RESEARCH PAPER

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Sevron Blue 5G as an Ion-Pairing Reagent for the Determination of Acidic Drugs in Pharmaceutical Formulations

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An extractive spectrophotometric technique was applied for the determination of four acidic drugs, viz., Piroxicam, Sulphinphyrazone, Frusemide and Trichlormethazide using an oxazine dye, Sevron blue 5G as reagent. The method of the determination is based on the measurement of the absorbance of the chloroform extract of the ion-association complex formed between the drug and the dye at pH 7.0, which exhibits an absorption maximum at 655 nm. The method is simple, rapid sensitive, reproducible and with an accuracy of ± 1%.

EXTRACTIVE spectrophometric procedures are normally adopted for the assay of drugs because of higher sensitivity, reproducibility and accuracy of these methods.[1] Basic dyes belonging to different chemical classes such as phenazine, thiazine, xanthane and triphenylmethane were used for the extractive spectrophotometric determination of drugs exihibiting acidic properties.[2-7] In the present investigation the authors proposed a simple spectrophotometric method for the determination of four acidic drugs viz., Piroxicam (PX, antiinflammatory agent), Sulphinpyrazone (SP, antigout agent), Frusemide, (FRU, diuretic) and Trichlormethazide (TCM, diuretic) with Sevron blue 5G (SB 5G, oxazine dye, C.I.No.51004) as an ion pairing reagent.

EXPERIMENTAL

A systronic model 106 and Milton Roy spectronic 1201 spectrophotometer with 1 cm matched quartz cells and an Elico LI- 120 digital pH meter were used.

A 0.1% solution of SB 5G (Dupont, Wilmington DE, USA) was prepared by dissolving the required amount in distilled water. The aqueous solution was washed with chloroform to remove the chloroform soluble impurities and residual solvent was removed by bubbling with nitrogen. Phosphate buffer, pH 7.0 was prepared by mixing 61.2 ml of Na_2HPO_4 (0.06 mole 1^{-1}) with 38.8 ml of KH_2PO_4 (0.06 mol 1^{-1}).

Standard Drug Solutions:

The stock solutions of the drugs consisting of 1 mg/ml were prepared by dissolving 100 mg of the drug in 10 ml of 0.1M sodium hydroxide, and diluted to 100 ml after bringing pH 7.0 with addition of suitable volume of dil. hydrochloric acid. These stock solutions were further diluted to working standard solutions with distilled water when ever required.

Sample Drug Solutions:

The powdered tablet/capsule equivalent to 100 mg of drug content was extracted with 3x10 ml of chloroform and 3x20 ml of water, successively for removing the extractable interfering substances such as reserpine. The remaining solid was dissolved in 10 ml of 0.1M sodium hydroxide and was diluted to 100 ml after bringing pH 7.0 with dilute hydrochloric

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*For Correspondence

Table 1: Analysis of Pharmaceutical Formulations of Acidic Drugs (PX, SP, FRU or TCM) by proposed and reference procedures

Pharmaceutical formulations	labelled amount (mg)	Amount found* (mg)		% Recovery** by proposed procedure
		Proposed	Reference	
PX				
Tablets	20	19.95 ± 0.05 t =1.70, F = 2.61	19.90 ± 0.03	99.75 ± 0.35
Capsules	10	10.02 ± 0.06 t = 1.24, F = 1.09	9.97 ± 0.06	100.20 ± 0.35
SP				
Tablets - I	200	199.90 ± 0.07 t = 1.25, F = 1.56	199.85 ± 0.05	99.95 ± 0.12
Tablets - II	200	200.02 ± 0.06 t = 1.20, F = 1.31	199.98 ± 0.05	100.02 ± 0.12
FRU				
Tablets	40	40.02 ± 0.57 t = 0.16, F = 1.26	39.95 ± 0.51	100.05 ± 0.10
Injections	20	20.01 ± 0.06 t = 1.44, F = 2.46	19.96 ± 0.04	100.05 ± 0.15
TCM				
Tablets - I	2	1.99 ± 0.05 t = 0.36, F = 1.85	1.98 ± 0.04	99.50 ± 0.22
Tablets - II	2	2.01 ± 0.05 t = 0.52, F = 1.39	1.99 ± 0.06	100.50 ± 0.31

* Average ± Standard Deviation (n = 6). The t- and F- values refer to comparison of the proposed method with the reference method (PX[4], SP[9], FRU[8], TCM[9]); theoretical values at 95% confidence limit t = 2.57, F = 5.05.

** Recovery 10 mg added to the preanalysed pharmaceutical preparation (Average of three determinations).

acid. An aliquot of the injection solution equivalent to 100 mg of the drug was diluted to 100 ml with distilled water to give a solution containing 1 mg/ml. Working solutions were prepared as required by suitable dilution of these sample solutions.

Recommended Procedure:

Aliquots of the standard drug solutions SP, PX: 0.5-7.0 ml, 5μg/ml; FRU: 0.5-6.0 ml, 10μg/ml; TCM: 0.5-6.0 ml, 100 μg/ml) were transferred in to series of 125 ml separating funnels. Then 2.0 ml of dye (0.1%) and 12.0 ml of buffer (pH 7.0) were added and total volume of the aqueous phase was adjusted to 20 ml with distilled water. Ten ml of chloroform was added to each flask and the contents were shaken for 2 min, and allowed to separate. The separated chloroform layer consisting of coloured ion-association complex was dried over anhydrous sodium sulphate and the absorbance was measured at λ_{max} (655 nm) against a reagent blank with in the stability period (1 min-24 h). The amount of the drug in sample was computed from its calibration graph.

RESULTS AND DISCUSSION

Optimum operating conditions used in the procedure were established adopting variation of one variable at a time (OVAT) method. The optical characteristics such as Beer's law limits (μg/ml), molar absorptivity (1. mole^{-1}. cm^{-1}) and Sandelk's sensitivity (μg/cm^2/0.001 absorbance unit) were found to be 0.25-3.5, 8.300x10^4, 0.004; 0.25-4.0, 8.1304x10^4, 0.005; 0.50-6.0, 4.167x10^4, 0.008 and 5.0-60.0, 0.455x10^4, 0.083 for PX, SP, FRU and TCM respectively. The slope, intercept, standard error of estimation and correlation co-efficients obtained by linear least squares treatment of the results were found to be 0.2501, -0.03x10^{-3}, 0.57x10^{-3}, 0.9999; 0.2007, -0.55x10^{-3}, 1.28x10^{-3}, 0.9999; 0.1257, -0.82x10^{-3}, 1.28x10^{-3}, 0.9999 and 0.0120, -0.61x10^{-3}, 0.89x10^{-3}, 0.9999 for PX, SP, FRU and TCM respectively. The precision and accuracy of the method was tested by measuring six replicate samples of the drug with in Beer's law limits (PX: 10 μg; SP: 25 μg; FRU: 40μg; TCM: 600μg). The percent standard deviation and the percent range of error at 95% confidence level have been found to be 0.18, 0.19; 0.34, 0.34; 0.39, 0.38 and 0.43, 0.42 for PX, SP, FRU and TCM respectively.

Commercial formulations containing each drug were successfully analysed by the proposed method. The results obtained from the proposed and official (FRU[8], TCM[9], SP[9]) or reported methods (PX[4]) were compared statistically by means of student t-test and by the variance ratio F-test and no significant difference **(Table 1)** was observed. It indicates that none of the usual excipients employed in the formulation of dosage forms interfere in the analysis of these drugs by the proposed method Substances having no acidic centres are not expected to interfere, since extraction of drug (acidic) proceeds the colour reaction. The interference caused by other drugs like reserpine, which is usually found in combination with FRU in formulation was avoided by preliminary extraction of reserpine with chloroform. As an additional check of accuracy, recovery experiments were performed by standard addition method. These results are also summarized in Table 1. The stoichiometric ratio of the drug to dye was determined with slope ratio method[10], and was found to be 1:1 in all instances.

The proposed method is advantageous over the other reported visible spectrophotometric methods of these drugs because of the higher sensitivity and higher λ_{max} exhibited by the ion-association complex. The above four drugs are the representative ones of a larger class of drugs having acidic properties. The proposed method is simple, rapid, precise and accurate and can be used in the routine analysis and quality control of acidic drugs in pharmaceutical formulations.

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