Determination of Catopril in Non-aqueous Media by Potentiometric and Enthalpimetric Techniques

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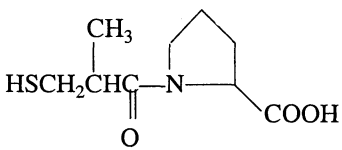
The most simple cost effective, time saving and precise method has been developed to determine captopril, an antihypertensive and weakly acidic drug using strongly basic titrants by potentiometric and enthalpimetric methods in acetone and DMF media.

INTRODUCTION

Different methods[1–6] are suggested for determination of captopril, an antihypertensive drug. The official method[7] involves the use of TLC and HPLC for determination of captopril. The literature survey reveals that the determination of captopril at mg level has not been carried out enthalpimetrically and potentiometrically in purely non-aqueous media using tetra-*n*-butyl ammonium hydroxide (*n*-Bu_4NOH) and alc. KOH as titrants. The present communication reports the determination of captopril in anhydrous acetone and DMF media using different titrants and techniques.

EXPERIMENTAL

All chemicals used were of AR grade. The solvents, *i.e.*, acetone, isopropyl alcohol, methyl alcohol, toluene and DMF were purified by standard methods[8]. The solutions of potassium hydroxide in isopropyl alcohol (alc. KOH) and tetra-*n*-butyl ammonium hydroxide (*n*-Bu_4NOH) in toluene-methanol as titrants were prepared as reported earlier[9]. Benzoic acid solution was prepared in acetone. AR acrylonitrile monomer was used as an indicator when DMF was used as solvent for enthalpimetric titration. Stock solutions in acetone and DMF containing 1.99 mg/mL of captopril was prepared. captopril I.P. with structure



was recrystallised from alcohol and used. The purity was checked by TLC.

For potentiometric titration digital pH-meter (Systronics, type 335) with a high input impedance and an accuracy of ±1 mV was used as potentiometer. Antimony rod was used as indicator electrode in non-aqueous medium since it has high sensitivity towards change in H^+ ion concentration[10, 11]. Morevover, this electrode

does not require conditioning and its surface can be easily cleaned when it loses its sensitivity. Its electrode reaction is

$$Sb_2O_3 + 6H^+ + 6e^- \rightleftharpoons 2Sb + 3H_2O$$

Calomel electrode was used as reference electrode and was modified by using methanol instead of water to prevent contamination of solvent by water and the electrode was conditioned in the solvent medium to be used for titration, for 1 h before use. For enthalpimetric titration a moisture-free glass apparatus used by Greenhow and Spenser[12] was slightly modified and used in the present investigation. The complete assembly of the apparatus consists of well insulated titration glass vessel fitted with thermometer, inlet gas tube for nitrogen gas and burette with side arm as reservoir for solution with guard tubes. The stirring was effected by magnetic stirrer.

Procedure

All titrations were carried out in nitrogen atmosphere in triplicate in acetone and DMF media and the procedure adopted in the present studies was as reported earlier[14].

Enthalpimetric Titration: An amount of requisite concentration of captopril was titrated in acetone medium in inert nitrogen atmosphere by continuous addition of titrant (alc. KOH and *n*-Bu_4NOH) with stirring and the temperature was recorded for every 0.2 mL addition. Near the end point, the temperature was recorded for every 0.02 mL addition. It was observed that as the titrant was added the temperature decreased slightly till the end point due to the endothermic nature of the reaction between weak acid (captopril) and titrant (base). However, at the end point the curve showed sudden break with sharp rise in temperature due to the reaction between acetone and excess base from burette which is an exothermic reaction and leads to the formation of diacetone[13]. Thus the heat liberated during dimerisation of acetone is responsible for the sharp rise in temperature which is taken as the end point. Hence in acetone medium no external indicator (monomer) is required for the polymerisation process. However, in DMF medium, the addition of acrylonitrile as monomer is required for polymerisation reaction in presence of base, since DMF alone does not polymerise like acetone at the end point. Due to the heat liberated during polymerisation of acrylonitrile in presence of base at the end point, there is sharp increase in temperature[12]. AR benzoic acid in acetone and DMF was used to standardise both the titrants.

Potentiometric titration: Before the thitrations, the electrodes described above were conditioned in the respective solvents. The required volume of solution of captopril was diluted to 20 mL with acetone or DMF and the electrodes were dipped in it. In the beginning 0.1 mL of titrant was added and the potential developed across the electrodes was measured. Near the end point 0.02 mL of titrant was added at a time and the end point was determined by sudden change in potential and the correct end point was computed by dE/dV *vs* V graph.

RESULTS AND DISCUSSION

Choice of Solvent

To study the effect of solvent on the accuracy of results, fixed amount of captopril was titrated with alc. KOH and *n*-Bu_4NOH as titrants in acetone and DMF media separately by enthalpimetric and potentiometric methods. The results indicate that both solvents are suitable for enthalpimetric and potentiometric titration with both the titrants. However, the results obtained in acetone medium are comparatively more accurate and moreover with acetone as solvent in enthalpimetric titration, no external indicator (acrylonitrile as monomer) is required to note temperature change at the end point, since acetone itself dimerises in basic medium with evolution of heat. Hence, further studies including effect of dilution, titrant and concentration of drug on the results have been undertaken only in acetone medium.

Effect of Titrant and Concentration of Drug

Different volumes of stock solution of captopril in acetone (1.99 mg/mL) were diluted to 20 mL with acetone and titrated with alc. KOH and *n*-Bu_4NOH by enthalpimetric and potentiometric methods. The results are incorporated in Table-1. It is observed from Table-1 that captopril with alcoholic KOH as well as *n*-Bu_4NOH as titrants can be quantitatively estimated between 1.9 to 9.9 mg, and 2.9 to 8.0 mg respectively by enthalpimetric technique. However, the optimum concentration ranges for the determination of captopril with alc. KOH and *n*-Bu_4NOH using potentiometric technique have been found to be 1.90 to 10.00 mg and 2.0 to 8.0 mg respectively. The comparison of the results shows that the potentiometric technique has been found to yield better results with alc. KOH as titrant.

Determination of captopril in Formulation

Ten tablets of same batch were accurately weighed and powdered. The powder containing 400 mg of captopril was accurately weighed, extracted with acetone and the volume was made up to 100 mL. The undissolved portion of the tablet was rejected. An aliquot of 10 mL of this solution was potentiometrically titrated with alc. KOH, previously standardised with standard benzoic acid solution in acetone. The amount of captopril present per tablet was determined. The results for five different samples were recorded in Table-2. The samples were also analysed by official (I.P.) method. It is observed from Table-2 that the present method gives results comparable to those obtained by I.P. method. Recovery studies carried out by addition of known standard solution to preanalysed sample varied from 99.7 to 101.4%. The mean and standard deviation have been found to be 0.26 and 0.36 respectively and coefficient of variance have been found to be 0.72.

TABLE-1
EFFECT TO TITRANT AND CONCENTRATION OF CAPTOPRIL
MEDIUM—ACETONE

Titrant	Weight taken	Enthalpimetric titrations		Potentiometric titrations	
		Weight found (%)	(%) Error	Weight found (%)	(%) Error
Alc. KOH	0.996	0.961	–3.5	0.962	–3.4
	1.992	1.941	–2.6	1.947	–2.3
	2.988	2.912	–2.5	2.955	–1.1
	3.984	3.912	–1.8	3.937	–1.2
	4.980	4.899	–1.6	4.928	–1.0
	5.976	5.849	–2.1	5.896	–1.3
	6.972	6.822	–2.2	6.852	–1.6
	7.968	7.769	–2.5	7.840	–1.6
	8.964	8.720	–2.7	8.782	–2.0
	9.960	9.658	–3.0	9.743	–2.2
	10.956	10.606	–3.2	10.680	–2.5
	11.952	11.495	–3.8	11.589	–3.0
n-Bu_4NOH	0.996	0.951	–4.5	0.958	–3.8
	1.992	1.921	–3.6	1.945	–2.4
	2.988	2.908	–2.7	2.949	–1.3
	3.984	3.878	–2.6	3.942	–1.1
	4.980	4.885	–1.9	4.894	–1.7
	5.976	5.847	–2.2	5.878	–1.6
	6.972	6.780	–2.8	6.830	–2.0
	7.968	7.715	–3.2	7.781	–2.3
	8.964	8.687	–3.1	8.712	–2.8
	9.960	9.615	–3.5	9.658	–3.0
	10.956	10.538	–3.8	10.600	–3.2
	11.952	11.446	–4.2	11.529	–3.5

TABLE-2
DETERMINATION OF CAPTOPRIL IN TABLETS BY POTENTIOMETRIC TECHNIQUE IN ACETONE (Titrant: Alc. KOH)

Sr. No.	Sample	Label Claim mg	Weight Found in mg*	
			By I.P. method	By proposed method
1	A	25	24.30	24.50
2	B	25	24.60	24.80
3	C	50	49.50	49.20
4	D	50	49.60	49.90
5	E	50	49.20	49.40

*Average of four determinations

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