Chem. Anal. (Warsaw), **47**, 613 (2002)

Conductometric Determination of Phenothiazine Derivatives by Precipitation Titration

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Key words: conductometric titration, triflupromazine hydrochloride, trifluoperazine dihydrochloride, prochlorperazine dimaleate

Results of the conductometric titration of phenothiazine derivatives: trifluoperazine dihydrochloride (TPE), triflupromazine hydrochloride (TFP) and prochlorperazine dimaleate (PCP) in aqueous and ethanol solutions, with ammonium molybdate(VI), sodium vanadate(V) and sodium arsenate(III) as the titrants, are reported. The method was found to be highly accurate, precise and having relative standard deviation of less then 1% (in 0.5×10^{-3} to 1.0×10^{-3} mol L^{-1} analyte concentration range). The conductometric titration was applied for the determination of the studied compounds in the presence of NaCl and revealed a good accuracy.

Przedstawiono wyniki miareczkowania konduktometrycznego pochodnych fenotiazyny: dichlorowodorku trifluoperazyny (TPE), chlorowodorku triflupromazyny (TFP) i dimaleinianu prochlorperazyny (PCP) w wodnym i etanolowym roztworze z molibdenianem(VI) amonu, wanadanem(V) sodu i arsenianem(III) sodu jako titrantami. Metoda okazała się bardzo dokładna, precyzyjna, z odchyleniem standardowym mniejszym niż 1% (w zakresie stężeń od 0.5×10^{-3} do 1.0×10^{-3} mol L^{-1}). W celu oznaczenia badanej substancji zastosowano miareczkowanie konduktometryczne w obecności NaCl, a uzyskane wyniki były zgodne z wynikami dla czystego leku.

The phenothiazine derivatives: triflupromazine hydrochloride (TFP), trifluoperazine dihydrochloride (TPE) and prochlorperazine dimaleate (PCP) (Fig. 1) are widely used as psychotropic drugs and are applied, among others, in the treatment of schizophrenia [1,2].

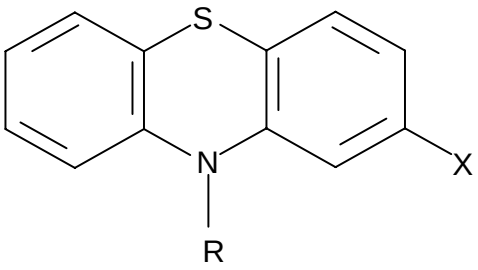
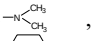
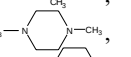


Figure 1. The general structure of the phenotiazine derivatives;
triflupromazine — x = CF_3, R =  ,
trifluoperazine — x = CF_3, R =  ,
prochlorperazine — x = CCl, R = 

The determination of phenothiazines in formulations and biological fluids was widely studied [3–11]. The reaction of phenothiazines with V(V) was used in spectrophotometric determination of vanadium [12]. In the recent years the main research interests were focused on such techniques as: HPLC [13–14], micellar electrokinetic chromatography [15], and capillary electrophoresis [16–17], which can handle the trace amounts of drugs. However, besides the mentioned above methods also: gravimetric, colorimetric [18–19], spectrophotometric UV–VIS [20–23], polarographic, amperometric [24–25], potentiometric [26] and conductometric [27–29] methods are still in use.

Conductometric titrations were successfully applied in the quantitative analysis of hydroxyzine dihydrochloride with ammonium molybdate(VI) [27]. Chlorpromazine, promazine and trifluoperazine were determined with sodium hydroxide, mercury(II) chloride, and silver nitrate [28], while periciazine required silicotungstic acid [29]. The reported conductometric titrations of trifluoperazine did not involve, as the titrants, ammonium molybdate(VI), sodium vanadate(V) and sodium arsenate(III), hence we have started the determination of the phenothiazine derivatives using these reagents.

The conductometric titration is applicable, when in due course of the reaction, either before or after the equivalence point, one ion is substituted by another with a different mobility. The method is well suited for the end-points observation when a precipitate appears during the titration. In this case the shape of the titration curve can be calculated from the ionic conductance of various species at any point during

the titration. The solubility of the formed precipitate affects the titration curve and must be considered also.

FP V recommends the phenotiazines determination in non-aqueous solution using acidimetric titration by $HClO_4$ with malachite green as indicator.

The present paper describes a method of the determination of the mentioned drugs in both the pure and dosage forms. These titrations have been studied due to their simplicity, precision, accuracy and therefore they could be recommended for routine analyses in the control laboratories. The presented paper aims to confirm the method applicability for the drug determinations.

EXPERIMENTAL

Apparatus

Conductivity measurements were carried out with an automatic conductivity meter CX–742 (Elmetron, Poland) and an EPS–2ZM bell-shaped electrode (Radelkis, Hungary).

Chemicals

Triflupromazine hydrochloride (99%), trifluoperazine dihydrochloride (99%) and prochlorperazine dimaleate (99%) were purchased from Sigma, whereas ammonium molybdate(VI), sodium vanadate(V), sodium arsenate(III) (all analytical grade) from POCH Gliwice (Poland) and were used as received.

Sample preparation

The triflupromazine hydrochloride and trifluoperazine dihydrochloride solutions were prepared in standard volumetric flaks (100 mL) by dissolving the appropriate amount of the drug in threefold distilled water. Prochlorperazine dimaleate was dissolved in ethanol (96%). The prepared solutions had concentrations similar to the ones determined in the pharmaceutical preparations (0.5×10^{-3} to 2.0×10^{-2} $mol^{-1} L^{-1}$). In order to minimise the volume correction, the titrants concentrations were 5–6 times higher than those of the drugs studied.

Procedure

Measurements were carried out in water or ethanol solutions at 298 K. After addition of 0.1 mL (or 0.2 mL depending on the sample concentration) of the titrant, solutions were stirred for 2 min and left for 2 min to reach the equilibrium. The titrations were repeated three times and the average values were calculated. Considering the volume change, the observed values were corrected by a factor of (V+v)/V, where V is volume of the starting solution and v is volume of the titrant added.

RESULTS AND DISCUSSION

An addition of ammonium molybdate(VI), sodium vanadate(V) and sodium arsenate(III) caused the formation of a precipitate, therefore sometime was needed to reach the equilibrium in the solution. The mole ratios calculated from the curves end-points for triflupromazine hydrochloride, trifluoperazine dihydrochloride and prochlorperazine dimaleate with ammonium molybdate(VI), sodium vanadate(V) and sodium arsenate(III) are listed in Table 1.

Table 1. Results of conductometric titration of triflupromazine hydrochloride (TFP), trifluoperazine dihydrochloride (TPE) and prochlorperazine dimaleate (PCP) with ammonium molybdate(VI), sodium vanadate(V) and sodium arsenate(III)

Compound	Amount of drug, mg		Standard deviation [a] SD, mg	Confidence limit [b]
	taken	found		
$[TFP\ H]_6[Mo_7O_{24}]$	77.73	79.21	0.04	79.21±0.10
$[TPE\ 2H]_3[Mo_7O_{24}]$	97.79	96.32	0.06	96.32±0.15
$[PCP\ 4H]_3[Mo_7O_{24}]_2$	80.00	78.79	0.04	78.79±0.10
$[TFP\ H][VO_3]$	77.73	79.21	0.02	79.21±0.05
$[TPE\ 2H][VO_3]_2$	97.79	96.32	0.01	96.32±0.02
$[PCP\ 4H][VO_3]_4$	80.00	78.44	0.04	78.44±0.10
$[TFP\ H][AsO_2]$	77.73	79.11	0.07	79.11±0.17
$[TPE\ 2H][AsO_2]_2$	97.79	98.21	0.05	98.21±0.12
$[PCP\ 4H][AsO_2]_4$	60.61	60.10	0.01	60.10±0.02

[a] Average of three determinations.
[b] Probability level = 0.95.

Conductometric titration curves in the studied range of concentration are typical for the reactions where precipitates are formed. They are presented at Figures 2a, 2b.

The reaction end-point was calculated by the extrapolation of two linear parts of the curve. The maximum difference between the lowest and highest results in a separate series of determinations was below 5%. The bias in the analytical results for the studied range of concentrations did not exceed 2%. The average results of three measurements for TFP, TPE and PCP with ammonium molybdate(VI), sodium vanadate(V) and sodium arsenate(III) are presented in Table 1.

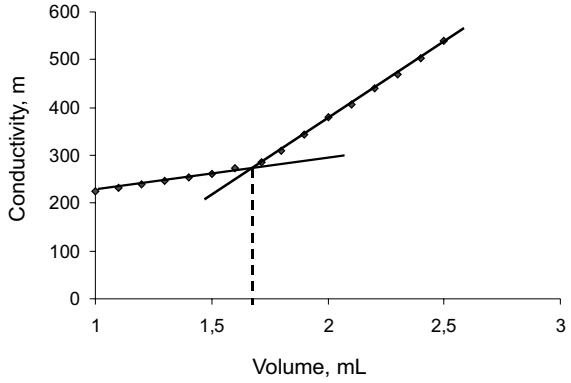


Figure 2a. Conductometric titration curve for triflupromazine hydrochloride (c = 0.013 mol L^{-1}, v = 15 mL) with ammonium molybdate(VI) (c = 0.0029 mol L^{-1})

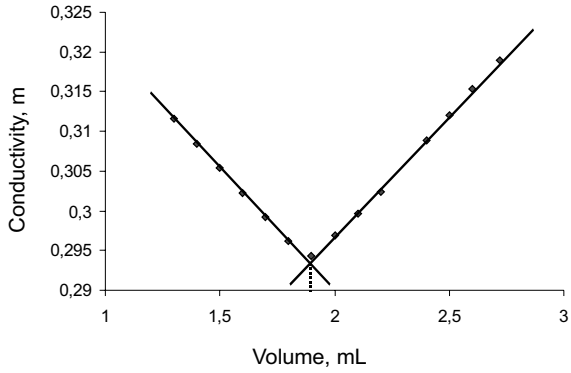


Figure 2b. Conductometric titration curve for trifluoperazine dihydrochloride (c = 0.002 mol L^{-1}, v = 15 mL) with sodium vanadate(V) (c = 0.015 mol L^{-1})

Due to the lack of adequate pharmaceutical preparations of the studied drugs, the conductometric titration was carried out with the pure compounds and NaCl added. The obtained results were of a good accuracy.

CONCLUSION

The proposed method can be applied for the determination of triflupromazine hydrochloride, trifluoperazine dihydrochloride and prochlorperazine dimaleate in pure and commercial standard solutions. The observed accuracy and precision of the conductometric titration indicates, that the method can be suitable for the routine quality control analysis of the pharmaceutical preparations.

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Received April 2001
Accepted December 2001