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Extractive Spectrophotometric Determination of Venlafaxine

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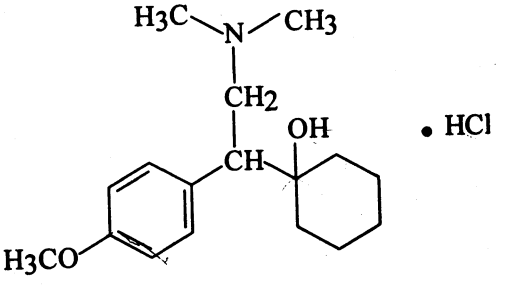
Three simple and sensitive extractive spectrophotometric methods (Method A, Method B and Method C) have been developed for the determination of venlafaxine in bulk drug and pharmaceutical formulations. The developed methods involve formation of coloured chloroform extractable complexes of drug with orange-II, bromocresol green and bromophenol blue in acidic medium. Extractable complexes showed absorption maximum at 490 nm, 430 nm and 420 nm. Beer's law is obeyed in the concentration ranges of 5–40 μg/mL, 2.5–25 μg/mL and 5–40 μg/Ll respectively. The results of analysis for all three methods have been validated statistically and by recovery studies.

Key words: Extractive, spectrophotometric, determination, venlafaxine

INTRODUCTION

Venlafaxine[1–3] is chemically (±)-1-[(2-dimethylamino)-1-(4-methoxyphenyl)-ethyl] cyclohexanol. It is an antidepressant drug and serotonin noradrenaline reuptake inhibitor. It is not official in any pharmacopoeia. Literature survey revealed that visible spectrophotometric methods are not reported for its quantitative determination in bulk drug and pharmaceutical formulations. In the present investigation, three simple and sensitive extractive spectrophotometric methods (Method A, Method B and Method C) have been developed for the determination of venlafaxine in bulk drug and pharmaceutical formulations. The developed methods involve formation of coloured chloroform extractable com-



Venlafaxine hydrochloride

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plexes of drug with orange-II, bromocresol green and bromophenol blue in acidic medium. Extractable complexes showed absorption maximum at 490 nm, 430 nm and 420 nm respectively. Beer's law is obeyed in the concentration ranges of 5-40 μg/mL, 2.5–25 μg/mL and 5–40 μg/mL respectively. The results of analysis for all three methods have been validated statistically and by recovery studies.

EXPERIMENTAL

Preparation of reagents: Buffer solution of pH 2.5 was prepared as per I.P.[4] by mixing appropriate quantities of 0.2 M potassium hydrogen phthalate and 0.2 M sodium hydroxide. Orange-II[5] (0.5%) solution was prepared by dissolving 500 mg in 100 mL distilled water. Bromocresol green[6] (0.04%) solution was prepared by dissolving 40 mg of bromocresol green in a mixture of 0.72 mL of 0.1 M NaOH and 20 mL of alcohol (95%) and made up to 100 mL with distilled water. Bromophenol blue[6] (0.1%) solution was prepared by dissolving 100 mg of bromophenol blue in 1.5 mL of 0.1 M sodium hydroxide and 20 mL of ethanol (95%) with gentle heating and added sufficient water to produce 100 mL.

All spectral measurements were made on Systronics 119 UV-visible spectrophotometer.

Standard and sample solutions: About 100 mg of venlafaxine (pure or equivalent formulation) was accurately weighed and dissolved in 20 mL of distilled water and made up to 100 mL with distilled water. Further dilutions were made with distilled water to get working standard solution of 100 μg/mL.

Assay

Method A: Volumes of standard venlafaxine solution (1 mL = 100 μg) ranging from 0.5 to 4 mL were transferred into a series of 150 mL separating funnels. To each 1 mL of orange-II dye (0.5%) solution and 0.5 mL of HCl (0.1 N) were added and the total volume of the aqueous phase was made up to 10 mL with distilled water. About 10 mL of chloroform was added to each funnel and the contents were shaken for 2 min. The chloroform layer was separated and made upto 10 mL. The absorbance of chloroform layer was measured at 490 nm against reagent blank. The amount of venlafaxine present in the sample solution was computed from its calibration curve.

Method B: Volumes of standard venlafaxine solution (1 mL = 100 μg) ranging from 0.25–2.5 mL were transferred into a series of 150 mL separating funnels. To each 3 mL of bromocresol green (0.04%) and 0.5 mL of HCl (0.1 N) were added and the total volume of the aqueous phase was made up to 10 mL with distilled water. About 10 mL of chloroform was added to each funnel and the contents were shaken for 2 min. The chloroform layer was separated and made up to 10 mL. The absorbance of chloroform layer was measured at 430 nm against reagent blank. The amount of venlafaxine present in the sample solution was computed from its calibration curve.

Method C: Volumes of standard venlafaxine solution (1 mL = 100 μg) ranging from 0.5 to 4 mL were transferred into a series of 150 mL separating funnels. To each 4 mL of bromophenol blue (0.1%) and 1 mL of buffer (2.5 pH)

were added and total volume of aqueous phase was made up to 10 mL with distilled water. About 10 mL of chloroform was added to each funnel and the contents were shaken for 2 min. The chloroform layer was separated and made up to 10 mL. The absorbance layer was separated and made up to 10 mL. The absorbance of chloroform layer was measured at 420 nm against reagent blank. The amount of venlafaxine present in the sample solution was computed from its calibration curve.

RESULTS AND DISCUSSION

The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are presented in Table-1. The % RSD and per cent range of error (0.05 level confidence limit) calculated from six measurements containing 3/4 amount upper Beer's law limit of venlafaxine are given in Table-1.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

Parameters	Method A	Method B	Method C
λ_{max}(nm)	490	430	420
Beer's law limit (μg/mL)	5–40	2.5–25	5–40
Sandell's sensitivity (μg/cm^2/0.001 abs. unit)	0.066	0.035	0.055
Molar absorptivity (L mole^{-1} cm^{-1})	0.5831×10^4	0.8213×10^4	0.6841×10^4
Regression equation (Y*)			
Slope (b)	0.0157	0.0285	0.0463
Intercept (a)	0.0025	0.0008	0.0166
Correlation coefficient (r)	0.9987	0.9998	0.9925
% RSD	0.6324	0.4826	0.4107
% Range of error (0.05 level confidence limit)	±0.5287	±0.3966	±0.3434

Y = a + bX where X is the concentration of venlafaxine in μg/mL and Y is the absorbance at the respective λ_{max}.

The values obtained for the determination of venlafaxine in pharmaceutical formulations (tablets) by the proposed and UV methods are compared in Table-2. To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analysed pharmaceutical formulations and the mixtures were analyzed by the proposed methods and the recoveries (average of six determinations) are given in Table-2. Interference studies reveal that the common excipients and the additives usually present in the dosage forms did not interfere in the proposed methods.

TABLE-2

Sample† (Tablets)	Labelled amount (mg)	Amount obtained (mg)				Recovery (%)		
		UV* method	Proposed method					
			A	B	C	A	B	C
T_1	75	74.6	74.8	74.5	74.4	99.3	98.3	98.0
T_2	75	74.4	74.7	74.6	74.9	98.6	99.0	99.6

*As the drug is not official in any pharmacopoeia, official method is not available for comparison. Hence UV method developed in our laboratory was selected.
†Tablets from different manufacturers.

The coloured complexes which are being extracted in chloroform layer are due to the formation of drug : dye complexes between the acidic dye and basic drug venlafaxine in the ratio of 1 : 1, 1.2 : 1 and 1 : 1 for method A, Method B and method C respectively. The results indicate that the proposed methods are simple, sensitive, reproducible and accurate and can be used for the routine determination of venlafaxine in bulk drug and dosage forms.

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