

PVC-Based Ion-Selective Electrode Using Clarithromycin-Bromophenol Blue Ccomplex

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ABSTRACT

In this research two electrodes were built using the clarithromycin-bromophenol blue ion pair complex in a PVC matrix and the extraction of clarithromycin from Claricide medication. The experimental section relied on using two plasticizers; tri-butyl phosphate and ortho-nitro-phenyl-octyl ether. The results indicated that slopes and linear ranges of the clarithromycin electrodes [C1 and C2] were 55.699 and 53.895 mV/decade and 10^{-5} - 10^{-2} and 7×10^{-5} - 10^{-2} M, respectively. Based on using TBP plasticizer, the best electrode [C1] had a lifetime of 16 days, a 55.699 mV/decade slope, a 0.9995 correlation coefficient, and 9×10^{-6} M detection limit. Therefore, the main findings of this research indicated that, C1 electrode, which demonstrated excellent stability, can be employed to measure the amount of clarithromycin in drug samples. In addition, the separated and mixed methods can be conducted to study the interference measurements in the presence of certain ions, sucrose, and gelatin in order to determine the selectivity coefficient.

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1. INTRODUCTION

CN with a molecular weight of 748 g/mole. It is soluble in methylene chloride but insoluble in water. CN is 6-o-methyl-erythromycin or 4-[(2,6-Dideoxy-3-Cmethyl-3-O-methyl-L-ribohexopyranosyl) oxy]. 3-[3,4,6-trideoxy-12,13-dihydroxy-7-methoxy-3,5,7,9,11,13-hexamethyl-6-oxa-cyclo-tetra-decane-2,10-dione, as seen in Figure. (1), with the empirical formula $C_{38}H_{69}NO_{13}$ (British Pharmacopoeia, 2014)

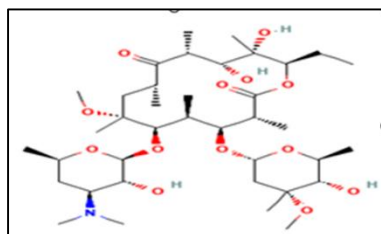


Figure 1. Structure of CN.

Chlamydia species, Rickettsia, Haemophilus influenzae, and Mycoplasmas are all commonly treated with CN. (Kanfer et al., 1998) (Langtry & Brogden, 1997) (Abraham et al., 2020) a number of analytical techniques, including spectrophotometry and HPLC (High Performance Liquid Chromatography) approaches, have been developed to identify the presence of clarithromycin in formulations and biological materials. Ion selective electrode applications are still essential in pharmaceutical industry (Amini & Ahmadiani, 2005) (Li et al., 2007) (Abraham, 2022) (Abraham et al., 2022) as these sensors have the benefits of low cost, rapid response, good selectivity, simple design and operation, and adaptability to turbid and colorful solutions. (Chandra et al., 2013) (Al-Baitai et al., 2020) (Koryta, 1977) (Craggs et al., 1974) The sensor used in this study is based on the detection of clarithromycin in pharmaceutical samples by employing the ion pair Clarithromycin-Bromophenol blue in PVC plasticized with various plasticizers. Additionally, the pH impact, selectivity, and characteristics of the produced electrodes were examined in this research.

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2. EXPERIMENTAL SECTION

2.1 Reagents and Solutions

- 500 mg clarithromycin-containing Claricide tablets in accordance with the published technique, clarithromycin was isolated from Claricide pills (British Pharmacopoeia, 2009). They were bought from Turkish-made Bilim Pharmaceuticals. Acetonitrile from Sigma-Aldrich, Tetrahydrofuran (E.Merck), Bromophenol blue (Bb), and ONPOE were acquired from Fluka AG, Switzerland, and Polyvinyl chloride (PVC) with a reasonably high molecular weight. Additional substances acquired from BDH.

- For KCl, MnSO₄, Fe₂(SO₄)₃·9H₂O, and gelatin, (0.1 M) stock solutions were made by dissolving 0.3722, 0.7550, 2.8100, and 1.5000 g in (50 mL) respectively.

- dissolved 0.6699 gm of pure Bromophenol blue in ethanol to obtain standard 0.01M of Bb

- 3.74 g of clarithromycin was dissolved in (1ml acetonitrile :3ml water) to obtain (0.01 M) clarithromycin standard solution.

-The practical fixes, the stock solution was serially diluted appropriately using the same solvent to create 10⁻⁶-10⁻² M clarithromycin.

2.2 Equipment

For potentiometric and pH measurements, this research relied on:

- (inoLab 740 of terminal 740, WTW, made in Germany) A pH/ion digital meter.
- (LMS-1003, Daihan Labtech) Hotplate stirrer
- Saturated Calomel reference electrode
- Silver-silver chloride wire
- And (SenTix® 82 WTW, made in Germany) pH combination electrodes.

2.3 Procedure

2.3.1 Preparation of ion pair

The ion pair was obtained by dissolving CN equimolar solution in acetonitrile and water (1:3) by combining with an equivalent amount of Bb which was obtained by dissolving 0.6699 gm of pure Bromophenol blue in ethanol to obtain standard 0.01M of Bb. After 24 hours, the precipitate developed.

2.3.2 Preparation of membrane, Potential Measurements and construction of Ion Selective electrode

A clear, viscous solution was prepared by dissolving PVC powder (0.1700 g), solution (0.0400 g), and a plasticizer (0.3600 g) combined with 5 ml of THF and stirred. The double junction electrode (Ag/AgCl) served as the exterior reference electrode after using the Ag/AgCl wire electrode as the inside reference electrode. A membrane that had been cut was affixed to the polyethylene tube in the shape of an electrode and

fastened to the last segment of the glass tube (Umezawa et al., 1995). The following is the electrochemical cell:

Ag/AgCl| internal filling solution||
membrane||test solution| SCE

The calibration curves were prepared by using Microsoft office Excel 2016.

2.3.3 Pharmaceutical Samples Preparation

Ten 500 mg pills of clarithromycin were completely ground up and precisely weighed. 5.8692 g was determined to be Ie. This powder weighed 0.0878 g. as the active weighed of single tablet was dissolved in 250 mL of acetonitrile and filtered. The resulted solution is left 1×10⁻³ M.

2.3.4 Selectivity Coefficient Calculation

a₁, a₂ are activities and z₁, z₂ are charge numbers for 1 ion, respectively, at a₁ = a₂.

The coefficients of selectivity were calculated using the fixed interference method (mixed method) (Shakir, 2016) (Abdulla et al., 2005) by using equation (1):

$$K_{1,2}^{pot} = a_1 / (a_2)^{z_1/z_2} \quad (2)$$

3. RESULTS AND DISCUSSION

The following are the calibration curves for two CN electrodes (C1 and C2), the C1 sensor was found at the junction of the extrapolated segments of the calibration curve's two linear sections. The slope value of electrode C1 was attributed to the high mixing between PVC and TBP, which resulted from the plasticizer's compatibility with the electro-active substance in terms of both composition and structure. Figure. (2) below displays a typical plot of electrode calibration curves of TBP & ONPOE.

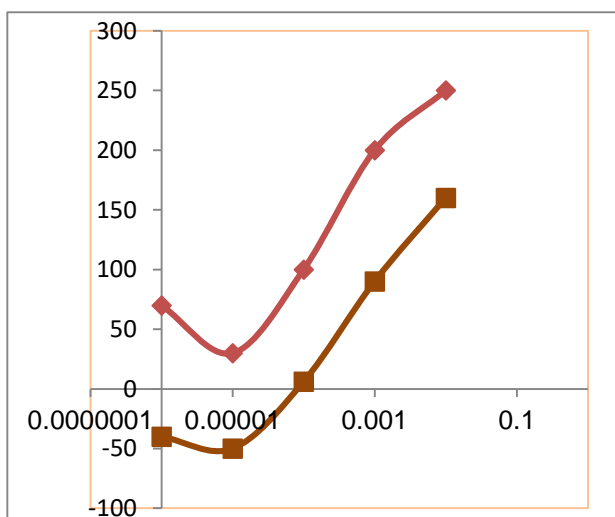


Figure 2: Selective electrodes CN Calibration curves with plasticizer TBP C1 (light red) ONPOE C2 (dark red)

The values of the slopes for the electrodes based on TBP and ONPOE were 55.699 and 53.895 mV/decade, respectively, and correlation coefficients were 0.9995, 0.9994. These electrodes have a linear range of 10^{-5} –0.01 and 7×10^{-5} –0.01M, with corresponding detection limits of 5×10^{-5} M and 9×10^{-6} M. Table (1) presents the outcomes together with other factors.

Table 1. C1 and C2 electrodes parameters

Electrode	C1	C2
Slope (mV/Decade)	55.699	53.895
Correlation coefficient(r)	0.9995	0.9994
Linear concentration range (M)	10^{-5} - 10^{-2}	7×10^{-5} - 10^{-2}
Detection limit (M)	9×10^{-6}	5×10^{-5}
Response time in sec.	1×10^{-2} M	23
	1×10^{-3} M	19
	1×10^{-4} M	13
Lifetime (day)	16	10

3.1 Effect of pH

The cell potential in CN solutions was measured at (0.01 and 0.001) M concentrations, where the pH varied from (0.5) to (11.0), the impact of pH was investigated. The right quantities of hydrochloric acid or sodium hydroxide solution were added to change the pH. Figure (3) displays the outcomes.

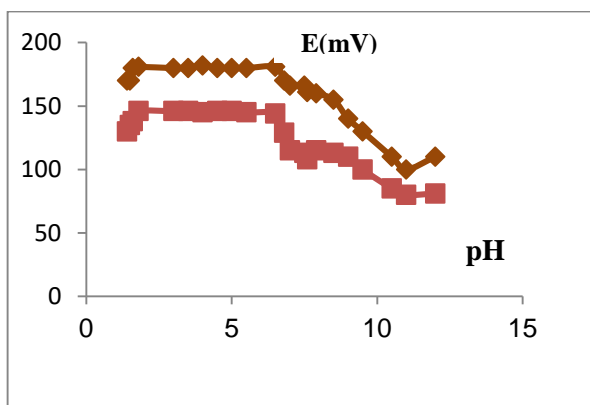


Figure 3. Effect of pH on C1 electrode at concentrations 0.01M (light red) 0.001 M. (dark red)

In very acidic environments or at pH values below 1.5, the electrode response has risen fairly erratically. This might be because the electrode begins to respond to ions and H+ activities. The electrode response starts to decline in an alkaline solution (pH over 7), which could be related to CN's diminishing solubility (Shakir, 2016) (Nassory et al., 2008) (Ismaeel & Al-Phalahy, 2020). Table (2) is a tabulation of the working pH.

Table 2. working pH Ranges, (CN) electrode C1.

C1 and range pH	
0.01 (M)	0.001 (M)
1.6-6.7	1.8-6.8

3.2 Interference studies

Equation (1) was used to examine the suggested membrane C1 electrode's selectivity toward clarithromycin in relation to interfering ions using a mixed solution approach.

Table 3. $K^{pot}_{A,B}$ Values - d FIM using electrode C1

	FIM	method
Interfering ions	a_a	$K^{pot}_{A,B}$
Mn^{+2}	4.9×10^{-5}	2.241×10^{-4}
Fe^{+3}	2.0×10^{-5}	5.433×10^{-5}
Cu^{+2}	3.9×10^{-5}	1.678×10^{-4}

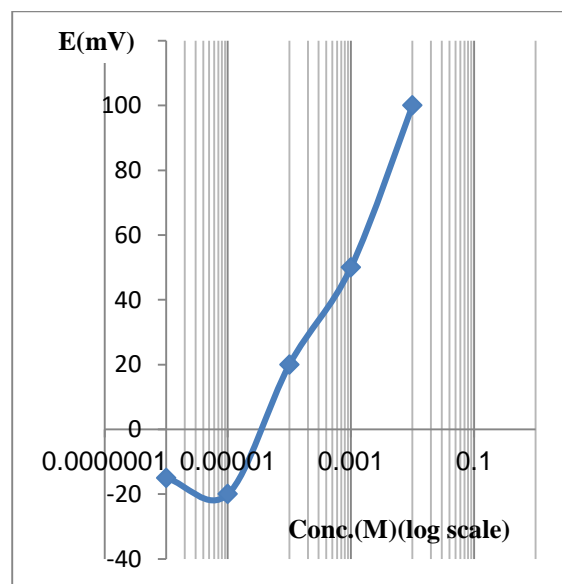


Figure 4. Clarithromycin selective electrode C1 Fe+3 interfering ion calibration curve for the fixed interfering technique

3.3 Sample Analysis

Clarithromycin was measured using potentiometric approaches, such as the standard addition method (SAM) and direct method, which both employed the equation:

$$CS = 10\Delta E/S [1+ (VU / VS)] = CU - (VU/VS)$$

If multiple standard additions (MSA) are calculated using the following equation, and CS, CU, VS and VU, stand for the volume as well as the concentration of the unknown in addition to the standard solution, respectively:

$$VS \times CS / VU = CU$$

where VS is the volume of standard solution, CS is the concentration of the unknown, and CU is the standard. The method was conducted as shown in Figure (5).

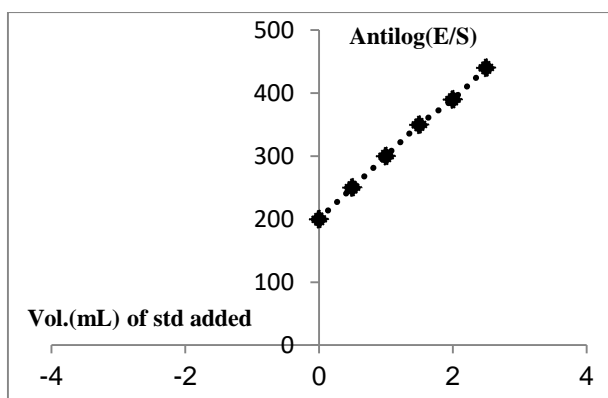


Figure 5. Clarithromycin selective electrode C1 Fe+3 interfering ion calibration curve for the fixed interfering technique

The concentration of clarithromycin may be examined and compared with the working range calibration curve of MSA by graphing antilog (E/S) with the volume of the five additions of standard clarithromycin. for titrating potentiometrically. Figure (6) displays a typical titration plot.

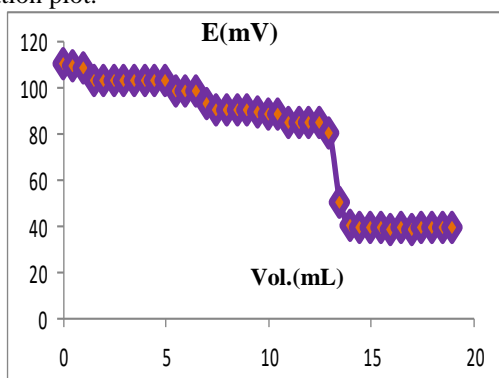


Figure 6. Titration curve of Electrode (a), a sample solution (15 mL) of clarithromycin (0.01 M) in a titrant solution containing 0.01 M of TPB

Table 4 presents the results of the calculation of (RSD %), the relative standard deviation, (Er %) relative error, recovery (Re %), and for the titration technique.

Table 4. CN Analysis - titration method using ISE C1

Method	Titration method**
Conc.(M)	1.000×10 ⁻³
Found(M)	0.969×10 ⁻³
RSD*%	0.700%
Re%	98.4%
Er%	-1.6%

For every approach, (Er %) the relative error, (RSD %) relative standard deviation, and (Re %) recovery were computed. Table (5) below displays the findings.

Table 5. CR Analysis by ISE (C1)

Parameter	Direct method *	SAM*	Multi SAM*	Titration method***
Conc.	1.000 × 10 ⁻³ (M)	1.000 × 10 ⁻³ (M)	1.000 × 10 ⁻³	1.000 × 10 ⁻³ (M)
Found	0.996 × 10 ⁻³ (M)	0.989 × 10 ⁻³ (M)	1.009 × 10 ⁻³	0.969 × 10 ⁻³ (M)
% RSD*	0.468%	0.414%	-----	0.700%
% Re	99.4%	99.2%	100.7%	98.4%
% Er	-0.6%	-0.8%	0.7%	-1.6%

RSD*% for n=5, t=2.7, RSD**% for n=3, t=4.3, RSD***% for n=2, t=12.7

In Table (6), the data acquired for pharmaceutical samples demonstrating the use of electrode C1 in the potentiometric assessment of clarithromycin in pharmaceutical industry.

Table 6. Analysis of CN in pharmaceutical sample

Parameter	Direct method *	SAM*	Multi SAM*	Titration method***
Conc. (M)	1.000 × 10 ⁻³	1.000 × 10 ⁻³	1.000 × 10 ⁻³	1.000 × 10 ⁻³
Found * (M)	0.979 × 10 ⁻³	0.993 × 10 ⁻³	1.02 × 10 ⁻³	0.978 × 10 ⁻³
% RSD *	0.577%	0.511%	-----	0.688%
Re %	98.8%	98.9%	101.1 %	98.1%
Er %	-1.2%	-1.1%	1.1%	-1.9%

4. CONCLUSION

Two electrodes of clarithromycin were prepared using the ionic complex clarithromycin-bromophenol Blue in a polyvinyl chloride matrix to form the membrane using two plasticizers, tributyl phosphate (TBP) and orthonitrophenyl octyl ether (ONPOE). Clarithromycin electrodes [C1 and C2] gave a slope of (55.699 and 53.895 mV/decade) and linear range of concentrations (10^{-5} - 10^{-2} and 7×10^{-5} - 10^{-2} m), respectively. (C1) the best electrode with TBP plasticizer presented a slope of 55.699 mV/decade, correlation coefficient 0.9995 and limit of detection (9×10^{-6}) M, at an age of 16 days. Electrode C1 showed high stability and thus, was important for clarithromycin determination in pharmaceutical samples. Interference measurements in the presence of some ions were calculated by relying on the method of mixed solution.

5. Acknowledgements

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6. Conflict of interest

The authors declare no conflict of interest in this reported work.

REFERENCES

- Abdulla, N. I., Al-Haideri, A. M., Al-Joboury, M. I., & Nassory, N. S. (2005). Construction and characterization of indium liquid ion selective electrodes based on crown ethers in a PVC matrix membrane. *Turkish Journal of Chemistry*, 29(6), 687–696.
- Abraham, S. A. (2022). Analysing aflatoxin production conditions in feed samples using a preparative thin layer chromatography (TLC) method. *Iraqi Journal of Science*, 9–20.
- Abraham, S. A., Ahmad, S. M., & Al-Phalahy, B. A. (2022). Novel potentiometric sensor for estimation of the moxifloxacin in the pharmaceutical samples, urine, and serum. *International Journal of Drug Delivery Technology*, 12(4), 1663–1668.
- Abraham, S. A., Saad, A., & Ibrahim, S. A. (2020). Various analytical methods for the determination of clarithromycin: A review. *International Journal of Research in Engineering and Innovation*, 4(1), 56–59.
- Al-Baitai, A. Y., Abdalhadi, S. M., Ibrahim, S. A., Ali, A. A., & Alzamly, G. H. (2020). The effect of temperature and storage time on the concentration of vitamin D in human serum. *Systematic Reviews in Pharmacy*, 11(4), 695–700.
- Amini, H., & Ahmadiani, A. (2005). Sensitive determination of clarithromycin in human plasma by high-performance liquid chromatography with spectrophotometric detection. *Journal of Chromatography B*, 817(2), 193–197.
- British Pharmacopoeia. (2009). *Specific monographs* (Vol. 3, p. 8359). The Stationery Office on behalf of the Medicines and Healthcare Products Regulatory Agency.
- British Pharmacopoeia. (2014). *Medicinal and pharmaceutical substances* (Vol. 1, No. 2, pp. 1406–1407). The Stationery Office on behalf of the Medicines and Healthcare Products Regulatory Agency.
- Chandra, S., Sharma, K., & Kumar, A. (2013). Mg(II) selective PVC membrane electrode based on methyl phenyl semicarbazone as an ionophore. *Journal of Chemistry*, 2013, Article 189464.
- Craggs, A., Moody, G. J., & Thomas, J. D. R. (1974). PVC matrix membrane ion-selective electrodes: Construction and laboratory experiments. *Journal of Chemical Education*, 51(8), 541.
- Ismaeel, Y. Q., & Al-Phalahy, B. A. (2020). A new cyproheptadine PVC ion selective electrode and their applications in pharmaceutical preparations and human fluids. *Al-Nahrain Journal of Science*, 23(2), 26–32.
- Kanfer, I., Skinner, M. F., & Walker, R. B. (1998). Analysis of macrolide antibiotics. *Journal of Chromatography A*, 812(1–2), 255–286.
- Koryta, J. (1977). Theory and applications of ion-selective electrodes. Part 2. *Analytica Chimica Acta*, 91(1), 1–85.
- Langtry, H. D., & Brogden, R. N. (1997). Clarithromycin: A review of its efficacy in the treatment of respiratory tract infections in immunocompetent patients. *Drugs*, 53, 973–1004.
- Li, W., Jia, H., & Zhao, K. (2007). Determination of clarithromycin in rat plasma by HPLC–UV method with pre-column derivatization. *Talanta*, 71(1), 385–390.
- Nassory, N. S., Maki, S. A., & Al-Phalahy, B. A. (2008). Preparation and potentiometric study of promethazine hydrochloride selective electrodes and their use in determining some drugs. *Turkish Journal of Chemistry*, 32(5), 539–548.
- Shakir, I. M. (2016). A novel online coupling of ion selective electrode with the flow injection system for the determination of vitamin B1. *Baghdad Science Journal*, 13(2), 458.
- Umezawa, Y., Umezawa, K., & Sato, H. (1995). Selectivity coefficients for ion-selective electrodes: Recommended methods for reporting $K_{A,B}^{pot}$ values (Technical report). *Pure and Applied Chemistry*, 67(3), 507–518.