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NOTE

Spectrophotometric Estimation of Flutamide in Pharmaceutical Dosage Forms

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Two simple and sensitive spectrophotometric methods (methods A and B) for the estimation of flutamide for both bulk and pharmaceutical dosage forms were developed. Method A is based on the formation of reddish pink colored chromogen with chromotropic acid having λ_{max} at 525 nm and method B is based on the formation of yellowish brown coloured complex with resorcinol exhibiting λ_{max} at 485 nm.

Flutamide (FMD) is α^1, α^1, α^1-trifluoro-4-nitrosobutyro-*m*-toludide[1], which is used in the treatment of prostatic carcinoma and as antiandrogenic agent. Few analytical methods which include HPLC[2], GLC[3], polarography[4], colorimetry[5,6] have been reported for the estimation of flutamide. The NO_2 group present in flutamide is reduced to primary aromatic NH_2 group with zinc dust and hydrochloric acid. The NO_2 group reacts with sodium nitrite and forms a diazo compound, which couples with chromotropic acid to form reddish pink chromogen that was measured at 525 nm (Method A). In the second method, after diazotization with sodium nitrite it is coupled with resorcinol to form yellowish brown chromogen having absorption maximum at 485 nm (Method B). These methods have been extended to the pharmaceutical formulations containing flutamide.

All the chemicals used were of analytical grade. HCl (5 N), sodium nitrite (0.1%) ammonium sulfamate (0.5%), chromotropic acid (1.0%), resorcinol (1.0%) and NaOH (5.0 N) were prepared in distilled water. All spectral measurements were made on Systronics UV-Visible spectrophotometer 117 with spectral bandwidth of 1 nm and using a pair of 10 mm matched quartz cells.

Standard and Sample Solution: About 100 mg of flutamide (pure or tablet powder) was accurately weighed and dissolved in 10 mL of methanol, then treated with 10 mL 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 and washed with 3 × 15 mL portions of distilled water and volume was made up to 100 mL with distilled water. The final concentration of reduced FMD was brought to 50 micrograms per mL by further dilution with distilled water.

Assay Procedure

Method A: To an aliquot of standard reduced flutamide solution ranging from 0.5 to 4 mL (1 mL = 50 μg), aqueous solutions of HCl (5 N) 0.5 mL and sodium nitrite (0.1%) 2 mL were added and kept a side for 5 min. Then aqueous solutions of

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ammonium sulfamate (0.5%) 0.5 mL, chromotropic acid (1.0%) 3 mL and sodium hydroxide (5 N) 1 mL were successively added and after 2 min the final volume was made up to 25 mL with distilled water. The absorbance of reddish pink coloured species was measured at 525 nm against reagent blank. The amount of flutamide present in the sample solution was computed from its calibration curve.

Method B: Volumes of standard reduced flutamide solution ranging from 0.2 to 1 mL (1 mL = 50 μg) were transferred into a series of 10 mL volumetric flasks. 1 mL of HCl (5 N) and 1.5 mL of sodium nitrite (0.1%) were added and kept aside for 5 min. Then aqueous solutions of 1.5 mL resorcinol (1.0%) and 2 mL sodium hydroxide (5 N) were added to each flask and the total volume was made up to 10 mL with distilled water. The yellowish brown coloured chromogen was measured at 485 nm against reagent blank. The amount of flutamide present in the sample solution was read from its calibration curve.

The optical characteristics such as Beer's law limits (μg/mL), molar extinction coefficient (L $mole^{-1}$ cm^{-1}), Sandell's sensitivity (μg/cm^2/0.001 absorbance unit), % relative standard deviation (calculated from eight samples), % range of error (0.05 and 0.01 confidence limits) for the proposed methods are 1–8, 2.5824×10^4, 0.01069, 0.76316, 0.6381, 0.9440 respectively for method A and 1–5, 4.143×10^4, 0.00666, 0.47750, 0.3992, 0.5907 respectively for method B. The results showed that the methods have reasonable precision and accuracy. Comparison of the results obtained with the proposed methods and the reference method for dosage forms and the recovery studies (Table-1) confirm the suitability of these methods for the routine determination of flutamide in pharmaceutical dosage forms.

TABLE-1
ESTIMATION OF FLUTAMIDE IN PHARMACEUTICAL FORMULATIONS

Sample	Labelled amount (mg)	Amount obtained (mg)		Per cent recovery of the proposed method	
		Method A	Method B	A	B
1.	250	250.1	249.4	100.04	99.76
2.	250	249.9	250.0	99.96	100.00
3.	250	248.9	249.6	99.86	99.84
4.	250	250.3	249.9	100.12	99.96

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