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NOTE

Use of Redox Reactions for Estimation of Carvedilol

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Simple and sensitive indirect spectrophotometric methods (M_1 and M_2) for the assay of Carvedilol in dosage forms based on their reactivity with N-bromo succinimide have been described. These methods involve the oxidation of drug with excess of N-bromo succinimide and estimating the unreacted N-bromo succinimide either with celestine blue (M_1) or p-N-methyl amino phenol sulfate-sulfanilamide (M_2). The results obtained are reproducible and are statistically validated.

Key Words: Spectrophotometric, Carvedilol, N-bromo succinimide.

In recent years, there has been growing interest in the role of N-bromo succinimide (NBS) as an analytical reagent in the assay of drugs. It contains weakly bound bromine and is used for brominations and dehydrogenations[1]. The present paper proposes two methods using NBS as an oxidant for the assay of Carvedilol. Carvedilol[2] (CAR) is a 2nd and 3rd degree AV blocking agent prescribed in the treatment of severe heart failure, bradycardia, hypotension, angina pectoris, asthma etc. Chemically, it is 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxy phenoxy)ethyl]amino]2-propanal. Literature survey revealed reports of the presence of HPLC methods[3–7] and visible spectrophotometric procedures[8, 9] for estimation of CAR in pharmaceutical formulations.

The analytically useful functional groups of CAR namely *vic*-aminodiol and carbazole moeity have not been fully exploited. Hence, attention was focussed on developing simple spectrophotometric methods exploiting the varied functional groups of the drug. The efforts in this regard resulted in the development of two such procedures based on the oxidation of CAR with NBS and estimating the unreacted NBS with celestine blue (CB) (M_1) or p-N-methyl amino phenol sulfate-sulfanilamide (PMAP-SA) (M_2). The reacted NBS (NBS originally added – NBS unreacted) corresponds to the concentration of the drug.

A Systronics model 117 UV-Visible spectrophotometer with 1 cm matched quartz cells was used for spectral and absorbance measurements in the UV and visible regions, respectively. All the chemicals and reagents used were of analytical grade and the solutions were freshly prepared. Aqueous solutions of NBS (BDH, 5.618×10^{-4} M for M_1 and M_2), CB (Chroma, 5.5×10^{-4} M), hydrochloric acid (E. Merck, 5 M), PMAP (Wilson Labs, 8.70×10^{-3} M), SA (S.D. Fine, 1.16×10^{-2} M) and acetic acid (Qualigens, 8.75×10^{-1} M) were prepared using distilled water.

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Standard drug solution: 1 mg/mL solution was prepared by dissolving 100 mg of CAR in 10 mL of aldehyde free methanol and further diluted to 100 mL with methanol. The solution was further diluted with methanol to obtain the working standard solution of concentration 50 μg/mL for method M_1 and 100 μg/mL for method M_2.

Sample drug solution: An accurately weighed amount of tablet powder equivalent to 100 mg of CAR was extracted with chloroform (4 × 15 mL) and filtered. The combined filtrate was evaporated to dryness and the residue was dissolved in 10 mL of aldehyde free methanol and further diluted to 100 mL of methanol to get a concentration of 1 mg/mL. The solution was further diluted with distilled water to get a working sample solution.

Recommended procedures

Method (M_1): Aliquots of drug solution (CAR, 1.0–3.0 mL, 50 μg mL^{-1}) were taken in a series of 25 mL calibrated tubes; 1.25 mL of (5.0 M) HCl and 2.5 mL of (5.618×10^{-4} M) NBS solution were added and the volume was made up to 20 mL with distilled water. After 10 min, 5 mL of (5.49×10^{-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 was computed from the corresponding calibration graph.

Method (M_2): Aliquots of the standard drug solution (1.0–3.0 mL; 100 μg mL^{-1} for CAR) were transferred into a series of 25 mL calibrated tubes containing 0.5 mL of (8.75×10^{-1} M) AcOH and 2.5 mL of (5.618×10^{-4} M) NBS solution. The volume was made up to 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 up to 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 the drug solution. The decrease in absorbance corresponding to drug content was obtained by subtracting the absorbance of the test solution from that of the blank solution. The amount of the drug solution was computed from its calibration graph.

The optimum conditions for the colour 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 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) are also presented in Table-1. The precision of the method was found by measuring absorbances of five replicate samples containing known amounts of drug. The per cent relative standard deviation and per cent range error (confidence limits) of the methods are given in Table-1. To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed samples and the mixtures were analyzed by the proposed methods. Commercial available formulations of CAR in the form of tablets from various

industries were analyzed by the proposed methods. The values obtained by the proposed and reported methods were summarized in Table-2.

TABLE-1
OPTICAL CHARACTERISTICS, PRECISION AND ACCURACY OF THE PROPOSED METHODS FOR CAR

Parameters	NBS/CB (M_1)	NBS/PMAP/SA (M_2)
λ_{max} (nm)	540	520
Beer's law limits (μg/mL)	2–6	4–12
Molar absorptivity (1 mol^{-1} cm^{-1})	3.455×10^4	1.857×10^4
Correlation coefficient (r)	0.9999	0.9997
Sandell's sensitivity (μg/cm^2/ 0.001 absorbance unit)	0.01176	0.02188
Regression equation (y = a + bc):		
(i) Slope (b)	0.09030	0.04505
(ii) Standard deviation on slope (S_b)	0.00057	0.00061
(iii) Intercept (a)	–0.00100	0.00100
(iv) Standard deviation on intercept (S_a)	0.00244	0.00520
(v) Standard error of estimation (S_e)	0.00182	0.00388
Optimum photometric range (μg/mL)	3–5.2	5–10.6
Relative standard deviation*	0.2647	0.2274
% Range of error (confidence limits):		
(i) 0.05 level	0.221	0.190
(ii) 0.01 level	0.327	0.281

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

TABLE-2
ASSAY OF CAR IN PHARMACEUTICAL FORMULATIONS

Pharmaceutical formulations	Labelled amount (mg)	% Recovery by proposed methods (mg)		Reference method[8]
		M_1	M_2	
Tablets 1	25	99.87	100.13	99.76
Tablets 2	25	99.89	99.93	99.86
Tablets 3	25	99.91	99.81	99.76

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