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APPLICATION OF N–BROMOSUCCINIMIDE AS AN OXIDANT FOR THE ASSAY OF CEFDINIR

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ABSTRACT

Two simple and sensitive indirect spectrophotometric methods (M_1 and M_2) for the assay of cefdinir in its dosage forms based on their reactivity with N–bromosuccinimide (NBS) have been described. These methods involve the oxidation of drug with excess of NBS and estimating the unreacted NBS either with celestine blue (CB) (M_1) or P–N–methyl amino phenol sulfate (PMAP) – sulfanilamide (SA) (M_2). The results obtained are reproducible and are statistically validated.

Key words: Spectrophotometry, Cefdinir, N–Bromosuccinimide, Sulfanilamide, Celestine blue, p–N–methyl aminophenol sulfate, Capsules

INTRODUCTION

In recent years, there has been growing interest in the role of N–bromosuccinimide as an analytical reagent in the assay of drugs. It contains weakly bound bromine and is used for brominations and dehydrogenations[1]. It is a highly selective oxidant. The present paper proposes two methods using NBS as an oxidant for the assay of cefdinir. Cefdinir (CEF)[2] is a chemotherapeutic agent and belongs to the caphalospoprin group. The chemical designation is {6R–[6,7β(z)]}–7–{[(2–amino–4–thiazolyl)(hydroxylamino)–acetyl]amino]–3–ethenyl–8 – oxo– 5–thia–1–azabicyclo [4,2,0]oct–2ene–2–carboxylic acid. A search of literature revealed a lack of visible spectrophotometric methods for its estimation. Hence, the authors focussed attention to develop sensitive and flexible visible spectrophotometric methods for the assay of CEF. The efforts in this regard resulted in the development of two such procedures based on the oxidation of CEF with NBS and estimating the unreacted NBS with CB[6] (M_1) or PMAP–SA[7] (M_2). The reacted NBS (NBS originally added – NBS unreacted) corresponds to the concentration of the drug. The results of the methods are statistically validated.

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EXPERIMENTAL

Instrument

A Systronics model 117 UV – Visible spectrophotometer with 1cm matched quartz cells was used for spectral and absorbance measurements in the UV and visible regions.

Reagents

All the chemicals and reagents used were of analytical grade and the solutions were freshly prepared. Aqueous solutions of NBS (BDH, 5.618 x 10^{-4} M for M_1 and M_2), CB (Chroma, 5.5 x 10^{-4} M), hydrochloric acid (E. Merck, 5 M), PMAP (Wilson labs, 8.70 x 10^{-3}M), SA (Sd fine, 1.16 x 10^{-2} M) and acetic acid (Qualigens, 8.75 x 10^{-1} M) were prepared using distilled water.

Standard drug solution

A 1mg/mL solution was prepared by dissolving 100 mg of CEF in 10 mL of 0.1N HCl and further diluted to 100 mL with distilled water. The solution was further diluted with distilled water to obtain the working standard solution of concentration of 50 µg/mL for Method M_1 and 100 µg/mL for Method M_2.

Sample drug solution

An accurately weighed amount of capsule powder equivalent to 100 mg of CEF was extracted with isopropanol (4 x 15 mL) and filtered. The combined filtrate was evaporated to dryness and the residue was dissolved in 10 mL 0.1N HCl and further diluted to 100 mL of distilled water to get a concentration of 1 mg/mL. The solution was further diluted with distilled water to get working sample solution.

Recommended Procedures

Method (M_1)

Aliquots of standard drug solution (CEF: 0.5–2.5 mL, 50 µg/mL^1) were taken in series 25 mL calibrated tubes, 1.25 mL of (5.0M) HCl, 2.5 mL of (5.618 x 10^{-4}M) NBS solution were added and the volume was made upto 20 mL with distilled water. After 10 min, 5 mL of (5.49 x 10^{-4}M) CB was added and mixed thoroughly. The absorbances were measured after 5 min at 540 nm against distilled water. The blank (omitting drug) and dye (omitting drug and oxidant) solutions were prepared in a similar manner and their absorbances measured against distilled water. The decrease in absorbance corresponding to the consumed NBS and in turn to the drug concentration, was obtained by subtracting the absorbance of test solution (dye–test) from that of the blank solution (dye – blank). The amount of drug in sample was computed from the corresponding calibration graph.

Method (M_2)

Aliquots of the standard drug solution (0.5 mL –2.5 mL; 100 µg/mL for CEF) were transferred into a series of 25 mL calibrated tubes containing 0.5 mL of (8.75 x 10^{-1}M) AcOH

and 2.5 mL of (5.618×10^{-4}M) NBS solution. The volume was made upto 10 mL with distilled water and kept aside for 15 min. Then 1.0 mL of (8.71×10^{-3}M) PMAP solution and after 2 min, 2.0 mL of (1.16×10^{-2}M) SA were added. The volume was made upto 25 mL with distilled water and the absorbance was measured after 10 min, at 520 nm against distilled water. A blank experiment was also performed omitting drug solution. The decrease in absorbance corresponding to drug content was obtained by subtracting the absorbance of the test solution from that of blank solution. The amount of drug in the solution was computed from its calibration graph.

RESULTS AND DISCUSSION

The optimum conditions for the color developments of methods (M_1 and M_2) were established by varying the parameters one at a time, keeping the others fixed and observing the effect produced on the absorbance of the coloured species. The optical characteristics such as Beer's law limits, molar absorptivity and Sandell's sensitivity for each method of CEF are given in Table 1. Regression analysis using the method of least squares was made to evaluate the slope (b), intercept (a), correlation coefficient (r) is presented in Table 1. The precision of the method was found by measuring absorbances of five replicate samples containing known amounts of

Table 1. Optical characteristics, precision and accuracy of the proposed methods

Parameters	NBS/CB	NBS/PMAP/SA
λ_{max} (nm)	540	520
Beer's law limits (µg/mL)	1–5	2–10
Molar absorptivity (l $mol^{-1}cm^{-1}$)	4.735×10^4	2.0006×10^4
Correlation coefficient (r)	0.9999	0.9998
Sandell's sensitivity (µg/cm^2/ 0.001 absorbance unit)	0.00835	0.01970
Regression equation (y = a + bc)		
(i) Slope (b)	0.1200	0.05055
(ii) Standard deviation on slope (S_b)	0.00092	0.00046
(iii) Intercept (a)	0.00060	0.00430
(iv) Standard deviation on intercept(S_a)	0.00304	0.00303
(v) Standard error of estimation (S_e)	0.00290	0.00289
Optimum photometric range (µg/ml)	2–4.8	2.5–9.6
Relative standard deviation *	0.2356	0.2774
% Range of error (confidence limits)		
(i) 0.05 level	0.197	0.232
(ii) 0.01 level	0.291	0.343

Y*= a + bC, where "C" is concentration in µg/mL and Y is absorbance unit.

drug. The percent relative standard deviation and percent range error (confidence limits) of the methods are given in Table 1. To evaluate the validity and reproducibility of the method, known amounts of pure drug were added to the previously analysed samples and the mixtures were analysed by the proposed method. Commercial available formulations for CEF in the form of CEF from various industries are analysed by the proposed method. The values obtained by the proposed and reported method were summarized in Table 2.

Table 2. Assay of CEF in pharmaceutical formulations

Pharmaceutical formulations	Labelled amount (mg)	% Recovery by proposed methods (mg)		Reference method*
		M_1	M_2	
Capsules 1	300	99.87	100.13	99.76
Capsules 2	300	99.89	99.93	99.86
Capsules 3	300	99.91	99.81	99.76

*UV method developed by the authors

CONCLUSIONS

The two proposed visible spectrophotometric methods are useful for the assay of cefdinir in dosage forms. These methods show good precession and accuracy and non–interference of other ingredients usually present in dosage forms. Hence, these methods can be used as alternatives for the rapid and routine assay of bulk samples and dosage forms of CEF in microgram quantities.

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