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Use of sodium tetraphenylborate reagent for conductometric titration of Amlodipine Besylate in pure and pharmaceutical forms

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Abstract— *Simple, accurate and reliable conductometric method for the quantitative determination of Amlodipine Besylate (AML) in pure form and pharmaceutical formulations using sodium tetraphenylborate (TPB) in aqueous solution at 20°C has been described. The method is based on the formation of ion association complex of cation coming from the cited drug with tetraphenylborate anion and the conductance of the solution is measured as a function of the volume of titrant. Many experimental conditions were evaluated. The described procedure allowed the determination of AML in double distilled water in the range of 0.200-1.000mM. The accuracy of the method is indicated by the excellent recovery 98.60-101.40%, and the precision is supported by the low relative standard deviation < 4.74 %. The method was further applied successively to pharmaceutical formulations with no interference from the excipients, the results obtained were compared statistically with those obtained by the official method and showed no significant differences regarding accuracy and precision.*

Keywords— ***Amlodipine Besylate, conductometric titration, sodium tetraphenylborate, pharmaceutical forms.***

I. INTRODUCTION

Amlodipine besylate (AML), has chemical name known as (4R,S)-3 ethyl-5-methyl 2-(2- amino-ethoxy-methyl)-4-(2 chlorophenyl)-1,4-dihydro-6-methyl pyridine-3,5 dicarboxylate monobenzene sulphonate and is one of the dihydropyridine class and long acting calcium channel blocking agents using as antihypertensive in cardiovascular diseases [1].

Several methods have been described for the quantitative determination of AML in pharmaceutical dosage forms by spectrophotometric methods [2-14], HPLC with ultra violet detection [15-20], fluorescence detection [21], HPTLC [22]. AML has been determined in human plasma and tablets by Glassy Carbon Electrode [23-25].

The present manuscript describes conductometric method that is simple and accurate for determination of Amlodipine Besylate (AML) in bulk samples and pharmaceutical preparations using sodium tetraphenylborate (TPB) as reagent.

II. EXPERIMENTAL

2.1. Apparatus

A conductometer – pH meter Consort C830 (Belgium) equipped with conductivity cell (cell constant of 1.0) and combined glass pH electrode was used. The desired temperature was maintained with circulating water bath thermostat connected to a jacket around the analysis vessel.

2.2. Chemicals

All chemicals and reagents used throughout this work were of analytical-reagent grade and supplied by Merck and solutions were made with doubly distilled water.

Amlodipine Besylate (AML) was obtained from Kunshan Chemical, India. The purity of AML was found to be 99.48%. Sodium tetraphenylborate (TPB) was obtained from (BDH). Methanol (Surechem products,LTD)) and ethanol (EuroLab) were also used. Pharmaceutical preparations containing AML were purchased from commercial sources in the local market.

2.3. Solutions

Solution of 10mM TPB was prepared by dissolving appropriate weight in 100 mL of double distilled water. The solution was standardized and kept in light-resistant, well-closed container. Stock standard solution, 1mM of AML was prepared in double distilled water, stored in dark bottle. Other concentrations of working solutions were then prepared by suitable dilution of the stock solution with double distilled water.

2.4. General procedure

Aliquot volumes (2.5-25mL) of standard stock solution (1mM, AML), were transferred separately into a series of 25mL calibrated flasks and completed to volume with double distilled water if necessary. The contents of the calibrated flask were transferred quantitatively to a conductometric titration cell, the conductivity cell was immersed in the sample solution, the solution was then titrated conductometrically against 10mM TPB and the conductance was measured subsequent to each addition of the reagent solution and after thorough stirring for one min. The conductance was corrected for dilution [26] by means of the following equation:

$$\Omega^{-1}\text{correct} = \Omega^{-1}\text{obs}\,[V_1+V_2/V_1]$$

where Ω^{-1} is the corrected electrolytic conductivity, Ω^{-1}obs is the observed electrolytic conductivity, V_1 is the initial volume and V_2 is the volume of reagent added.

2.5. Procedure for the pharmaceutical formulations

Twenty tablets of the selected drug were weighed and finely powdered. An accurately weighed amount of the powder equivalent to 56.705mg of AML was dissolved in a 100 mL of ethanol, and sonicated for 5 minutes and then filtered. The combined filtrate was evaporated to the dryness. The remaining portion of the solution was dissolving in a 100 mL volumetric flask to the volume with double distilled water, and the resulting solution was used for analysis by the recommended procedure in the concentration range mentioned above.

III. RESULTS AND DISCUSSION

Conductometric measurements can be used in quantitative titrations of ionic solutions in which the conductance of the solution varies before and after the equivalence point, so that two intersecting lines can be drawn to indicate the end-point. The shape of the titration curve depends on all the species present during the titration process and other factors such as viscosity, dielectric constant, solvation, ion-pair association and proton transfer.

Amlodipine Besylate is able to form precipitate with sodium tetraphenylborate so the applicability of conductometric titration of this drug with the mentioned reagent, was tested. The different parameters affecting the end point, such as solvent, electrolyte concentration (drug and reagent) and temperature were studied.

3.1. Effect of solvent

The effect of solvents on the specific electrical conductivity was shows that the values were increased as follows MeOH>H_2O>EtOH for AML and TPB (Figure 1).

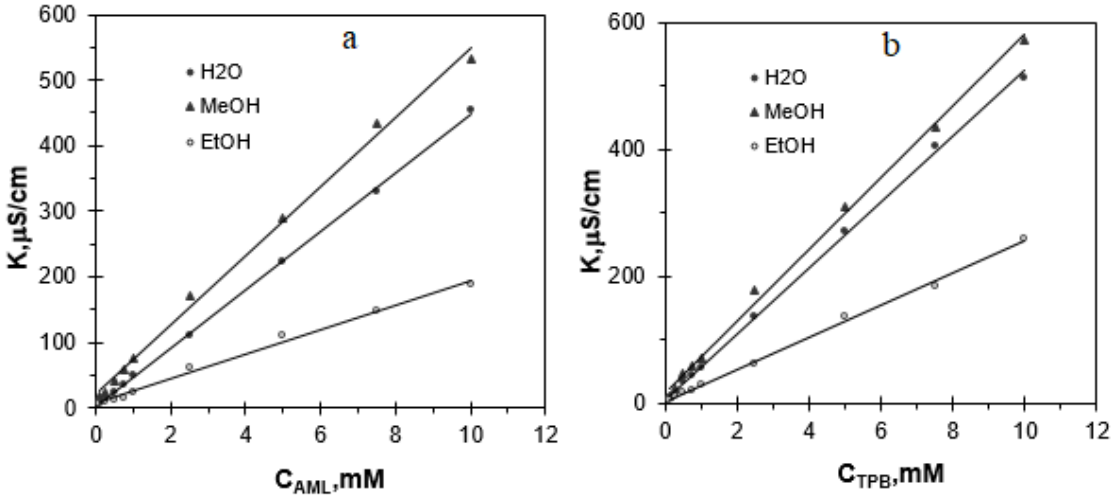


Fig.1. Effect of solvent on the conductance values: (a) AML 1mM, (b) TPB 1mM.

The effect of solvent on the end point of the conductometric titration was tested by three different titrations: (i) aqueous drug solution with aqueous reagent solution; (ii) methanolic drug solution with methanolic reagent solution and (iii) ethanolic drug solution with ethanolic reagent solution at 20 ºC.. Preliminary experiments showed that procedure (i) was the most suitable for successful results, because in procedures (ii) and (iii) the end-point detection is very difficult and so the precision is very low, whereas in water medium sharpest end point was detected as shown in Figure 2. So water was the best and cheapest choice medium for conductometric titration.

3.2. Effect of electrolyte concentration (drug and reagent)

The relationship between the conductance values and the concentration of AML, and TPB solutions in aqueous and alcoholic media was linear increasing in the range of 0.1-10 mM for AML and TPB, and indicated that the values were as follows TPB > AML in water and ethanol ,and TPB ≈ AML in methanol as shown in Figure 3.

A solutions 1mM of AML were prepared with double distilled water in 25 mL and titrated against 1mM, 5mM and 10mM TPB solution. The results indicated that, the optimum concentration of TPB was 10mM to achieve a constant and highly stable conductance reading after 1 minute mixing.

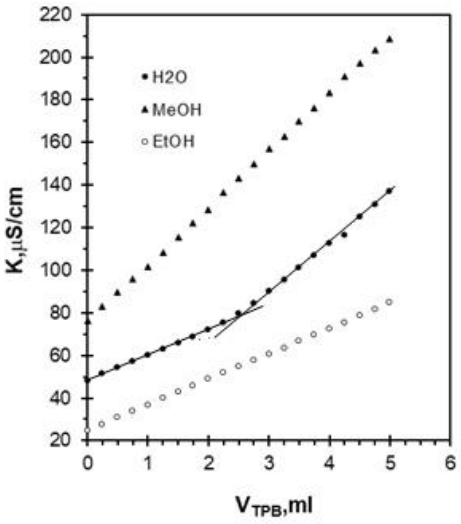


Fig.2. Effect of solvent on the end point of the conductometric titration of 25 mL of AML1mM with 10m M TPB at 20ºC.

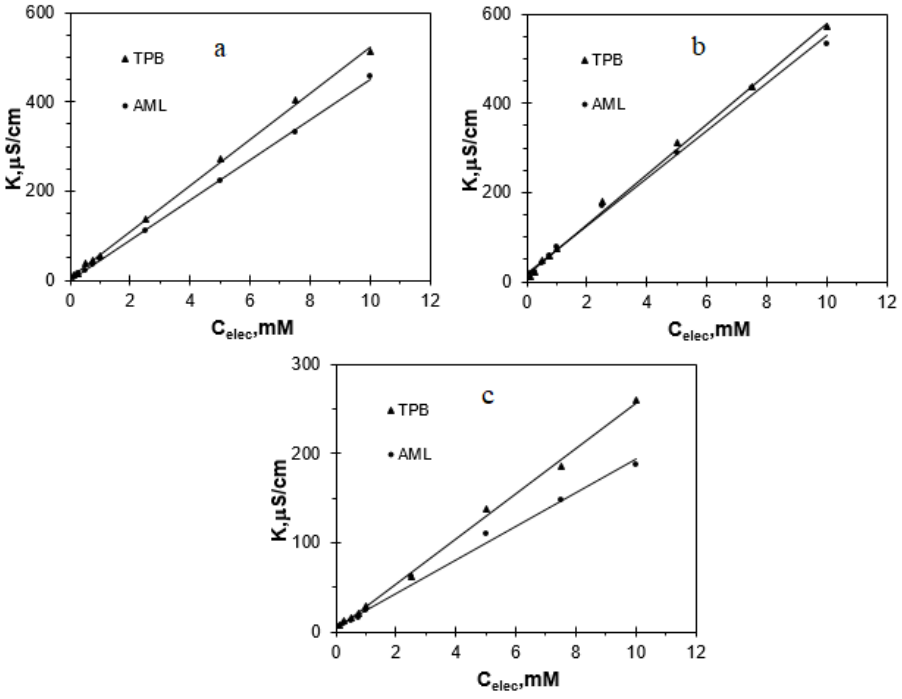


Fig.3. Effect of electrolyte concentration on the conductance values in rang 0.1-10mM: (a) water, (b) Methanol, (c) Ethanol.

3.3. Effect of temperature

The relation between the conductance values and temperature of the solutions of AML, and TPB was linear increasing in aqueous media in the range of 20-60 ºC, (Figure. 4).

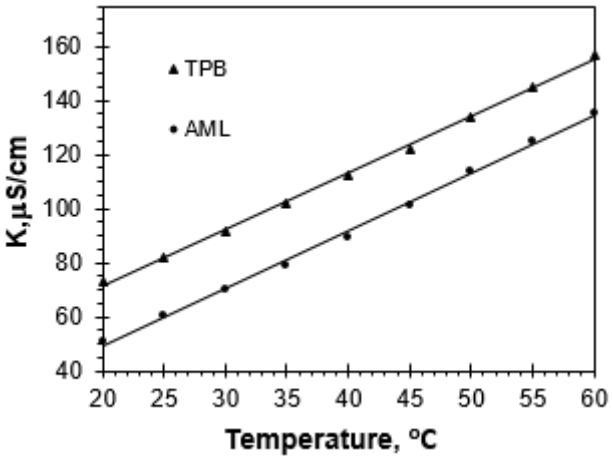


Fig.4. Effect of temperature on the conductance values AML 1mM and 1mM TPB in aqueous medium

The effect of temperature on the end point of the conductometric titration was tested by carrying out titrations at 20 - 60 °C. The results showed that as the temperature increases, the conductivity of the whole solution increases, and no effect was observed on the shape of the titration curve and the position of the end point up to 40 °C, then 20 °C was used for carrying out the other variables (Figure. 5).

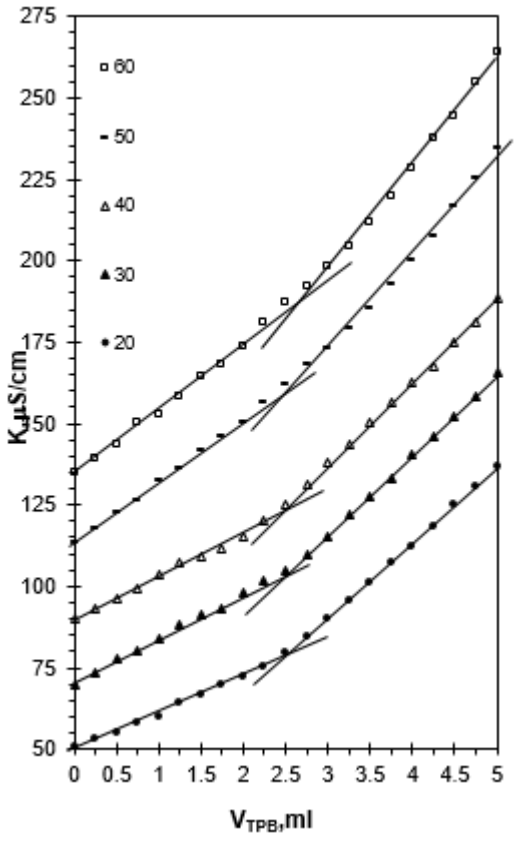
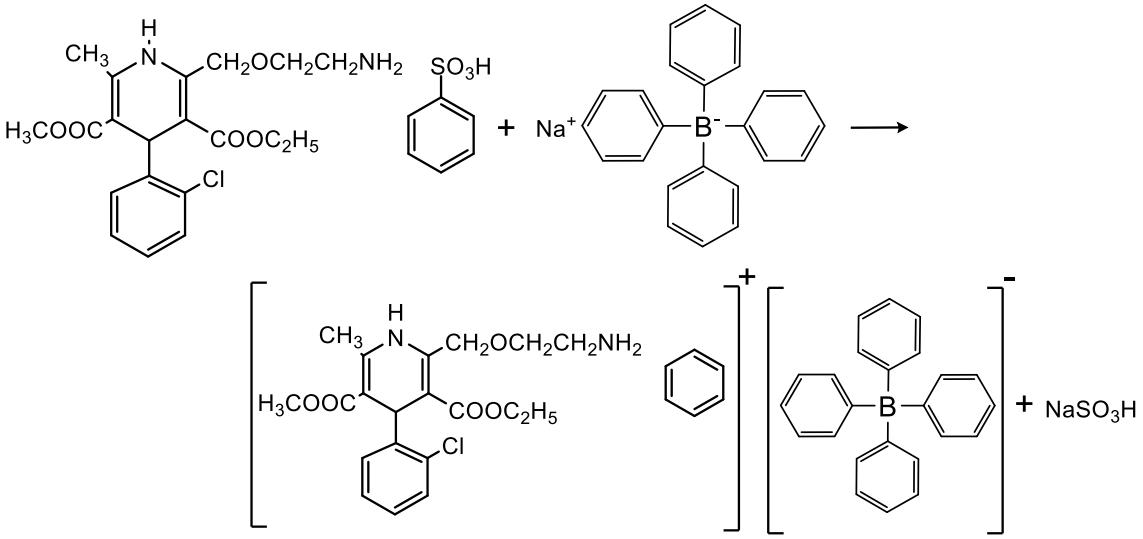


Fig.5. Effect of temperature on the end point of the conductometric titration of 25 mL of AML 1mM with 10mM TPB in aqueous medium at 20 -60 oC.



3.4. Determination of the drug–titrant ratio

The conductometric titration was used for the determination of AML using TPB as a titrant; the ion-associate is formed as shown in the following equation

Representative titration curve is shown in Figure 6. Two straight lines are obtained, intersecting at the end-point, the titration curve showed a steady increase in conductance values up to the equivalence point where a sudden change in the slope occurs. This divergence from linearity can be attributed to the formation of an ion-associate in the solution as a result of the reaction, so the conductivity increases. After the end-point, the titration

curve indicate a sharply increase of conductance. This may be due to the ionization of the reagent added.

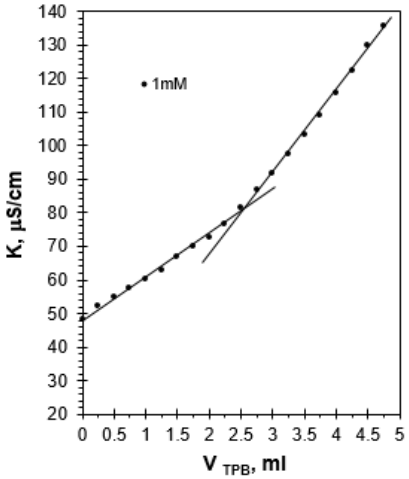


Fig.6. Conductometric titration curve of 25 mL of AML1mM with 10mM TPB at 20°C.

3.5. Linearity and Validation of the method

In order to establish whether the proposed method exhibits any fixed or proportional bias, a simple linear regression [27] of observed drug concentration against the theoretical values (5 points) was calculated (Table 1), and showed that it did not differ significantly from the ideal value of unity. Hence, it can be concluded that there are no systematic differences between the determined and true concentrations over the cited range.

The optimum concentration range for determining AML using TPB was 0.200-1.000mM at which well-definite inflections and stable conductance values as shown in Figure 7. The validity of the method for the analysis of AML in pure state was examined by analyzing the samples using the proposed procedure. The results obtained are given in Table 2. The precision and accuracy of the method were tested by analyzing five replicates of the drug. The low values of relative standard deviation (RSD %) indicate good precision and reproducibility of the method and the average percent recoveries obtained, indicating good accuracy of the method.

Table 1. Linear regression analysis for AML using TPB

Parameters	TPB
Optimum concentration range (mM)	0.200-1.000
Intercept of regression line[a]	0.0019
Slope of regression line	0.9995
Correlation coefficient, r	0.9999
Range of Error %	± 0.790

[a]Observed vs. theoretical

Table 2. Accuracy and precision of the proposed conductometric titration of AML using TPB

mM			RSD %	Recovery %	Relative error (%)
Taken	**Found***	**S.D.**			
0.200	0.203	0.006	3.05	101.50	1.50
0.400	0.401	0.008	2.00	100.25	0.25
0.600	0.602	0.009	1.50	100.33	0.33
0.800	0.805	0.007	0.82	100.62	0.62
1.000	0.998	0.007	0.73	99.80	-0.20

*Average of five determinations

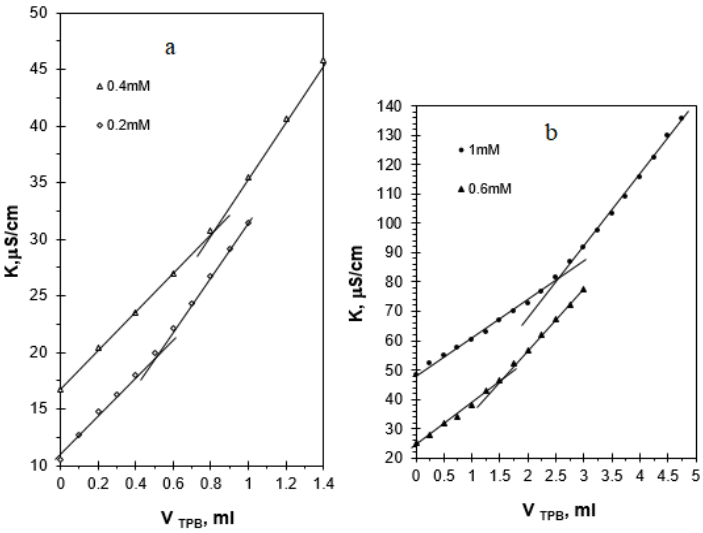


Fig.7. Conductometric titration curve of 25 mL of AML a) 0.2, 0.4 mM, b) 0.6, 1 mM with 10mM TPB at 20°C.

3.6. Application to the pharmaceutical dosage form

The proposed technique was applied to the tablets. The ingredients in the tablets did not interfere in the experiments. The applicability of the proposed method for the assay of AML in formulations was examined by analyzing various formulations and the results are

tabulated in Table 3 were compared to the reference method [14] by means of *t*- and *F*-values at 95% confidence level.

Table 3: Determination of AML in tablets by the proposed and reference methods

Formula	% Found* ± S.D	
	Proposed method	**Reference method**
Amlodipine 5mg/tab	100.26±0.59 *t* =1.04 *F* =3.20	99.87±0.33 *t* =1.32
Amlodipine Oubari 5mg/tab	101.30±1.20 *t* =2.48 *F* =1.03	100.42±1.22 *t* =1.88
Amlodipine Ultra Medica 10mg/tab	100.35±0.72 *t* =0.99 *F* =1.37	98.94±1.16 *t* =1.46

* Five independent analyses. At 95% confidence level t^- value is 2.776 and F^-value is 6.26

In all cases, the average results obtained by proposed method and reference method were statistically identical, as the difference between the average values had no significance at 95% confidence level. The low values of (RSD %) show the results are reproducible.

IV. CONCLUSION

The simple, rapid and accurate conductimetric method described in this paper can be an alternative to the more complex and expensive methods for assay of AML without interference from common excipients. The proposed method is easy, cheap, accurate and very useful for the determination of AML in their pharmaceutical formulations and can be applied in laboratories for routine analysis.

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