NEW SPECTROPHOTOMETRIC ANALYSIS OF FLUTAMIDE IN PURE AND DOSAGE FORMS

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ABSTRACT

A simple rapid and sensitive visible spectro photometric method for the assay of flutamide drug, based on the oxidation of the drug with excess quantity of the Oxidant Nitrous acid and the excess Nitrous and is determined using a dye cresyl fast violet acetate CFVA, with a maximum absorption at 555 nm. The method is applicable to pure samples as well as dosage forms of the drug. The results obtained by the proposed method were in good agreement with the labelled amounts.

Keywords: Flutamide, Cresyl fast violet acetate CFVA, Nitrosation Spectro photometry.

Introduction:

Flutamide (FMD) chemically known as propanamide, 2-methyl-N-[4-nitro-3-(trinfluoromethyl) phenyl] is an anti-androgen drug which is used for to treat prostate cancer.

Floutamide[1] is official is USP[2] analytical methods for the determination of flutamide are chromatography[3] polarography[4] gas chromatography[5], high-performance liquid chromatography[6-7] UV spectrophotometric and visible spectrophotometric methods[8-16] have been reported for this drug. The present communication reports new visible spectrophotometric method based on the formation of diazotization followed by reduction with HON_2 & CFVA. Sastry et al[17] developed an indirect method for the assay of some drugs using Nitrous acid/cresyl fast violet acetate (CFVA, benzo, phenoxazin-5-ium-5-imino-9-aminoacetic acid). In this method the drug is treated with known excess of oxidant Nitrous acid and the excess nitrous and is estimated with known excess of CFVA. The pinkish violet colour with red fluorescence (original dye) changes to yellow. The change

may be due to alteration of the dye structure in which the original chromophore and auxochromes change due to nitrosation with involvement of amino group of the drug.

MATERIALS AND METHODS

A Milton Roy spectronic 1201 and systronic 106 spectrophotometers with 1cm matched quartz cells were used for all spectral and absorbance measurements.

Preparation of Reagents:

All the chemicals and reagents used were of analytical or pharmacopocial grade and all solutions were freshly prepared in doubly distilled water.

$NaNO_2$ solution (E.Merck, 0.002% 0.2899×10^{-3} M)	Prepared by dissolving 100mg of sodium nitrite in 100ml of distilled water and standardized. Two ml of this solution was further diluted to 100 ml to get desired concentration (20µg/l) or 0.2899×10^{3}M)
CFVA Solution Croma, 0.005% 1.5560×10^{-4}M	Prepared by dissolving 25mg of CFVA in 500ml with distilled water.
Hydrochloric acid E.Merck 5M	Prepared by diluting 217.5ml of Conc. HCl to 500ml with distilled water.

Preparation of solutions:

Reduced FMD for Analysis

Fifty mg of FMD was dissolved in 10ml of Methanol. The solution was treated with 4.0 ml of 2M HCl and 1gm of Zinc dust was added in portion. After standing for 45min at room temperature the solution was filtered subsequently the solution was treated with 4MNaoH solution for bringing down the pH (6.5 – 7.0) almost neutrality.

The working standard solution for this method was prepared by suitable dilution of the corresponding stock solution with distilled water (50µg/ ml).

Procedure:

Aliquots of standard FMD solution (0.5 – 2.5 ml, 50 µg/ ml) were added to a series of 25 ml graduated test tubes. Then 1.25 ml of 5M HCl and 2.0 ml of $NANO_2$ (20 µg/ml) solutions were added successively and the volume in each flask was brought to 15.0 ml with distilled water. After 3 min 10.0ml of CFVA solution was added, mixed thoroughly

and the absorbance was measured. After 5 minutes at 555 nm against distilled water. A blank experiment was carried out in a similar manner omitting drug. The decrease in absorbance correspond to consumed $NaNO_2$ which in turn to drug concentration was obtained by subtracting the absorbance of the blank solution from that of the test solution. The amount of drug present was calculated from the Beer-Lambert plot drawn between the amount of drug and decrease in the absorbance of CFVA.

Analysis of pharmaceutical preparations:

Tablet powder equivalent to 100mg was weighted for this method and the solution was prepared as under standard solution preparation and filtered if insoluble portion present and analysed as per the assay procedure described for pure sample.

Results and Discussion:

The optical characteristics such as beer's law limits molar extinction coefficient, sandell's sensitivity, correlation coefficient, slope and intercept data from linear least squares treatment and percent relative standard deviation (from six replicate samples) were present in Table 1.

Table – 1

Optical and regression characteristics, precision and accuracy of proposed method for FMD

Parameter	Method
λ_{max} (nm)	555
Beer's law limits (µg/ml)	1 - 5
Molar absorptivity ($1mol^{-1}$ cm^{-1})	2.50×10^4
Sandell's sensitivity µg. cm^{-2}/0.001 Abs. units	1.11×10^{-2}
Regression equation ($\gamma = a + bc$) slope (b)	9.0×10^{-2}
Intercept (a)	5.0×10^{-4}
Correlation coefficient (r)	0.9999
Relative standard deviation (%)*	0.37
Range of error (Confidence limits) 0.005 level 0.01 level	0.40 0.62

Calculation from 6 determinations

The proposed method have been applied to dosage from (Tablets). The accuracy of the method was ascertained by comparing the results from the proposed and reported methods, statistically by the t and f-tests and found not to differ significantly. To evaluate the validity and reproducibility of the method, known amounts of pure drug was added to previously analysed samples and the mixtures by the proposed methods and the results are incorporated in Table-2. There is no interference of other ingredients present in the formulation.

Table-2

Assay of flutamide in pharmaceutical formulation

Pharmaceutical formulations*	Labelled amount	Amount found in proposed method**%	Found reference method	% recovery by proposed method***
Cytomid	250	99.9 ± 0.20 t = 0.235 F = 1.326	99.6 ± 0.19	99.8 ± 0.60
Drogenil	250	99.8 ± 0.26 t = 0.278 F = 2.589	99.2 ± 0.17	99.4 ± 0.17
Flutacane	250	99.4 ± 0.48 t = 0.452 F = 1.407	99.4 ± 0.36	99.5 ± 0.64
Plutamide	250	99.6 ± 0.45 t = 0.550 F = 2.455	100.1 ± 0.72	99.7 ± 0.49

* Formulations manufactured by four different pharmaceutical companies

** Average ± standard deviations of six determinations the t – and f- values refer to comparision of proposed with reference methods. Theoretical values at 95% confidence limits, f=5.05, t2.57.

*** Recovery of compared to the pharmaceutical formulation (average of three determinations)

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