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VISIBLE SPECTROPHOTOMETRIC DETERMINATION OF BICALUTAMIDE IN BULK DRUG AND PHARMACEUTICAL FORMULATIONS

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ABSTRACT

Two new simple, sensitive and cost effective visible spectrophotometric methods were developed for the estimation of bicalutamide in both; bulk drug samples and formulations. The first method was based on the oxidative coupling of the drug with the reagent namely 3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH, Method A) and ferric chloride solution. Second method was based on reaction of 1, 2 – naphthoquinone - 4 - sulphonic acid (NQS, Method B). The absorbance of the chromogens was measured at their respective absorption maxima at 630 nm for MBTH and 453 nm for NQS against the corresponding reagent blank. The methods obeyed Beer's law between 10-60 µg/mL for MBTH and 2.5-25 µg/mL for NQS. The results of the recovery experiments indicated that average recovery was above 99.83%. The interference studies also revealed the common excipients and other additives usually present in pharmaceutical dosage forms did not interfere in the proposed methods. The proposed methods are precise, accurate, sensitive and cost effective and can be used in routine analysis in quality control laboratories.

Key words : Bicalutamide, Spectrophotometry, Bulk drug, Formulation, MBTH, NQS

INTRODUCTION

Bicalutamide is an oral non-steroidal anti-androgen for prostate cancer. It was first launched in 1995 as a combination treatment (with surgical or medical castration) for advanced prostate cancer and subsequently launched as monotherapy for the treatment of earlier stages of the disease. It is mainly indicated for the treatment of stage D2 metastatic prostate cancer in combination with a luteinizing hormone-releasing hormone analogue or as a monotherapy. It is chemically N-[4-cyano-3-(trifluoromethyl)phenyl]- 3-(4-fluorophenyl)sulfonyl-2-hydroxy-2-methyl-propanamide. The drug is official in

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Martindale, The Extra Pharmacopoeia and also in Merck Index [1, 2]. Its chemical structure is shown in Fig. 1.

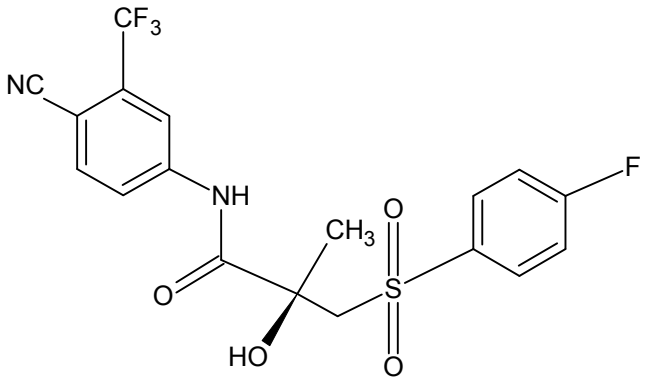

Fig. 1: Chemical structure of bicalutamide

Only few HPLC methods for quantitative determination of bicalutamide were reported in the literature. Majority of these HPLC methods were applied in the determination of bicalutamide and it's metabolites in biological fluids[3, 4] and are mainly useful for therapeutic monitoring of the drug. No visible spectrophotometric method for quantitative determination of bicalutamide in bulk drug samples and formulations was reported. The objective of this research was to develop and validate rapid, economical and sensitive visible spectrophotometric method for quantitative determination of bicalutamide in bulk drug samples and formulations. Bicalutamide has a secondary amino group in the molecular structure making it possible to undergo oxidative coupling of the drug with MBTH in ferric chloride solution in method A[5-11] and method B was based on reaction of the drug with NQS in sodium hydroxide[12].

EXPERIMENTAL

Instruments

Pharmaspec -1700 Ultraviolet-Visible spectrophotometer (double beam) was used for all spectral measurements.

Digisun model DI-707 pH meter was used for all the pH measurements.

Chemicals and reagents :

All the chemicals used were of analytical grade.

(i) 3-Methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) : 100 mg of MBTH was dissolved in 50 mL of distilled water.

(ii) Ferric chloride ($FeCl_3$) (0.3 % w/v): 300 mg of ferric chloride hexahydrate was dissolved in 100 mL of distilled water.

(iii) 1, 2–Naphthoquinone – 4 – sulphonic acid (NQS) (0.5% w/v) : 500 mg of NQS was dissolved in 100 mL of distilled water.

(iv) Sodium hydroxide (NaOH) (2 % w/v): 2 g of NaOH was dissolved in 100 mL of distilled water.

Procedure :

Preparation of standard drug solution:

Method B : A standard drug solution of bicalutamide was prepared by dissolving 100 mg of drug in 100 mL of methanol in a standard volumetric flask to obtain a stock solution of 1 mg/mL.

Method A : 10 mL of 1 mg/mL solution was further diluted to 100 mL with methanol to get 100 μg/mL working standard.

Preparation of sample solution

A quantity of the powder from tablets equivalent to 10 mg of drug was dissolved in 10 mL methanol, filtered and analyzed by taking an aliquot and treated as per the procedure for standard.

Method A : Aliquots of standard drug solution (1.0-6.0 mL) were transferred into series of 10 mL graduated test tubes, 2 mL of ferric chloride and 1 mL of MBTH were added to each test tube, mixed well and volume was made upto 10 mL with methanol. The absorbance of resulting solution was measured at 630 nm against reagent blank prepared simultaneously and a linear graph was obtained. The amount of bicalutamide present in the sample solution was computed from its calibration curve.

Method B : Aliquots of standard drug solution (0.25-2.5 mL) were transferred

into series of 10 mL graduated test tubes, 0.5 mL of NQS and 2 mL of NaOH were added to each test tube, mixed well and volume was made upto 10 mL with methanol. The absorbance of resulting solution was measured at 453 nm against reagent blank prepared simultaneously and a linear graph was obtained. The amount of bicalutamide present in the sample solution was computed from its calibration curve.

RESULTS AND DISCUSSION

Analytical data and method validation

The optimum conditions were established by varying one parameter at a time and keeping the others fixed and observing the effect on absorbance of chromogen.

Bicalutamide has a secondary amino group in the molecular structure making it possible to undergo oxidative coupling of the drug with MBTH in ferric chloride solution in method A and method B was based on reaction with NQS in sodium hydroxide. The effect of temperature of the reaction, quantity, concentration and order of addition of various reagents were studied and optimized after several experiments with respect to maximum sensitivity, colour stability, adherence to Beer's law and then other optimum conditions are incorporated in the procedure.

The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are presented in Table 1.

Table 1 : Optical characteristics, precision and accuracy of the method

Parameter	Method A	Method B
λ_{max} (nm)	630	453
Beer's law range (μg/mL)	10-60	2.5-25
Molar extinction coefficient (L. mole^{-1} cm^{-1})		
Sandell's sensitivity	0.35 x 10^4	0.89 x 10^5
(μg/cm^2/0.001)	0.657	0.026

Cont…

Parameter	Method A	Method B
Regression equation (y = mx + b) *		
Slope (m)	0.0015	0.0379
Intercept (b)	-0.0046	0.0014
Correlation coefficient (r)	0.9998	0.9999
Precision (% Relative standard deviation)	0.77	0.16

The regression analysis using the method of least squares was made to evaluate the slope (m), intercept (b) and correlation coefficient (r) obtained from different concentrations and the results are presented in Table 2. The graph showed negligible intercept as described by the regression equation y = mx + b, where y is the absorbance and x is the concentration in μg/mL.

Table 2 : Determination of bicalutamide in formulations

Sample	Reagent	Label claim (mg)	Amount*(mg) found by proposed method	% Recovery**
1	MBTH	50	49.92	99.84%
	NQS	50	49.95	99.90%
2	MBTH	50	49.95	99.90%
	NQS	50	49.83	99.66%

*Average of three determinations **After spiking the sample

Commercially available tablets of bicalutamide were analyzed by the proposed methods and as additional check on the accuracy of the method, recovery experiments were also conducted by spiking known amounts of pure drug in preanalysed formulation and the recovery was calculated in each of the case using the regression line equation

developed under the linearity experiment. The results of recovery experiments were given in the Table 2 for both the methods**.** The interference studies revealed the common excipients and other additives usually present in pharmaceutical dosage forms did not interfere in the proposed method.

CONCLUSION

The proposed visible spectrophotometric methods enable quantitative determination of bicalutamide in bulk drug samples and tablets. Efficient visible spectrophotometric detection at the absorption maximum was found to be suitable without any interference from the excipients. The calibration curve was linear over a concentration range from 10-60 µg/mL for method A and 2.5-25 µg/mL for method B. The relative standard deviations (R. S. D.) were less than 1% and average recovery was above 99.83 %. Analytical results of samples were in accordance with those of standard solution in the same concentrations. The proposed methods are fast, precise, accurate, sensitive and efficient and can be used in routine analysis in quality control laboratories.

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REFERENCES

1. Martindale, The Extra Pharmacopoeia, 34th Edition, (2005) p. 530.

2. S. Budavari, Merck Index, 14th Edition, Monograph No. 1200, Edited by Maryadele, J. O. Neil, Merck Research Lab, Division of Merck & Co., NJ (2006).

3. R. Nageswara Rao, A. Narasa Raju, R. Narsimha, J. Pharm. Biomed. Anal., **46**, 505 (2007).

4. R. Török, A. Bor, G. Orosz, F. Lukács, D. W. Armstrong and A. Péter, J. Chromatogr. A., **1098**, 75 (2005).

5. C. S. P. Sastry, B. S Reddy and D. S Mangala, Indian Drugs, **21**, 526 (1984).

6. V. Das Gupta, Indian J. Pharm., **35**, 77 (1973).

7. D. M. Shingbal, Indian J. Pharm., **35**, 160 (1973).

8. T Kyoji, M Shoh and U. Toru, Talanta, **29**, 103 (1982).

9. B. S. Reddy and C. S. P. Sastry, J. Inst. Chemists (India), **5**, 69 1983).

10. B. S. Sastry, E. V. Rao, M. K. Tummuru and C. S. P. Sastry, Indian Drugs**, 24**, 105 (1986).

11. N. Viswanadham, M. N. Reddy and C. S. P. Sastry, Indian J. Pharm. Sci, **45**, 81(1983).

12. L. X. Xu, Y. X. Shen, H. Y. Wang and J.G. Jiang, Y. Xiao, Spectrochim. Acta A Mol. Biomol. Spectrosc., **59**, 3103 (2003).

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