formulation by proposed procedures and the chosen reference[1] procedure are given in Table 2. The application of t and F-tests to these results show that they do not differ significantly. The results are summarised in Table 2.

The proposed method exploits the oxidation reaction of TS with sodium metaperiodate due to the presence of vicinol diol in TS. This method does not involve any critical reaction conditions and has distinct edge over the reported methods. Thus the proposed method is simple and sensitive with good precision and accuracy for the assay of TS in the pure form and pharmaceutical formulations.


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# Spectrophotometric Methods for the Determination of Flutamide in Tablets


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**Simple and sensitive spectrophotometric methods for the determination of flutamide in either pure form or in its pharmaceutical preparations are described. The first method is based on the reaction of reduced flutamide with Ehrlich reagent in alcohol medium to produce a yellow Schiff base with a $\lambda_{max}$ of 430 nm. In the second method, the diazotisation of reduced flutamide followed by complexation with molybdate ions and pyrocatechol in sulphuric acid medium to give a pink coloured complex with a $\lambda_{max}$ of 540 nm. Both the methods are highly reproducible and results of the assay of flutamide in tablets compare favourably with the reported method.**


Flutamide (FLA), chemically known as 2-methyl-N[4-nitro-3-(trifluoromethyl)phenyl]propanamide is widely used as antineoplastic and antiandrogen drug[1]. This new drug is recently included in the USP, which involves a chromatographic method for the analysis of the pure drug and FLA capsules[2]. The reported methods for the determination of FLA include polarography[3], gas-chromatography[4], HPLC[5,6] and spectrophotometric methods[7-12]. In continuation of our work on the spectrophotometric determination of organic compounds of pharmaceutical importance[13-15], we have succeeded in developing two visible spectrophotometric methods (A and B) for the determination of FLA. Method A is based on the reaction of 4-dimethylaminobenzaldehyde (DAB) with the reduced flutamide. Method B is based on the reaction between the diazotisation product of reduced FLA with molybdate ions and pyrocatechol. The methods offer the advantages of sensitivity, selectivity and rapidity without the need for extraction or heating.

A JASCO model UVIDEC-610 UV/VIS spectrophotometer with 1 cm matched cells was used for absorbance mea-


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surements. Pharmaceutical grade FLA was obtained as a gift sample from Cipla Ltd, Mumbai. DAB was purchased from Aldrich Chemical Co, Milwaukee, WI, USA. Both pyrocatechol and sodium nitrite were BDH samples and molybdic acid was purchased from Merck, Germany. AR HCl, AR $H_2SO_4$, absolute methanol and alcohol were used. All other chemicals and solvents used were of analytical reagents grade. Deionized water was used to prepare all solutions. Commercial dosage forms were purchased from Cipla, Fulford, Criticare, Torrent and BDH. Accurately weighed (100 mg) FLA was transferred to a 100 ml beaker containing 4.0 ml of methanol. Half a gram of zinc dust and 4 ml of concentrated HCl were added and the mixture was left for 30 min. The solution was filtered into a 100 ml standard flask and made upto the mark. The working standard solution of reduced FLA containing 25 µg/ml was prepared by further dilution. A 5% Ehrlich reagent (DAB) solution was prepared in alcohol. An aqueous solution of 1% $NaNO_2$, 2% sulphamic acid, 4% sodium molybdate (prepared by dissolving molybdic acid in 4 ml of 5 mol $dm^{-3}$ NaOH and neutralised by dilute HCl to get a clear solution), 0.2% aqueous pyrocatechol and 1:1 $H_2SO_4$ were used.

Aliquots of the working standard solution of reduced flutamide (25-40 µg/ml for method A; 10-200 µg/ml for method B) were transferred into 25 ml calibrated flasks. For the method A, 3 ml of 5 M $H_2SO_4$ was added followed by the addition of 5 ml of 5% Ehrlich reagent and the volume was made up with alcohol. After mixing the solution thoroughly, the absorbance was measured at 430 nm against the corresponding reagent blank. For method B, 2 ml of 1% $NaNO_2$ was added, cooled, in an ice bath, 2 ml of 2% sulphamic acid was added, cooled, followed by the addition of 2 ml of each of 4% sodium molybdate and 0.2% of pyrocatechol, mixed well, left for 15 min and the solution was diluted to the mark with 1:1 $H_2SO_4$. The solution was mixed well and the absorbance was measured at 540 nm against the corresponding reagent blank. The calibration graphs were constructed for the both the methods.

Twenty tablets were powdered and mixed thoroughly. An amount equivalent to 50 mg of FLA was dissolved in 4 ml of methanol and the substance was subjected to reduction using zinc and HCl. The solution was filtered and the filterate was made up to 100 ml and an aliquot of this solution was treated as described above for the pure sample either by method A or by method B.

The optical characteristics and precision data for both the methods are given in Table 1. The relative standard deviation (%) given in Table 1 is for five replicates. For the method A, it was found that 2-4 ml of 5 M $H_2SO_4$ and 3-7 ml of Ehrlich reagent were necessary for the maximum colour development. In the method B, 1% $NaNO_2$ in the range of 1-3 ml, 2% sulphamic acid in the range of 1-3 ml, 1-3 ml of 4% sodium molybdate and 1-3 ml of 0.2% pyrocatechol were required to achieve the maximum colour intensity. Hence, the required volumes of all the reagents were used as mentioned in the recommended procedure. Some of the common excipients which often accompany the pharmaceutical preparations like starch, gum acacia, talc, carboxymethycellulose, glucose, lactose, sucrose, sodium alginate and magnesium stearate (50 mg each) do not interfere in both the methods (9 µg/ml of FLA for methods A and B). The percentage recovery of FLA in presence of these excipients ranged from 99.3 to 101.4.

The application of the methods for the assay of pharmaceutical preparations were examined. The results of the assay of available tablets of FLA are summarized in Table 2. The percentage relative standard deviation given is for five determinations. The results are highly reproducible and the assay of tablets were cross checked by the reported (NEDA)

TABLE 1: OPTICAL CHARACTERISTICS AND PRECISION DATA.

| Parameters / Characteristics | Method A | Method B |
|---|---|---|
| $\lambda_{max}$ (nm) | 430 | 540 |
| Stability (h) | 4.0 | 1.5 |
| Beer's law range (µg/ml) | 1.0-18 | 0.4-18 |
| Limit of detection (µg/ml) | 0.58 | 0.32 |
| Limit of quantification (µg/ml) | 1.92 | 1.067 |
| Molar absorptivity (l/mol.cm) | $0.56 \times 10^4$ | $0.15 \times 10^5$ |
| Sandell's sensitivity (µg/cm²) | 0.033 | 0.019 |
| Optimum photometric range (µg/ml) | 3.0-15 | 0.9-15 |
| Regression equation Y = bx+a | | |
| Slope (b) | 0.0227 | 0.0368 |
| Intercept (a) | 0.01168 | 0.0093 |
| Correlation coefficient (r) | 0.9995 | 0.9996 |
| Relative standard deviation (%) | 0.32 | 0.48 |
| Range of error | ±0.44 | ±0.67 |

TABLE 2: DETERMINATION OF FLUTAMIDE IN PHARMACEUTICAL PREPARATIONS.

| Tablet | Label claim (mg) | Amount of FLA found (mg) | | |
|---|---|---|---|---|
| | | Proposed methods | | NEDA method[9] |
| | | A | B | |
| Cytomid | 250 | 249.3 ± 0.4 | 249.4 ± 0.5 | 249.4 ± 0.6 |
| Drogenil | 250 | 249.6 ± 0.3 | 249.5 ± 0.5 | 249.4 ± 0.6 |
| Flutacare | 250 | 249.2 ± 0.4 | 249.4 ± 0.6 | 249.3 ± 0.6 |
| Plutamide | 250 | 249.5 ± 0.4 | 249.6 ± 0.7 | 249.6 ± 0.7 |
| Prostamid | 250 | 250.6 ± 0.4 | 250.7 ± 0.5 | 250.6 ± 0.7 |

method which agree favourably. The present method can compete with a few reported spectrophotometric procedures and could be considered for the determination of FLA both in pure form as well as in pharmaceutical preparations.


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