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Estimation of Flupentixol in Bulk and Its Pharmaceutical Formulations by Precipitation Reagents

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Simple spectrphotometric methods (**A-C**) for the assay of flupentixol based on the formation of its complexes with alkaloidal precipitants are described. Flupentixol under quantitative precipitation in the form of molecular complexes with iodine (I_2, method **A**), ammonium molybdate (method **B**) or phosphomolybdic acid (method **C**) when used in excess. In addition to precipitation reactions, colour reactions have also been combined to estimate flupentixol. They are based on the colour formation with either unreacted precipitant of the filtrate (I_2) or released precipitant from the molecular complex (ammonium molybdate or phosphomolybdic acid) with chromogenic reagent such as P-N-methyl amino phenol sulphate (PMAP)-sulphanilic acid (Sac) (for I_2), potassium thiocyanate (for ammonium molybdate), cobalt nitrate (Co(II)-disodium salt of ethylene diamine tera acetic acid (EDTA) complex (for phosphomolybdic acid).

Key Words: Estimation, Flupentixol, Precipitation reagents.

INTRODUCTION

Flupenthixol[1] is a pronounced antipsychotic and anxiolytic agent and chemically it is 4-[-[2-(trifluoromethyl)-9*H*-thioxanthen-9-ylidene]propy]-1-piperzineethanol. The careful literature survey indicate that a few methods such as spectrophotometry[2,3] high performance liquid chromatography[4-8], GC[9,10], flourimetry[11-13], LC-MS[14] and GC-MS[15-17]. The analytically important functional groups of flupenthixol were not properly exploited for designing suitable spectrophotometric methods for the determination of flupenthixol. The aim of the present work is to provide simple and sensitive visible spectrophotometric methods for the estimation of flupenthixol in bulk form and formulations.

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EXPERIMENTAL

Spectral and absorbance measurements were made on Systronics UV-Visible Spectrophotometer 117 with 10 mm matched quartz cells.

All the chemicals and reagents used analytical grade and the solutions were freshly prepared. Aqueous solution of I_2 (0.089 %) in 0.83 % of potassium iodide, P-N-methyl amino phenol sulphate (PMAP) (2 %), sulphanilic acid (Sac) (0.4 %), hydrochloric acid (1 M) for method **A**; ammonium molybdate (AM) (2 %), potassium thiocyanate (PTC) (10 %), conc. HCl (used as it is) for method **B**; phosphomolybdic acid (PMA) (4 %) Co(II) (3 %), EDTA (4 %) for method **C**, 0.01 M HCl for methods **B** and **C** were prepared in triple distilled water. A one mg/mL solution was prepared by dissolving 100 mg of pure flupenthixol in 100 mL of distilled water and this stock solution was diluted stepwise with distilled water to obtain the working standard solution of concentrations 200 mg/mL for method **A**, **B** and **C**, respectively.

Recommended procedures

Method A: Aliquots of standard flupenthixol solution (0.5-2.5 mL, 200 µg/mL) were transferred into a series of centrifuge tubes containing 1.0 mL of 0.1 M HCl and the volume in each tube was adjusted to 4 mL with distilled water. Then 2.0 mL of iodine solution was added and centrifuged for 5 min. The precipitate was collected through filtration and subsequently washed with 1.5 mL of distilled water. The filtrate and washings were collected into a 25 mL graduated tube. Then 14 mL of pH 3.0 buffer and 1.5 mL of PMAP solutions were successively added. After 2 min, 2.0 mL of Sac solution was added. The absorbance was measured after 10 min at 520 nm against distilled water. A blank experiment was also carried out omitting the drug. The decrease in absorbance and in turn the drug concentration was obtained by subtracting the absorbance of the test solution from the blank. The amount of flupenthixol was calculated from Beer -Lambert's plot.

Method B: Aliquots of standard flupenthixol solution (0.5-2.5 mL, 200 µg/mL) were delivered into a series of centrifuge tubes and the volume in each tube was adjusted to 3.0 mL with 0.01 N HCl. Then 1.0 mL of ammonium molybdate was added and centrifuged for 5 min. The precipitate was collected through filtration followed by washing with 50 % alcohol until it is free from the reagent. The precipitate in each tube was dissolved in 5 mL of acetone and transferred into a 10 mL graduated tube. 3 mL each of conc. HCl and potassium thiocyanate solutions were successively added and the tubes were heated for 10 min, at 60 ºC. The test tubes were colled and the solution in each tube was made upto the mark with distilled water. The absorbance was measured at 480 nm against a similar reagent blank. The amount of flupenthixol was calculated from Beer-Lambert's plot.

Method C: Aliquots of standard flupenthixol solution (0.5-2.5 mL, 200 µg/mL) were delivered into a series of centrifuge tubes containing 0.25 mL of conc. HCl and the volume in each tube was adjusted 3.0 mL with distilled water. 1.5 mL of phosphomolybdic acid was added and centrifuged for 5 min and the precipitate was collected through filtration, followed by washing with distilled water until it is free from reagent. The precipitate in each tube was dissolved in 5.0 mL of acetone and transferred into a 25 mL graduated test tube. One mL each of cobalt nitrate and EDTA solutions were successively added and the tubes were heated for 10 min, at 60-70 ºC. The test tubes were cooled and solution in each tube was made upto the mark with distilled water. The absorbance was measured after 10 min at 840 nm against a similar reagent blank. The amount of flupenthixol was calculated from Beer-Lambert's plot.

RESULTS AND DISCUSSION

The optimum conditions for the colour development of methods (**A**, **B** and **C**) were established by varying the parameters one at a time, keeping the others fixed and observing the effect produced on the absorbance of the coloured species.

The optical characteristics such as Beer's law limits, molar absorptivity and Sandell's sensitivity for the methods (**A-C**) are given in Table-1. The precision of the method to the drug was found by measuring the absorbance of 6 separate samples containing known amounts of drug and the results obtained are incorporated in Table-1. Regression analysis using the method of least squares was made to evaluate the slope (b), intercept (a) and correlation coefficient (r) and standard error of estimation (Se) for each system and is presented in Table-1.

The accuracy of the methods was ascertained by comparing the results by proposed and reference methods (UV) statistically by the t- and F- tests (Table-2). The comparison shows that there is no significant difference between the results of studied methods and those of the reference ones. The similarity of the results is an obvious evidence that during the application of these methods, the excipients are usually present in pharmaceutical formulations do not interfere in the assay of proposed methods. As an additional check of accuracy of the proposed methods, recovery experiments were carried out. The recovery of the added amounts of standard drug were studied at 3 different levels. Each level was repeated for 6 times. From the amount of drug found, the % recovery was calculated in the usual way.

The higher λ_{max} values of all the proposed methods have a decessive advantage since the interference from the associated ingredients should be generally less at higher wavelengths than at lower wavelengths. Thus the

TABLE-1
OPTICAL CHARACTERISTICS, PRECISION AND ACCURACY OF THE PROPOSED METHODS OF FLUPENTIXOL

Parameters	Method **A**	Method **B**	Method **C**
λ_{max} (nm)	520	480	840
Beer's law limits (µg mL)	4-20	10-50	4-20
Molar absorptivity (1 mol^{-1} cm^{-1})	1.497×10^4	7.56×10^3	1.345×10^4
Sandell's sensitivity (µg/cm^2/0.001 absorbance unit)	0.0344	0.0679	0.0382
Regression equation y = a + bc*			
Slope (b)	0.0290	0.0147	0.0261
Intercept (a)	0.0004	-0.0007	0.0001
Correlation coefficient (r)	0.9999	0.9999	0.9999
Relative standard deviation (%)**	0.5350	0.2680	0.3070
% Range error** (0.05 level confidence limit)	0.2950	0.2240	0.2570

*Y = a + bc, where c is the concentration in µg/mL.
**From 6 determinations.

TABLE-2
DETERMINATION OF FLUPENTIXOL IN PHARMACEUTICAL FORMULATIONS

Sample* (Tablets)	Labeled method (mg)	Amount obtained (mg)				Recovery (%)		
		UV** method	Proposed method					
			A	**B**	**C**	**A**	**B**	**C**
T_1	1	0.99 ± 0.005	0.990 ± 0.004 F= 1.50 t= 0.60	0.990 ± 0.007 F= 1.50 t= 0.50	0.990 ± 0.005 F= 1.34 t= 0.90	99.73 ± 0.46	99.60 ± 0.70	99.86 ± 0.49
T_2	20	19.91 ± 0.039	19.91 ± 0.062 F= 2.58 t= 1.11	19.94 ± 0.05 F= 1.58 t= 2.2	19.87 ± 0.080 F= 4.97 t= 1.86	98.98 ± 0.41	99.56 ± 0.42	99.67 ± 0.09
T_3	40	39.69 ± 0.695	40.1 ± 1.97 F= 2.93 t= 1.46	39.88 ± 1.21 F= 2.07 t= 0.99	39.96 ± 1.60 F= 2.88 t= 0.87	100.19 ± 0.49	99.82 ± 0.30	99.76 ± 0.40
T_4	40	40.32 ± 2.668	39.9 ± 2.35 F= 2.91 t= 1.52	39.85 ± 1.61 F= 1.62 t= 0.99	39.8 ± 2.71 F= 2.41 t= 0.90	99.98 ± 0.58	99.62 ± 0.13	99.92 ± 0.12

*Four different batches of tablets from a pharmaceutical company.

proposed visible spectrophotometric methods are simple and sensitive with reasonable precision, accuracy and constitute better alternatives to the existing ones to the routine determination of flupenthixol in bulk forms and pharmaceutical formulations.

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