

form. Ten milliliters of final dilution was taken in a separating funnel and treated as per procedure described for the preparation of calibration curve. Absorbance was measured at 414 nm and the concentration of drug in sample solution was determined from calibration curve. Results of analysis are presented in Table 1.

Recovery studies were carried out by addition of known quantities of standard drug solution to pre-analysed sample at three different concentration levels and the determination was repeated for all the three methods. Results of recovery studies are presented in Table 1.

The proposed methods are colorimetric methods for determination of clarithromycin from tablet dosage form. The methods are very simple and accurate. Reproducibility of each method was checked by recovery studies and results of which were found to be close to 100% and values of stan-

dard deviation were satisfactorily low. Since no spectrophotometric method is reported for the estimation of clarithromycin from pharmaceutical formulations, the methods developed in the present investigation may perhaps be used for the analysis of clarithromycin from tablets.

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## Spectrophotometric Determination of Amiodarone and Ondansetron in Pharmaceutical Dosage Forms with Citric Acid - Acetic Anhydride Reagent

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**A sensitive spectrophotometric method is presented for determining amiodarone and ondansetron. The drugs are extracted from formulations with chloroform from an alkaline medium and reacted with citric acid-acetic anhydride reagent to produce a bluish-violet colour having absorption maximum at 580 nm. Beer's law is obeyed between 2-12 µg/ml for amiodarone and ondansetron. The results agree within ± 1.0% with official method.**

Amiodarone (as hydrochloride, AD) is a class III antiarrhythmic drug and is chemically known as 2-butyl-3-benzofuranyl-4[2-(diethylamino)ethoxy]-3,5-diiodophenyl

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ketone hydrochloride. Ondansetron (as hydrochloride, OST) is an antiemetic and is chemically known as 1, 2, 3, 9-tetrahydro-9-methyl-3-(2-methyl-1H-imidazol-1-yl)4H-carbazol-4-one monohydrochloride. AD is official in IP<sup>1</sup> and BP<sup>2</sup>, while OST is official in USP<sup>3</sup>. A number of methods such as HPLC (OST)<sup>4,7</sup>, UV (AD)<sup>8</sup> and visible spectrophotometric (OST)<sup>9-11</sup> are reported in the literature. No visible spec-

trophotometric method has been reported for the assay of AD in literature. The present method is based on the involvement of tertiary amino group<sup>12</sup> (acyclic, AD; imidazolyl, OST) in drug with ( $\alpha$ ,  $\gamma$ -aconitic anhydride (dehydrated product of C-A) as coloured internal salt ( $\lambda_{\max}$  : 580 nm). This method has been successfully used for the determination of AD or OST in the pure and pharmaceutical dosage forms.

A Milton Roy spectronic 1201 and Systronics 106 spectrophotometer with 1 cm matched quartz cells were used for all spectral absorbance measurements. All chemicals used were of analytical reagent grade. C-A was prepared by dissolving 1.2 g citric acid monohydrate (E. Merck) in 5 ml anhydrous methanol and diluting upto 100 ml with acetic anhydride (E. Merck).

AD or OST (25 mg) was treated with 20 ml of 0.1 N NaOH solution and transferred into a 125 ml separator. The free base of the drug was extracted with 4 successive 25 ml portions of chloroform. The total chloroform extract was filtered through a pledget of cotton carrying 2 g anhydrous sodium sulphate and made upto 250 ml with chloroform for getting the working standard solution (100  $\mu$ g/ml of AD or OST). Tablets powder equivalent to 25 mg of the drug (AD or OST) was taken and the sample solution was prepared

in same manner as mentioned under standard drug solution preparation.

Aliquots of standard and sample solutions (50-300  $\mu$ g of AD or OST) were taken into a series of 25 ml graduated tubes and gently evaporated on a boiling water bath to dryness. To this, 1.0 ml C-A reagent was added and the tubes were immersed in a boiling ( $95 \pm 2^\circ$ ) waterbath for 30 min. The tubes were cooled to room temperature and made upto the mark with acetic anhydride. The absorbances of the coloured solutions were measured after 15 min at 580 nm against reagent blank. The amount of the drug was computed from the calibration graph.

Beer's law limits, molar absorptivity, regression equation, correlation coefficient obtained for each drug by a linear least squares treatment of the results are given in Table 1. The precision and accuracy of the method was tested by measuring six replicate samples of the drug within Beer's law limits (200  $\mu$ g of AD or OST) and the results are summarised in Table 1.

The percent recovery values obtained are listed in Table 2. Commercial tablets containing each drug were analysed by the proposed and reference methods and compared sta-

TABLE 1: OPTICAL CHARACTERISTICS, PRECISION AND ACCURACY OF THE PROPOSED METHOD.

Parameters	AD	OST
$\lambda_{\max}$ (nm)	580	580
Beer's law limits ( $\mu$ g/ml)	2.0 - 12.0	2.0 - 12.0
Molar absorptivity (1.mole <sup>-1</sup> cm <sup>-1</sup> )	$3.589 \times 10^4$	$1.585 \times 10^4$
Sandell's sensitivity ( $\mu$ g.cm <sup>-2</sup> /0.001 absorbance unit)	$1.72 \times 10^{-2}$	$2.08 \times 10^{-2}$
Regression equation (Y = a + bC)*		
Slope (b)	$5.56 \times 10^{-2}$	$4.48 \times 10^{-2}$
Intercept (a)	$6.66 \times 10^{-5}$	$4.0 \times 10^{-4}$
Correlation coefficient (r)	0.9999	0.9999
Relative standard deviation (%)**	0.368	0.481
% range of error (confidence limits)**		
0.05 level	0.386	0.505
0.01 level	0.605	0.790
% Error in bulk samples***	0.157	0.182

\*Y=a+bC, where C is concentration of analyte and Y is absorbance unit; \*\*Average of six determinations considered; \*\*\*Average of three determinations considered.

TABLE 2: ASSAY OF AD AND OST IN PHARMACEUTICAL DOSAGE FORMS.

Drug*	Lable claim mg/tablet	Amount found		% Recovery by Proposed method***	
		Proposed method**	Reference method (AD <sup>o</sup> , OST <sup>o</sup> )		
AD	Tablet 1	100	99.83 ± 0.15 F = 2.39 t = 1.28	99.79 ± 0.24	99.83 ± 0.15
	Tablet 2	100	99.63 ± 0.48 F = 1.82 t = 0.42	99.66 ± 0.36	99.63 ± 0.48
	Tablet 3	200	199.67 ± 0.31 F = 1.12 t = 0.62	199.62 ± 0.33	99.89 ± 0.18
	Tablet 4	200	199.39 ± 1.05 F = 2.15 t = 1.00	199.39 ± 0.71	99.69 ± 0.52
OST	Tablet 1	4	3.992 ± 0.007 F = 1.92 t = 0.95	3.985 ± 0.012	99.81 ± 0.18
	Tablet 2	4	3.995 ± 0.008 F = 1.85 t = 0.95	3.99 ± 0.009	99.88 ± 2.0
	Tablet 3	8	7.979 ± 0.018 F = 1.23 t = 1.50	7.985 ± 0.021	99.74 ± 0.22
	Tablet 4	8	7.951 ± 0.03 F = 1.13 t = 1.14	7.970 ± 0.03	99.39 ± 0.39

\*Drug from different pharmaceutical companies; \*\* Average ± Standard deviation of 6 determinations, the t- and F-test values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limit, F = 5.05, t = 2.57; \*\*\* Recovery of 10 mg added to the preanalysed pharmaceutical dosage forms (average of three determinations).

tistically by means of student's t-test and by the variance ratio F-test and no significant difference was observed. It indicates that none of the usual excipients employed in the dosage forms interfere in the analysis of AD or OST by the proposed method. The proposed method is superior over the reported ones for OST as it possesses higher  $\lambda_{max}$  and  $\epsilon_{max}$  values. The proposed method is sensitive, rapid, selective and accurate for the determination of AD or OST in pharmaceutical dosage forms.

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## Sensitive Spectrophotometric Methods for the Analysis of Some Anesthetic Drugs

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**Two simple and sensitive visible spectrophotometric methods for the analysis of some anesthetic drugs in pure and available pharmaceutical preparations have been developed. The first method is based on the formation of colored ion-pair complexes by the drugs, ketamine hydrochloride, lignocaine hydrochloride, bupivacaine hydrochloride and tetracaine hydrochloride with bromothymol blue. The ion-pair complexes formed are quantitatively extracted into dichloromethane and absorbance is measured at 420 nm. The second method is based on the coupling of the diazotized drugs benzocaine and procaine hydrochloride with a new and highly sensitive coupling agent, monosodium salt of 4-amino-5-hydroxynaphthalene-2,7-disulfonic acid. The absorbance of the red azo-dye is measured at 530 nm. These methods are quantitatively evaluated and found to be precise and accurate. Beer's law is obeyed in the concentration range 1-15 µg/ml and 0.1-7 µg/ml for first and second methods, respectively.**

Anesthetics are drugs, which produce anesthesia, a condition of inability to feel sensation<sup>1</sup>. Two types of anesthetic drugs are generally recognized: local and general. Local anesthetic drugs can be conveniently divided into two groups: esters and nonesters, benzocaine (BzC), tetracaine hydrochloride (TC) and procaine hydrochloride (PC) belong to p-aminobenzoic acid ester group, whereas lignocaine hydrochloride (LC) and bupivacaine hydrochloride (BpC) are nonester or amide type anesthetic drugs. Local anesthetics with an ester linkage and those with amide linkage differ significantly in hypersensitivity, metabolism and duration

of action<sup>1</sup>. Ketamine hydrochloride (KT) is a general anesthetic drug.

The official method of IP describes nitrite titration method for BzC<sup>2</sup>, BpC<sup>3</sup>, KT<sup>4</sup>, LC<sup>5</sup> and PC<sup>6</sup> (TC is not included in IP) and USP describes HPLC method for BzC<sup>7</sup>, TC<sup>7</sup>, BpC<sup>8</sup>, KT<sup>9</sup>, LC<sup>10</sup> and PC<sup>11</sup>. A few contemporary analytical techniques employed for the analysis of these drugs include HPLC<sup>12</sup>, chemiluminescence<sup>13</sup>, potentiometry<sup>14</sup> and titrimetry<sup>15,16</sup>. A few spectrophotometric methods have already been reported for the determination of anesthetic drugs. Reported methods in one way or the other have disadvantages like lack of sensitivity<sup>17-19</sup>, long time for reaction to complete<sup>20</sup> and tedious heating procedures<sup>21</sup>. However, no single method has

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