk and pharmaceutical preparations.

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