SHORT COMMUNICATIONS

Spectrophotometric Estimation of Pyrantel in Pharmaceutical Formulations

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Four simple and sensitive visible spectrophotometric methods have been described for the determination of pyrantel based on the formation of coloured charge-transfer complex between drug and chloranilic acid (method A, λmax : 540 nm) or by the reduction of Folin-Ciocalteau reagent (method B, λ_{max}: 760 nm) or by finding the oxidant [N-bromosuccinimide (NBS) or potassium permanganate ($KMnO_4$)] reacted with pyrantel using a dye [celestine blue λ_{max} : 540 nm (method C) or cresyl fast violet acetate λ_{max} : 600 nm (method D)]. The results obtained are reproducible with coefficient of variation of less than 1.0%.

A SURVEY of literature revealed a few visible[1] and UV[2,3] spectrophotometric methods for the estimation of pyrantel. This paper describes the development of four visible spectrophotometric methods for its determination by exploiting its basic behaviour and reducing characteristics. Method A is based on the formation of coloured charge-transfer complex (λ_{max} : 540 nm) between drug and chloranilic acid (CA). Method B is based on the reaction of drug with Folin-Ciocalteau (F-C) reagent[4] in the presence of sodium carbonate solution to form a blue coloured product having λmax at 760 nm. Methods C and D are indirect ones, involving the addition of excess oxidant (NBS, for method C, and $KMnO_4$ for method D) to known concentration of the drug and determination of the unreacted oxidant by measuring the reduction in absorbance of celestine blue[5] (CB for method C) or cresyl fast violet acetate[6] (CFVA for method D) at a suitable maximum wavelength (λmax 540 nm for method C and λmax : 600 nm for method D).

A Milton Roy spectronic 1201 UV-Visible spectrophotometer and a Systronics 106 digital spectrophotometer with 1 cm matched quartz cells were used for all absorbance measurements. An Elico LI 120 digital pH meter was used for pH measurements. Aqueous solutions of NBS (100 µg/ml),CB (100 µg/ml), HCl (5M), $KMnO_4$ (2.0×10^{-3}M) in 2.0 M H_2SO_4, CFVA (100 µg/ml) and sodium carbonate (10%) were prepared. F-C reagent (2.0N) supplied by the Loba-Chemie Company was used directly. CA solution was prepared by dissolving 500 mg of p-chloranilic acid in 20 ml isopropyl alcohol initially, followed by dilution to 100 ml with $CHCl_3$.

The stock solution of pyrantel was prepared by dissolving an appropriate amount of its pamoate equivalent to 50 mg of free base in 10 ml of DMF to which 5 ml of 1M NaOH was added. The free base was extracted with chloroform (5 x 20 ml). The stock solution (500 µg/ml) was directly used as a working solution for method A. For methods B, C and D, the residue obtained after evaporating 10 ml of stock solution was redissolved in 10 ml of 0.1M NaOH (for method B) or CH_3COOH (for methods C and D) and then diluted to 100 ml with distilled water (for method B) or CH_3COOH (for methods C and D) to get the working solution (50 µg/ml). An accurately weighed or measured amount of tablet powder or suspension of pyrantel pamoate equivalent to 50 mg of pyrantel was treated with 10 ml of DMF and filtered if insoluble portion left. The filterate was used in the same manner as under standard solution preparation for methods A, B, C and D and assayed as per the procedure.

Into a series of 20 ml volumetric flasks containing different aliquots of drug solution (0.5-2.5 ml, 500 µg/ml),

Table 1 : Optical Characteristics, Precision and Accuracy

Parameters	Methods A	B	C	D
Beer's law limits (μg/ml)	12.5-62.5	2.0-10.0	1.0-10.0	1.0-10.0
Molar absorptivity (1 $mole^{-1}$ cm^{-1})	0.43×10^4	3.55×10^4	4.91×10^4	3.79×10^4
Sandell's sensitivity (μg/cm^2/0.001 absorbance unit)	0.104	0.016	0.012	0.016
Regression equation* (Y)				
Slope (b)	7.61×10^{-3}	5.89×10^{-2}	8.20×10^{-2}	6.42×10^{-2}
Intercept (a)	-3.92×10^{-3}	0.10×10^{-2}	1.10×10^{-3}	-0.40×10^{-3}
Correlation coefficient (r)	0.9996	0.9999	0.9999	0.9999
% RSD**	0.35	0.91	0.54	0.86
% Range of error** (95% confidence limits)	0.38	0.96	0.57	0.91

* : $Y = a \pm bC$ where C is the concentration in μg/ml
** : For six determinations

0.2 ml of chloranilic acid was added and the volume was made upto the mark with chloroform. The absorbance of the coloured species was measured at 540 nm against a reagent blank during the stability period (5-40 min). The amount of drug present was calculated from its calibration graph.

Aliquots (1.0-5.0 ml, 50 μg/ml) of the standard drug solution were transferred into a series of 25 ml volumetric flasks. Then 2.0 ml of 2N F-C reagent and 9.0 of 10% Na_2CO_3 were added successively and kept aside for 10 min at laboratory temperature. The solutions were made upto the mark with distilled water and the absorbances were measured at 760 nm against a reagent blank, during the stability period (10 min-2 h). The amount of drug was computed from the Beer-Lambert plot.

To each of 25 ml volumetric flasks containing standard drug solution (0.5-5.0 ml, 50 μg/ml for methods C and D), 1.25 ml of 5.0 M HCl (for method C) and 2.5 ml of NBS (for method C) or 2.0 ml of $KMnO_4$ (for method D) were added and the solutions were diluted to 15 ml with distilled water. After 10 min, 10 ml of dye solution (CB for method C and CFVA for method D) was added, mixed thoroughly and the absorbances were measured after 5 min at 540 nm (for method C) or 600 nm (for method D) against distilled water. The blank (omitting drug) and dye (omitting drug and oxidant) solutions were prepared in a similar manner and their absorbances were also measured against distilled water. The decrease in absorbance corresponding to consumed oxidant, which reflects the drug concentration, was obtained by subtracting the decrease in absorbance of the test solution (dye-test) from that of the blank solution (dye-blank). Calibration graphs were prepared by plotting the decrease in the absorbance of dye, against the amount of drug. The amount of drug was calculated from its calibration curve.

Beer's law limits, molar extinction coefficient, Sandell's sensitivity and regression characteristics of proposed methods are presented in Table 1. the relative standard deviation and % range of error at 95% confidence level are also given in Table 1. The values obtained by the proposed and reference[1] methods for the estimation of drug in pharmaceutical formulations are compared in Table 2 and are in good agreement. These methods can be used for the routine determination of pyrantel in pharmaceutical formulations.

Table 2
Result of Assay and Recovery Experiments

Sample	Labelled amount (mg)	Amount found* by proposed methods				Reference method	% Recovery by proposed methods**			
		A	B	C	D		A	B	C	D
Tablets I	250	248.88±0.92	250.18±1.08	248.98±0.51	250.01±0.85	249.65±0.65	99.2±0.38	100.1±0.69	100.1± 0.69	99.4±0.42
Tablets II	250	249.12±0.65	249.99±0.98	248.56±0.72	249.52±0.63	249.66±0.52	100.1±0.71	99.8±0.35	99.8±0.35	99.6±0.60
Suspension I	250 mg/5 ml	250.56±1.41	249.98±1.24	250.08±1.03	249.60±0.95	249.65±1.23	99.8±0.50	100.6±0.75	100.6±0.75	99.8±0.44
Suspension II	250 mg/5 ml	249.52±1.15	248.91±0.42	249.12±0.65	249.91±0.91	249.40±0.82	99.8±0.52	100.3±0.50	100.3±0.50	99.8±0.43

*Average±standard deviation (six determinations)

**Recovery of amount added to the pharmaceutical formulation (Average of three determinations)

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