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Cobalt Thiocyanate as Chromogenic Reagent for Determination of Trandolapril and Aripiprazole

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A new spectrophotmetric method for the assay of trandolapril and aripiprazole has been described. The coloured species formed by interaction of cobalt thiocyanate and the experimental drugs. They form the coordination complex of the drug (electron donor) and the central metal atom of cobalt thiocyanate which is extractable into nitrobenzene from aqueous solution. The coloured complexes when trandolapril or aripiprazole is treated with cobalt thiocyanate due to the presence of secondary or tertiary amino group respectively, is the basis in the present investigation. It has maximum absorption at 620 nm. Beer's law limits, precision and accuracy of the methods are checked suitable for the assay of trandolapril and aripiprazole in the presence of other ingredients that are usually present in tablets.

Key Words: Trandolapril, Aripiprazole, Cobalt thiocyanate, Spectrophotometric.

INTRODUCTION

Trandolapril (TRA), Sec H-indole-2- carboxylic acid, 1-(2S)-2- [(1S)-(ethoxy carbonyl)-3-phenyl propyl]amino-1-oxopropyl]octahydro-(2S,3aR,7as)-[87679-37-6], is an inhibitor of angiotensin converting enzyme and blocks the formation angiotensin II thereby lowering blood pressure. It is antihypertensive. It is available in capsules and tablets. Literature survey reveals that only a few methods based on HPLC (TRA)[1,2], LC-MS, (TRA)[3] are reported, while no effective spectrophtometric method is reported.

Aripiprazole is an antipsychotic and chemicaly is 7-[4-[4-(2,3-dichloro phenyl)-1-piperazinyl]butoxy]-3-dihydro carbostyril. It is available in tablets and oral solution. Literature survey reveals that only a few methods based on HPLC (ARI), LC-MS (ARI), LC-UV (ARI) are reported[4-7] for this drug and no specific spectrophtometric method is reported. Cobalt thiocyanate (CTC) has been proved to be a valuable chromogenic reagent for the detection and determination of amino compounds[8-10]. Cobalt thiocyanate has been proved to be a valuable chromogenic agent. Surprisingly the coloured species formed is the coordination complex of the drug TRA or ARI and the central metal atom of cobalt thiocyanate which is extractable into nitrobenzene from aqueous solution. These methods are applicable for the determination of TRA and ARI in formulations.

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EXPERIMENTAL

An Elico, UV-visible digital spectrophotometer with 1 cm matched quartz cells were used for the spectral and absorbance measurements. An Elico L1-120 digital pH meter was used for pH measurements.

All the chemicals and reagents used were analytical grade and the solutions were prepared freshly. Aqueous solution of cobalt thiocyanate (BDH, 2.5×10^{-1} M) was prepared and pH 2.0 trisodium citrate was also prepared. Nitrobenzene (Qualigens) was used as it is. Double distilled water was used throughout the experiment.

Preparation of standard drug solution: A 1 mg/mL stock solution of TRA (in free base form) was prepared by treating 100 mg of TRA with 5 mL of 10 % sodium carbonate, followed by extraction with chloroform (3 × 15 mL) and dilution to 100 mL with the same solvent.

A 1 mg/mL stock solution of ARI was prepared by dissolving 100 mg of it in 0.1 N sodium hydroxide or isopropanol.

The standard stock solutions of these drugs were further diluted with appropriate solvent to get the working standard solutions of TRA (800 µg/mL) and ARI (800 µg/mL)

Recommended procedure: Into a series of 125 mL separating funnels containing aliquots of standard drug solution (0.5-3.0 mL, 800 µg/mL) for TRA and ARI. 2.0 mL of buffer (pH 2.0) and 5.0 mL of CTC (1.25×10^{-1} M) solutions were added. The total volume of aqueous phase in each separating funnel was adjusted to 15.0 mL with distilled water. To each separating funnel 10.0 mL of nitrobenzene was added and the contents were shaken for 2 min. Two phases were allowed to separate and the absorbance of the separated nitrobenzene was measured at 620 nm against a similar reagent blank within the stability period 5-60 min. The amount of drug (TRA or ARI) was deduced from its calibration curve.

RESULTS AND DISCUSSION

Fixation of optimum conditions: The optimum conditions for the development of colour were established by varying the parameters one at a time, keeping the others fixed and observing the effect produced on the absorbance of the coloured species. Variation of pH beyond upper and lower limits results in decrease of absorbance. pH 2.0 was fixed with maximum absorption. For covering broad range of Beer's law limits and to give maximum absorbance, CTC volume was varied from 4 to 7 mL, but 5 mL CTC was found to be necessary. Among the various water immiscible organic solvents tested for the extraction of coloured coordinate complex into organic layer, nitrobenzene was preferred for selective extraction of coloured complex. The product was stable upto 5 min. The ratio of organic to aqueous phase was fixed as 1:1.5 and the shaking time was 2 min. Beer's law limits, molar absorptivity, Sandell's sensitivity and regression characteristics of the proposed methods are presented in Table-1. The relative standard deviation and % range of error at 95 % confidence level also given in Table-1. A few commercial formulations (tablets) containing

TABLE-1

Parameter	TRA	ARI
λ_{max} (nm)	620	620
Beer's law limits (µg/mL)	16-96	16-94
Detection limits (µg/mL)	0.3709	1.4115
Molar absorptivity (1 $mol^{-1}cm^{-1}$)	0.2805×10^4	0.2164×10^4
Sandell's sensitivity (µg cm^{-2}/0.001 absorbance unit)	0.1535	0.2073
Optimum photometric range (µg/mL)	40-100	32-50
Regression equation (Y = a+bx)		
i) Slope (b)	0.0066	5.001×10^{-3}
ii) Standard deviation on slope (S_b)	1.9343×10^{-5}	9.6435×10^{-5}
iii) Intercept (a)	-2.87×10^{-3}	-0.00691
iv) Standard deviation on intercept (S_a)	0.1840	0.9023
v) Standard Error of Estimation (S_e)	1.294×10^{-3}	1.9223×10^{-3}
vi) Correlation co-efficient (r)	0.9999	0.9999
vii) Relative standard deviation (%)*	0.4481	0.6025
% Range of error (confidence limits)*		
i) 0.05 level	0.4703	0.6324
ii) 0.01 level	0.7376	0.4918
% Error in bulk samples**	0.9874	0.0021

*Average of six determinations, **Average of three determinations.

TRA or ARI were successfully analyzed by the proposed method. The results obtained by the proposed and reference method were compared statistically by means of F- and t-tests and were found not to differ significantly at the 95 % confidence level. Recovery studies were performed by adding a fixed amount of the drug to the preanalyzed formulations and the results are present in Table-2.

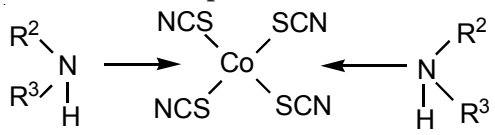
TABLE-2

Sample		Labelled amount (mg)	Amount found by methods*	Reference method	% Recovery by proposed method
TRA	Tablet 1	4	3.85 ± 0.49 F = 1.135 t = 0.217	3.79 ± 0.46	99.74 ± 0.15
	Tablet 2	2	1.975 ± 0.015 F = 2.25 t = 1.998	1.99 ± 0.01	99.78 ± 0.17
	Tablet 3	1	0.997 ± 0.25 F = 1.7313 t = 0.0551	0.99 ± 0.19	99.76 ± 0.12
ARI	Tablet 1	10	9.92 ± 0.163 F = 1.700 t = 0.4811	9.96 ± 0.125	99.29 ± 0.63
	Tablet 2	15	15.10 ± 0.201 F = 2.5848 t = 0.5312	15.15 ± 0.125	99.29 ± 0.63

*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.

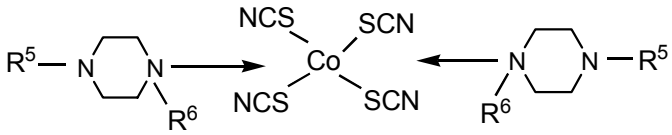
Interference studies in the determination of TRA and ARI in pharmaceutical formulations revealed that normally existing excipients and additives were found not to interfere even when present in excess than anticipated amount.

Chemistry of the coloured species:



TRA
Table 1.04
P.30&31

TRA
Table 1.04
P30&31



ARI
Table 1.04
P.32

ARI
Table 1.04
P.32

Conclusion

This newly proposed spectrophotometric method for the assay of TRA and ARI is simple, sensitive, selective and reliable. The colour reaction does not require stringent conditions or many reagents or solvents. The statistical data is in agreement with the reference method. Hence, this method can be suitable for the micro-determination of TRA or ARI in pure and pharmaceutical formulations in quality control laboratories depending upon the needs of situation and availability of facilities.

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