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Spectrophotometric Determination of Flutamide in Pharmaceutical Formulation

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Two simple, sensitive and precise spectrophotometric methods **(Method A** and **Method B)** are developed for the determination of flutamide (FMD) in pure and dosage forms. These methods are based on the formation of coloured species on treatment of reduced FMD with 1,10-phenanthroline and Fe(III) **[Method A]** and diazotization followed by coupling with α-naphthylamine **[Method B].**

Key Words: Spectrophotometric determination, Flutamide, Pharmaceutical formulation.

INTRODUCTION

Flutamide is 2-methyl-N-[4-nitro-3-(trifluoromethyl) phenyl] propanamide[1] which is used in the treatment of prostatic carcinoma and as anti-androgenic agent. Few methods have appeared in literature for the determination of FMD in biological fluids and pharmaceutical formulations. The techniques used include HPLC[2–5], GLC[6], polarography[3, 7], extractive spectrophotometry[11], colorimetry[8–10], UV-spectrophotometry[9] and planar chromatography[12]. This paper describes the development of two simple, sensitive spectrophotometric methods for the routine quality control analysis of pharmaceutical formulations containing flutamide (FMD). The NO_2 group present in FMD is reduced to primary aromatic (amine) NH_2 group with zinc dust and hydrochloric acid. The primary aromatic amine reacts with 1,10-phenanthroline and Fe(III) or α-naphthylamine reagent to form coloured species having maximum absorbances at 510 and 540 nm respectively.

EXPERIMENTAL

All spectral measurements were made on Systronics Model No. 2201 UV-Vis double beam spectrophotometer.

All the chemicals used were of analytical grade. All the solutions were freshly prepared with double distilled water. Aqueous solutions of 1,10-phenanthroline (0.01 M), ferric chloride (0.003 M) and orthophosphoric acid (0.2 M) were prepared for **Method A**. Alcoholic solution of α-naphthylamine (0.1%) and aqueous solutions of $NaNO_2$ (0.1%), ammonium sulfamate (0.5%) and HCl (5 N) were prepared for **Method B.**

Standard and sample solutions of FMD: About 100 mg of FMD (pure or formulation) was dissolved in 20 mL of methanol and treated with 10 mL of 5 N HCl and 5 g of zinc dust was added in portions. After standing for 1 h at room temperature, the solution was filtered through cotton wool, the residue was washed with 3 × 15 mL portions of distilled water and the volume of the filtrate was made up to 100 mL with distilled water. The final concentration of FMD was brought to 20 μg/mL **(Method A)** and 50 μg/mL **(Method B).**

Recommended Procedures

Method A: Aliquots of standard solutions containing 0.2–2.0 mL (1 mL = 20 μg) of reduced FMD were transferred into a series of 10 mL graduated tubes. Then 1 mL of ferric chloride (0.003 M) and 1.5 mL of 1,10-phenanthroline (0.01 M) were added to each tube. The tubes were then heated on boiling water bath for 10 min, cooled to room temperature and 2 mL of orthophosphoric acid (0.2 M) was added to each tube and the total volume was brought to 10 mL with distilled water. The absorbance of the red coloured species was measured at 510 nm against the reagent blank. The amount of FMD in the sample was computed from the calibration curve.

Method B: To a series of 10 mL graduated test tubes aliquots of reduced FMD ranging from 0.2–2.0 mL (1 mL = 50 μg) and aqueous solution of HCl (5 N, 1 mL) and sodium nitrite (0.1%, 1 mL) were added and kept aside for 5 min. Then aqueous solution of ammonium sulfamate (0.5%, 1 mL) and α-naphthylamine reagent (0.1%, 1 mL) were successively added and diluted to 10 mL with distilled water. The absorbance of the pink coloured species was measured at 540 nm against reagent blank. The amount of FMD was read from the calibration curve.

RESULTS AND DISCUSSION

The optical characteristics such as Beer's law limits, molar absorptivity, Sandell's sensitivity are presented in Table-1. The regression analysis using the method of least squares was made for the slope (a), intercept (b) and correlation coefficient (r) and the results are summarized in Table-1. The per cent relative standard deviations and per cent range of error (0.05 and 0.01 level confidence limits) are given in Table-1. The results showed that the methods have reasonable precision. Comparison of the results obtained with the proposed and reported methods for the dosage forms (Table-2) confirm the suitability of these methods for pharmaceutical dosage forms. The other ingredients and excipients usually present in the pharmaceutical dosage forms did not interfere.

The presence of NH_2 group in reduced FMD enables the use of redox reaction followed by complexation with 1,10-phenanthroline. The red coloured complex is due to the formation of ferroin in **Method A.** The pink coloured complex formed in **Method B** is due to the diazo coupling reaction of reduced FMD with α-naphthylamine reagent.

The proposed methods are found to be simple, sensitive, accurate and can be used in the determination of flutamide and their pharmaceutical dosage forms in the routine manner.

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

Parameters	Method A	Method B
λ_{max} (nm)	510	540
Beer's law limits (μg/mL)	0.4–4.0	1.0–10.0
Molar absorptivity (L mol^{-1}, cm^{-1})	8.985×10^4	2.756×10^4
Sandell' s sensitivity (μg/cm^2/0.001 abs. unit)	0.0031	0.012
Correlation coefficient (r)	0.9998	0.9999
Regression equation (y)†:		
Slope (a)	3.18×10^{-1}	1.004×10^{-1}
Intercept (b)	0.0021	0.0015
Per cent relative standard deviation (% RSD)†	0.7208	0.6727
% Range of error		
0.55 level confidence limit	±0.6027	±0.5624
0.01 level confidence limit	±0.8917	±0.8321

* Y = a + bx, where x is the concentration of FMD in μg/mL and y is the absorbance unit.
† For six replicate samples.

TABLE-2
ESTIMATION OF FLUTAMIDE IN PHARMACEUTICAL FORMULATIONS

Formulations	Labelled amount (mg/tablet)	Amount found by proposed method*		Reference[8] method	% Recovery	
		Method A	Method B		Method A	Method B
1	250	250.1 ± 0.56 t = 0.97 F = 1.25	249.9 ± 0.71 t = 1.35 F = 3.49	251.0 ± 0.38	100.04	99.76
2	250	249.9 ± 0.38 t = 1.08 F = 2.40	250.0 ± 0.40 t = 0.19 F = 2.52	249.6 ± 0.60	99.96	100.10
3	250	248.9 ± 0.36 t = 0.80 F = 1.53	249.6 ± 0.26 t = 0.92 F = 3.23	249.8 ± 0.40	99.86	99.84

*Average standard deviation of six determinations; the t- and F-values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limits, t = 2.57, F = 5.05.

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