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Spectrophotometric Determination of Flutamide, Nimesulide and Meloxicam

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Three simple and sensitive visible spectrophotometric methods have been developed for the assay of flutamide, nimesulide and meloxicam in bulk samples and pharmaceutical formulations. All the methods are based on the oxidation of the drug with a known excess of oxidant, potassium permanganate ($KMnO_4$). The excess permanganate is determined using the dye, Fast Green FCF (FGFCF) at 625 nm. The results obtained are reproducible and are statistically validated.

INTRODUCTION

Flutamide is α′,α′,α′-trifluoro-4′-nitrosobutyro-*m*-toludide, which is used in the treatment of prostatic carcinoma and as anti-androgenic agent. Nimusalide chemically is N-(4-nitro-2-phenoxy phenyl) methane sulphonamide, which is a histamine release and prostaglandin synthesis inhibitor used as NSAID and also as an analgesic and antipyretic. Meloxicam is 4-hydroxy-2-methyl-N-(5-methyl-2-thiazolyl) 2H-1,2-benzothiazine, 3-carboximide-1,1-dioxide used as NSAID, which acts by inhibiting cyclooxygenase.

Literature survey revealed very few analytical methods for the estimation of flutamide (HPLC[1], GLC[2], polarography[3] and colorimetry[4]), nimesulide (HPLC[5], polarography[6], UV[7] and colorimetry[8–10]) and meloxicam (UV[11, 13], HPLC[11, 12] and TLC densitometry[13]). The present communication reports three new visible spectrophotometric methods for the determination of above drugs based on the susceptibility of these drug molecules to undergo oxidation. In these methods the drug is treated with a known excess of potassium permanganate, and the excess permanganate remaining is estimated by utilizing its ability to oxidize the dye (fast green FCF) and thereby decrease the colour intensity of the solution of a known strength of the dye measured at 625 nm. The decrease in the colour intensity of the dye solution is proportional to the concentration of the drug under estimation.

EXPERIMENTAL

All chemicals used were of analytical grade. Aqueous solutions of $KMnO_4$

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(BDH, 2.0×10^{-3} M) in 2 M H_2SO_4, fast green FCF (FGFCF) (Loba Chemie, 1.23×10^{-4} M) in 1 M H_2SO_4, Na_2SO_4 (GS Chemicals, 1 M) in distilled water were prepared. Systronics UV-visible spectrophotometer-117 with 1 cm matched quartz cells was used for all the absorbance measurements.

Standard and Sample Solutions

For Flutamide and Nimesulide: About 100 mg of flutamide or nimesulide (pure or formulation) was accurately weighed and dissolved in 10 mL of methanol, then treated with 10 mL of 5 N HCl and 2 g 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 the volume was made up to 100 mL with distilled water for flutamide. whereas for nimesulide it was washed with 3 × 15 mL portions of methanol and finally the volume was made up to 100 mL with methanol.

For Meloxicam: 20 mg of meloxicam (pure or formulation) was accurately weighed and dissolved in 100 mL of 0.1 N NaOH. The final concentration of each drug was brought to 20 μg/mL by further dilution with distilled water.

Assay Procedure

Aliquots of standard drug solution (0.5 to 2 mL of flutamide, 0.2 to 2 mL of nimesulide, 0.5 to 3.5 mL of meloxicam, 1 mL = 20 μg) were taken into a series of 25 mL calibrated tubes. To each of these tubes, 0.5 mL of $KMnO_4$ solution was added and the total volume in each was brought to 10 mL with distilled water and kept aside for 15 min. at room temperature. Then 5 mL of FGFCF solution and 4 mL of sodium sulfate for flutamide and meloxicam whereas 4 mL of FGFCF solution and 3 mL of sodium sulfate for nimesulide were added successively. After 10 min. the volume was made up to the mark with distilled water. The absorbance was measured at 625 nm against distilled water. A blank experiment was carried out in a similar manner omitting the drug. The decrease in absorbance corresponding to the drug was obtained by subtracting the absorbance of the blank from that of the standard solution. The amount of drug present in the sample solution was computed from the standard calibration graph.

RESULTS AND DISCUSSION

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, per cent relative standard deviation (calculated from the eight measurements containing 3/4th of the amount of the upper Beer's law limits), % range of error (0.05 to 0.01 confidence limits) were calculated for all the methods and the results are summarized in Table-1.

The values obtained for the determination of flutamide, nimesulide and meloxicam in several pharmaceutical formulations by the proposed and reported methods are compared in Table-2. To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analysed pharmaceutical preparations and the mixtures were analysed by proposed methods and the per cent recoveries are given in Table-2.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

Parameters	Flutamide	Nimesulide	Meloxicam
Beer's law limit (μg/mL) (C)	0.2–1.6	0.2–1.6	0.4–2.8
Sandell's sensitivity (μg/cm^2/0.001 absorbance unit)	0.00202	0.00223	0.00404
Molar extinction coefficient (1 mole^{-1} · cm^{-1})	1.367×10^5	1.3783×10^5	0.8697×10^5
% Relative standard deviation	0.81814	1.1961	0.9363
% Range of error			
0.05 confidence limits	± 0.6841	± 1.0001	± 0.7829
0.01 confidence limits	± 1.0121	± 1.4760	± 1.1583
Regression equation (b + ac)			
Slope (a)	0.0201	0.0176	0.0102
Intercept (b)	–0.0009	0.0078	–0.0066
Correlation coefficent	0.9999	0.9997	0.9999

TABLE-2
ESTIMATION OF FLUTAMIDE, NIMESULIDE AND MELOXICAM IN PHARMACEUTICAL FORMULATIONS

Formulation tables	Labeled amount (mg)	Amount obtained (mg)		% recovery by proposed method
		Reference method[4, 7, 11]	Proposed method	
Flutamide				
1	250	249.80	250.3	100.12
2	250	250.20	249.6	99.80
3	250	250.10	249.9	99.96
Nimesulide				
1	100	100.10	99.90	99.90
2	100	99.90	99.82	99.82
3	100	99.92	99.79	99.79
4	100	99.80	100.10	100.10
Meloxicam				
1	7.5	7.54	7.52	100.26
2	7.5	7.45	7.53	110.40
3	7.5	7.48	7.49	99.86
4	7.5	7.55	7.48	99.73

Interference studies revealed that the common excipients and other additives usually present in the dosage form such as parabens, lactose, sucrose, starch, sodium benzoate, sodium phosphate, calcium gluconate, gelatin, talc, magnesium stearate did not interfere in the proposed methods. In conclusion the proposed

methods are simple, sensitive and accurate and can be used for the routine determination of flutamide, nimesulide and meloxicam in bulk as well as in pharmaceutical preparations.

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