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Spectrophotometric determination of trandolapril and aripiprazole in pharmaceutical dosage forms with citric acid- acetic anhydride reagent

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ABSTRACT

A Simple and sensitive method is presented for determining Trandolapril and Aripiprazole. The drugs were extracted from formulations with chloroform in an alkaline medium and reacted with citric acid – acetic anhydride reagent to produce a red-violet color having absorption maximum at 590nm. Beer's law is obeyed between 2-12 µìg/ml for Trandolapril and Aripiprazole. The results obtained are statistically validated.

Key words: Spectrophotometric, citric acid, acetic anhydride, determination, formulation.

INTRODUCTION

In the recent years there has been growing interest in the role of citric acid and acetic anhydride as analytical reagent in the assay of pharmaceutical dosage forms. Trandolapril[1-3] is a hypertensive and inhibitor of angiotensin converting enzyme (ACE) and blocks the formation of angiotensin (II) thereby lowering blood pressure. It is [(2s, 3aR, 7aS)-1-carboxy-3-phenyl propyl] alanyl hexahydro- 2-indoline carboxylic acid, 1- ethyl ester. Aripiprazole[4] is an antipsychotic and chemically known as sec 2 (IH)- Quinoline, 7[-4-(2,3- dichloro-phenyl)-1-piperazinyl] butoxyl –3,4-dihydro[129722-12-9] CAS NO. In the present investigations, the presence of tertiary amino group in TRA[5,6,12] and ARI[7-11,13-15,16] permits the development of new spectrophotometric method for its determination through the formation of red-violet color, internal salt[17] of aconitic anhydride[18].

EXPERIMENTAL

Instruments

An ELICO, UV- Visible spectrophotometer with 1 cm matched quartz cells were used for the spectral and absorbance measurements. An ELICO L 1-120 digital pH meter was used for pH measurements.

Chemicals

All the chemicals used were of analytical reagent grade. CIA was prepared by dissolving 1.2 g of citric acid monohydrate in 5ml of methanol (anhydrous) and diluting upto 100ml with acetic anhydride (Qualigens).Tablets containing ARI or TRA were treated with 20ml of 0.1N NaOH solution and transferred into a 125ml separator. The free base of the drug was extracted with 3 successive 25ml portions of chloroform. The total extract of each drug was filtered through anhydrous sodium sulfate

and made upto, with chloroform to get the working standard solution (100µg/ml).

METHOD

Aliquots of standard and simple solutions (50-300µg/ml) in free base form were taken into a series of 25ml graduated tubes and gently evaporated on a boiling water bath to dryness. To this 10.0ml of CIA- AC_2O reagent was added and the flasks were immersed in boiling water bath for 30min. The tubes were cooled to room temperature and made upto the mark with acetic anhydride. The absorbance of the colored solutions were measured after 15 min. at 590nm against reagent blank. The amount of the drug in the dosage forms was computed from the calibration graph.

RESULTS

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 and the results are summarised in Table1.

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 statistically 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 TRA and ARI by the propose method. The proposed is superior over the reported ones for TRA and ARI. The proposed method is sensitive, rapid, selective and accurate for the determination of TRA and ARI in pharmaceutical dosage forms.

Table 1: Optical, regression characteristics, precision and accuracy of the proposed method for TRA and ARI

Parameter	TRA	ARI
λ_{max} (nm)	590	590nm
Beer's law limits (µg/mL)	2-12	2 -12
Detection limits (µg/mL)	0.2547	0.3712
Molar absorptivity ($1.mol^{-1}cm^{-1}$)	0.1479×10^{3}	0.3374×10^{5}
Sandell's sensitivity ($\mu g.cm^{-2}$/0.001 absorbance unit)	0.0547	0.0133
Optimum photometric range (µg/mL)	4-8	40-100
Regression equation (Y=a+bx)		
i) Slope (b)	0.0214	0.0754
ii) Standard deviation on slope (S_b)	3.124×10^{-5}	6.28×10^{-5}
iii) Intercept (a)	-3.32×10^{-2}	-0.0009
iv) Standard deviation on intercept (S_a)	2.564×10^{-2}	0.9022
v) Standard Error of Estimation (S_e)	5.3691×10^{-4}	5.26×10^{-4}
vi) Correlation co-efficient (r)	0.9989	0.9999
vii) Relative standard deviation (%)*	0.5587	0.3586
% Range of error (confidence limits)*		
i) 0.05 level	0.5471	0.3764
ii) 0.01 level	0.7854	0.5904
% Error in bulk samples**	0.2647	0.2417

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

Table 2: Determination of TRA & ARI in pharmaceutical formulations

Sample	Labelled amount (mg)	Amount found by Proposed Methods*	Ref. method	% Recovery by Proposed methods **
TRA Tab 1	4	3.987±0.49 F=1.1347 t=0.7108	3.79±0.46	99.75±0.22
Tab. II	2	2.00±0.028 F=4.0 t=0.9116	1.99±0.01	99.75±0.22
Tab III	1	0.995±0.20 F=1.1080 t=0.0433	0.99±0.19	99.75±0.22
ARI Tab I	10	9.88±0.183 F=2.143 t=0.8997	9.96±0.125	100.01±0.72
Tab II	15	14.990±0.152 F=1.481 t=1.994	15.15±0.125	100.01±0.72

*Tablets from four different pharmaceutical companies.

**Average ± standard deviation of six 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 10mg added to the pre analyzed pharmaceutical formulations (average of three determinations).

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