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# Conductometric Titration Method for the Determination Chlorpheniramine Maleate (CPM)in Pure and Pharmaceutical

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**Abstract**

A straightforward, accurate, quick, and inexpensive conductometric approach has been described for determining chlorpheniramine maleate (CPM) in pure form and in pharmaceutical formulations utilizing sodium hydroxide, Silver Nitrate, and sodium tetraphenylborate (TPB). The proposed method is based on the cation association of the drug with the anion of the base used .Sodium hydroxide was used instead of TPB and $AgNO_3$ because it is a strong, effective, readily available, inexpensive base that dissolves easily in water. The solution's conductivity was measured in relation to the titrant volume. The substance under study was tested in double-distilled water at concentrations between 0.39 and 1.9 mg. The effect of different temperatures (20-55°C) on the endpoint was evaluated. The obtained results demonstrated positive recovery rates (94%-102%) with a relative standard deviation less than 1.0% for chlorpheniramine maleate. These medications' pharmaceutical compositions were successfully analyzed using the suggested methods.

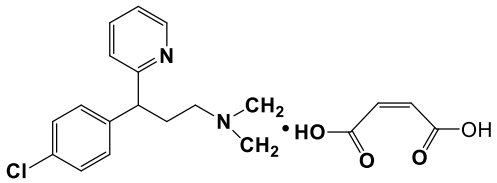


## 1. Introduction

Chlorpheniramine, with the molecular formula C20H23ClN2O4 (scheme1)and a molecular weight of 390.9 g/mol, is formally known as (Z)-3-(4-chlorophenyl)-N,N-dimethyl-3-pyridin-2-ylpropan-1-amine. This compound exists as a white, odorless crystalline powder with a pH ranging from 4 to 5 .

As a first-generation antihistamine, chlorpheniramine is commonly used to alleviate allergy symptoms. Its sedative properties[4,5], often referred to as a "sleepy antihistamine,"[1] make it particularly effective in reducing symptoms such as rhinorrhea, pruritus, conjunctivitis, and sneezing. Oral administration results in a relatively long serum half-life of approximately 20 hours, indicating sustained therapeutic effects. While

food intake does not significantly impact the drug's absorption, it can delay the peak plasma concentration."[2,3].




**CPM**

**Scheme 1. Chlorpheniramine maleate structure**

Chloroquine enhances the efficacy of treating acute, uncomplicated falciparum malaria. On the other hand, it may cause negative side effects like fatigue, lightheadedness, disorientation, constipation, anxiety, nausea, blurred vision, restlessness, poor coordination, and more [6, 7]. Chlorpheniramine maleate (CPM) in pharmaceutical formulations can be quantitatively determined using a variety of analytical techniques. These consist of various UV mass spectrometry detectors in conjunction with high-performance liquid chromatography[8-14], Using micellar electrokinetic chromatography to quantify paracetamol and CPM simultaneously [15], direct current polarography[16]., and differential pulse stripping voltammetry with electrodes made of modified glassy carbon [17]. Additionally, first derivative UV spectrophotometry in dosage forms has been used to determine CPM and phenylpropanolamine hydrochloride (PPM) simultaneously using quick and easy spectrophotometric techniques [18]. Chlorpheniramine maleate and phenylephrine hydrochloride in bulk and in a combination capsule dose form can also be estimated using the spectrophotometric technique[19]. Analytical methods based on measuring systems are the essence part of therapeutic drugs monitoring (TDM). Analytical systems reliability for drug concentrations measurement in pharmaceutical preparations is crucial. A number of analytical techniques are capable to measure numerous drugs after their separation from the matrix, which called "separative", whilst other techniques are measuring drug concentrations without the demand for separating them from the matrix, which called "non-separative"[20-21]. This study introduces a novel, cost-effective conductometric titration method using sodium hydroxide to quantify CPM in pharmaceutical products.

## 2. Experimental

### 2.1 Materials

Every chemical and reagent employed in this investigation was of analytical- reagent quality, and double - distilled water was used to make the solutions. The purity of the chlorpheniramine maleate (CPM), which was acquired from Sama AI-Fayhaa Company in Basrah , was determined to be 99.7%.and different (CPM), (Al-Kindi), (Pioneer) and (Samarra Drug Iraq Company).

### 2.2 Solutions

Dissolved appropriate weight of CPM in 100 ml double -distilled water to prepared 10 mM of TPB, AgNO3 and NaOH. Stock standard solution 1mM of CPM was prepared in double distilled water kept of each solution in dark place and closed container . The stock solution was then suitably diluted with double-distilled water to yield different concentrations of the working solution.

2.3 Pharmaceutical preparations

Twenty tablets of each (CPM), (Al-Kindi), (Pioneer) and (Samarra Drug Iraq Company) were weighed and ground into a fine powder.A precisely weighed amount of powder, equal to 100 mg of the medication, was dissolved in 100 milliliters of ethanol, filtered, and then evaporated until it was completely dry before being dissolved in 100 milliliters of double-distilled water in a volumetric flask.

## 3. General procedure

A 20 mL calibrated flask was filled with aliquots of standard solution containing 1mM and 5 mM of CPM, and the volume was adjusted accordingly. A conductometric titration cell was quantitatively filled with the contents of the calibrated flask and immersed in the sample solution. Following each addition of the reagent solution and a minute of vigorous stirring, the conductance was measured and the solution was titrated conductometrically against solutions of 10Mm of NaOH, $AgNO_3$ and TPB. Under the assumption that conductivity is a linear function of dilution, the conductance was adjusted for dilution using equation (1).

$$\Omega^{-1}_{correct} = \Omega^{-1}_{obs} [V_1+V_2/V_1] \quad (1)$$

Where $\Omega^{-1}_{correct}$ is the corrected electrolytic conductivity, $V_1$ is the initial volume and $V_2$ is the volume of reagent added, $\Omega^{-1}_{obs}$ is the observed electrolytic conductivity.

The endpoint was ascertained conductometrically by creating a graph of corrected conductivity against the volume of added titrant.

Equation (2) was used to determine the quantity of medications under investigation,

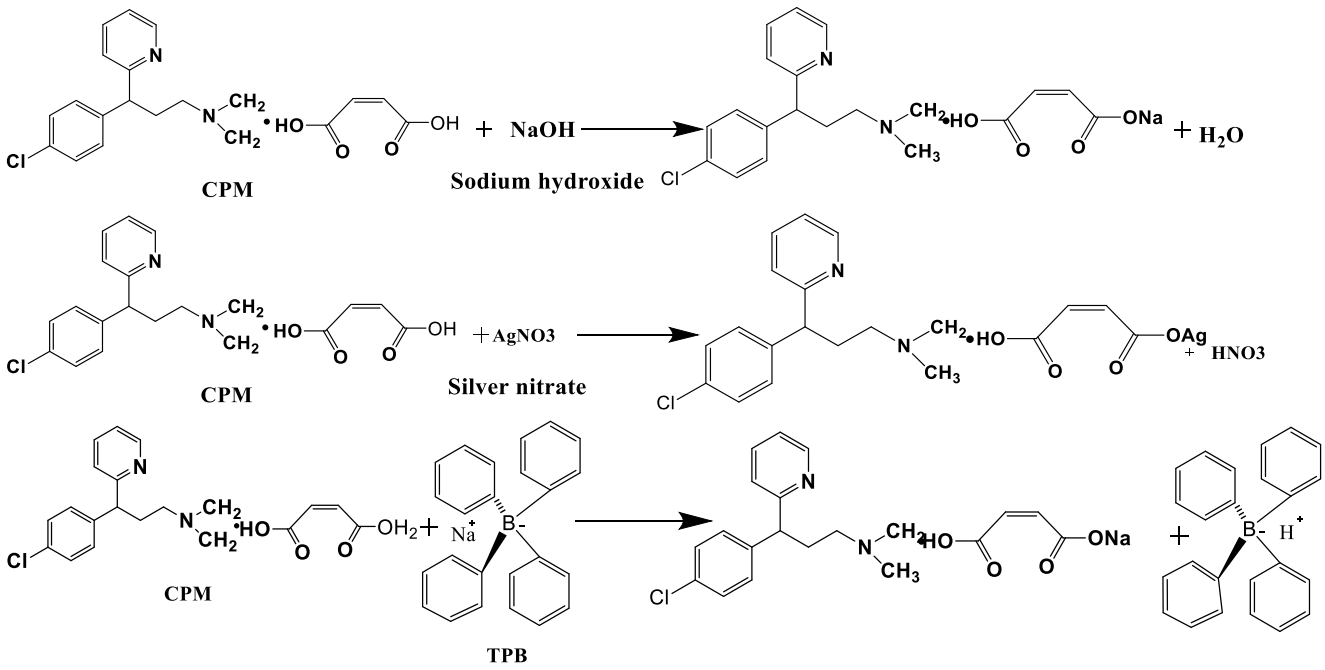
$$\text{Amount of drug} = V.M.R / N \quad (2)$$

where M is the drug's molecular weight, R is the titrant's molar concentration, N is the number of moles of titrant consumed by one mole of drug, and V is the titrant's volume (mL).

## 4. Result and Discussion

Since the conductance of the solution varies before and after the equivalency point, conductometric measurements can be used for quantitative titrations of ionic solutions, where the end-point can be shown by drawing two intersecting lines. In addition to the species present during the titration process, other parameters that affect the form of the titration curve include viscosity, the solvation, proton transport, ion-pair interaction, and dielectric constant of the solvent. A 20 mL calibrated flask was filled with aliquots of standard solution containing 1mM and 5 mM of CPM, and the volume was adjusted accordingly. A conductometric titration cell was quantitatively filled with the contents of the calibrated flask and immersed in the sample solution. Following each addition of the reagent solution and a minute of vigorous stirring, the conductance was measured and the solution was titrated conductometrically against solutions of 10Mm of NaOH, $AgNO_3$ and TPB. Under the assumption that conductivity is a linear function of dilution, the conductance was adjusted for dilution using equation (1).

The applicability of conductometric titration of chlorpheniramine maleate with the aforementioned reagents was investigated because of its capacity to interact with sodium tetraphenylborate, sodium hydroxide and silver nitrate (scheme 2).




Scheme 2. Reaction Chlorpheniramine maleate (CPM) with reagent (NaOH,$AgNO_3$ and TPB)

## 5. Study of optimum conditions:

Many factors influencing the end point, including titrant concentrations and temperature, were examined.

### 5.1. Effect of titrant concentrations:

In the range of 0.001-0.6 M for CPM, NaOH , $AgNO_3$ and TPB solutions, there was a linear increase in the conductance values with the concentration of these solutions. This relationship is depicted in Figure 1 within the 0.1-10 mM range. At the same concentration, the conductance values of the NaOH, $AgNO_3$ and TPB were approximately two and three times higher, than CPM solutions respectively, than those of solution (Fig.2). The following figures dropped when the effect of electrolyte content on specific electrical conductivity was examined: NaOH>TPB>$AgNO_3$>CPM in an aqueous media.

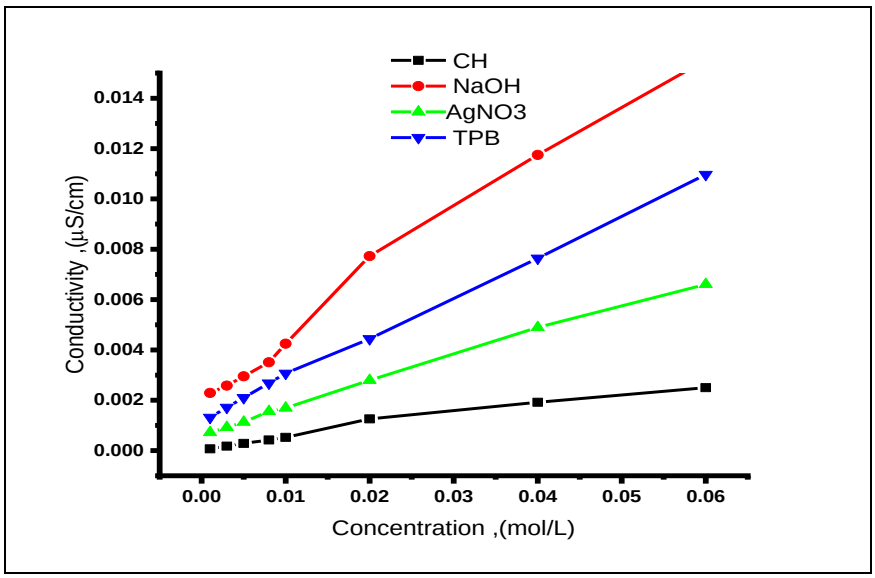



**Fig. 1. The impact of electrolyte concentration on double-distilled water's conductivity.**

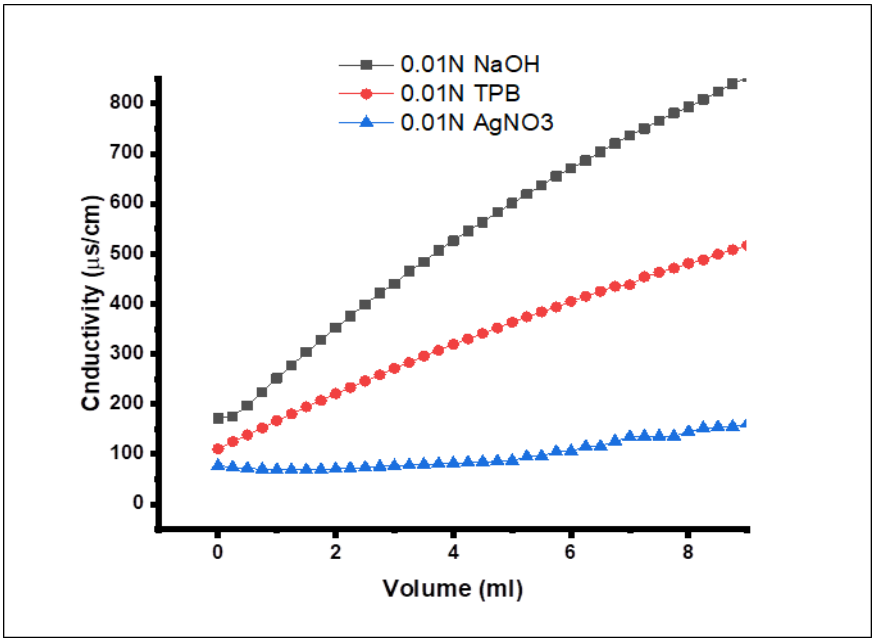



**Fig. 2. Effect of electrolyte concentration $10^{-2}$mol/L with $10^{-3}$ mol/L CPM on the end point conductivity titration**

On determining CPM using NaOH ,$AgNO_3$ and TPB as a titrant. displays a typical titration curve. The system under study demonstrated a consistent increase in conductance until it reached the equivalency point, at which time the slope abruptly changed. The hydrolysis that produces ( $H^+$ )and ($OH^-$) is most likely the cause of this behavior. By substituting mobile $Na^+$ for the $H^+$ cations, adding NaOH increases conductivity. More reagent is added after the end point is achieved, and conductivity increases faster.

## 5.2 Effect of temperature

In the 20–55 $^oC$ range, In aqueous media, the temperature and conductance values of the CPM and NaOH solutions rose linearly. Titrations were conducted between (20 -55) $^oC$ to investigate the impact of temperature on the conductometric titration's end point. The findings demonstrated that the conductivity of the entire solution increases with temperature, although up to 55 $^oC$, there was no discernible change in the titration curve's form or the end point's location. Thus, room temperature was used for the experiment (Fig. 3).

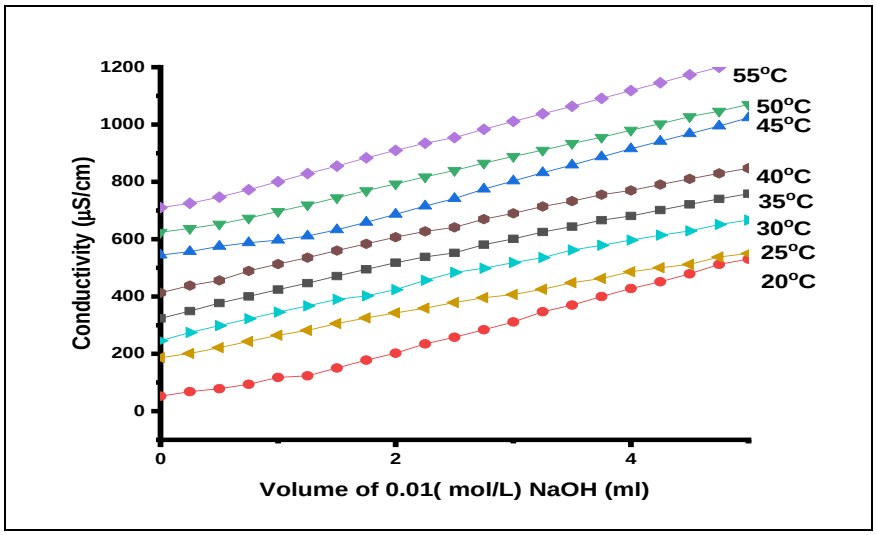



**Fig .3. Effect of temperatures on the end point conductivity of 0.001mol/L CPM with 0.01mol/L NaOH.**

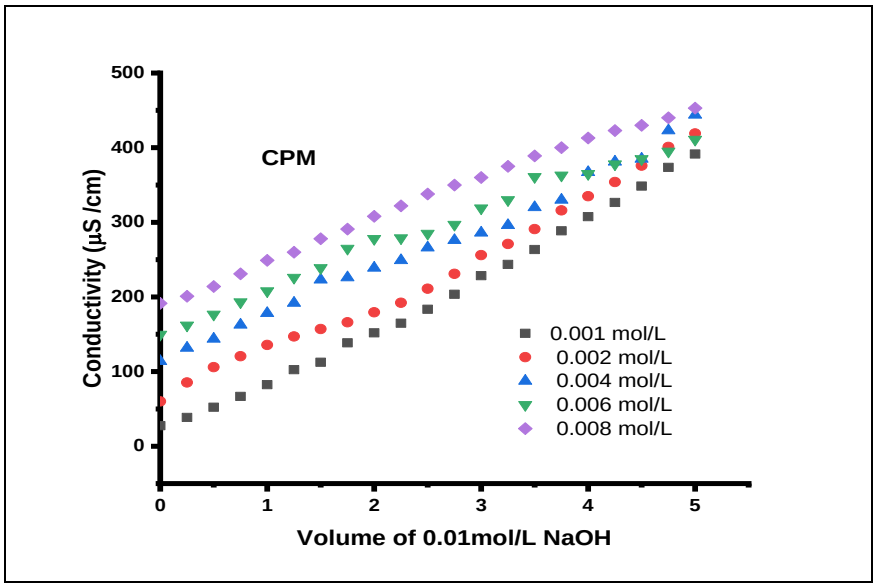
## 5.3 Validation of the Studied Method

A statistical analysis of the data gathered from the method's application on the medication in both its pure form and in formulations was carried out to verify the method's recovery, as indicated in table 1.

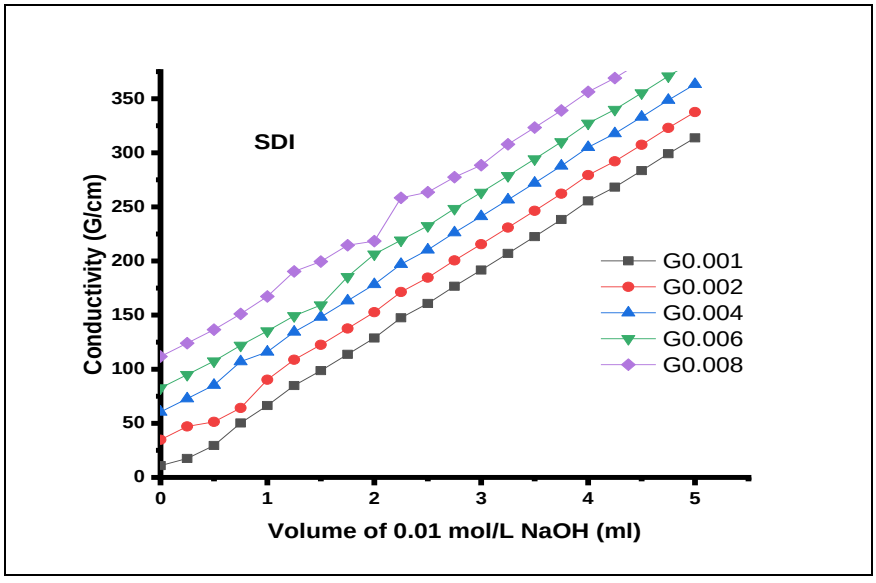
**Table 1.Dermination of CPM in different pharmaceutical formations**

| Method | Taken mg | Found mg | Relative Error % | Recovery % |
|---|---|---|---|---|
| Pure Drug | 39.09 | 39 | 0.002 | 99.7 |
| CPM | 78.18 | 78 | 0.009 | 99.7 |
| | 156.36 | 156 | 0.002 | 99.7 |
| $\bar{X}$=99.82 | 234.54 | 234.54 | 0 | 100 |
| SD =∓0.16 | 312.7 | 312.7 | 0 | 100 |
| SDI | 39.09 | 39.09 | 0 | 100 |
| | 78.18 | 78.18 | 0 | 100 |
| | 156.36 | 154.79 | 0.01 | 99 |
| $\bar{X}$=99.82 | 234.54 | 237 | -0.01 | 101 |
| SD =∓0.16 | 312.7 | 309.59 | 0.009 | 99 |
| Pioneer | 39.09 | 39.09 | -0.1 | 100 |
| | 78.18 | 78.18 | 0.009 | 100 |
| | 156.36 | 152.29 | 0.02 | 97.3 |
| $\bar{X}$=99. | 234.54 | 244 | -0.040 | 104 |
| SD =∓3 | 312.7 | 296.4 | 0.05 | 95 |
| Al-Kindi | 39.09 | 36.7 | 0.06 | 94 |
| | 78.18 | 79.7 | -0.01 | 102 |
| | 156.36 | 156.36 | 0 | 100 |
| $\bar{X}$=99.06 | 234.54 | 228.28 | 0.13 | 97.33 |
| SD =∓1.30 | 312.7 | 312.7 | 0 | 100 |

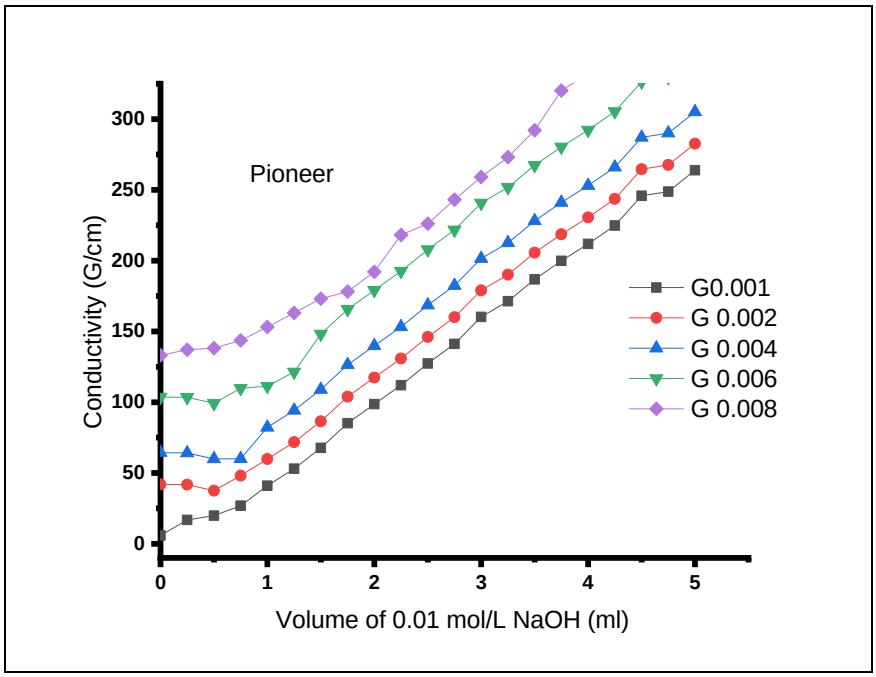
Table shows the measured quantities (Taken) with the detected ones (Found) using different pharmaceutical formations ( SDI ,Pioneer and Al -Kindy company). Observations the SDI company achieves perfect recovery 100% for all samples the Pioneer company shows varied results with recovery rates ranging from 95%to 101% but ,the Al-Kinday company shows some discrepancies in the detected amounts with recovery rates between 94%-102% that show in (Fig. 4) for CPM, SDI, Poneer and Al-Kindy company .



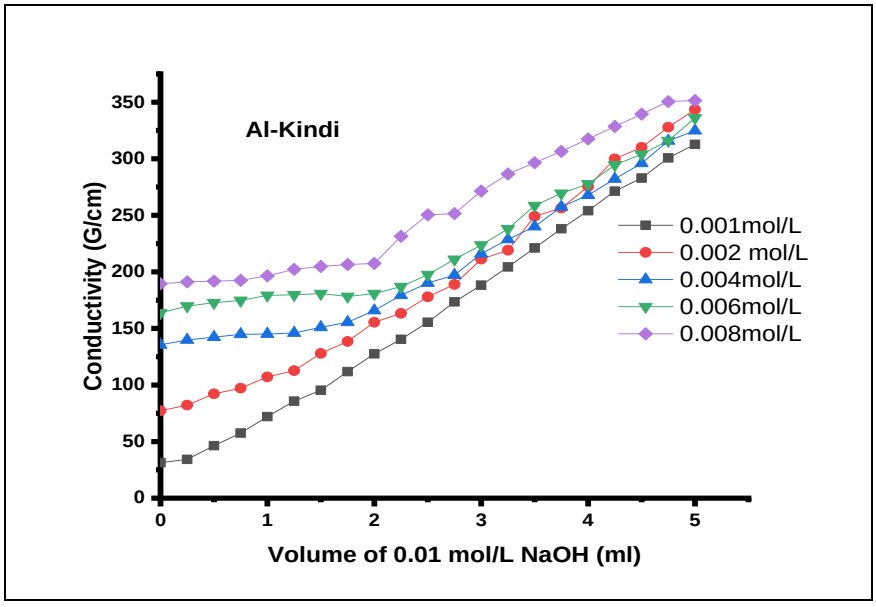

**(a)**




**(b)**




**(c)**




**(d)**

**Fig. 4.Condumatric titration of $10^{-3}$ mol/L of CPM ,SDI, Pioneer and Al-Kindy company with $10^{-2}$mol/L of NaOH**

## 6. Conclusion

Given its cost-effectiveness and ease of use, the proposed method presents a compelling alternative to conventional CPM assay methods. The suggested approach is straightforward, effective, and suitable for routine laboratory analyses. It can be reliably used to detect CPM in pharmaceutical formulations.

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