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Development of Coated Graphite and Wire Electrodes for Methyldopa Determination in Pharmaceutical and Pure Products

Hasan Amer Katif [1a]* and Omar Salih Hassan[2b]

[1,2]*Department of Chemistry, College of Education for pure Science, Tikrit University, Tikrit, Iraq.*

[a]E-mail: ha5772500@gmail.com , [b]E-mail: : Omar.s.hassan@st.tu.edu.iq
[a*]Corresponding author:ha5772500@gmail.com

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Abstract*— Two designs of methyldopa-selective electrodes were compared: electrode A, which was copper-coated and electrode B, which was a coated graphite electrode (CGE) based on the ion-exchanger complex of methyldopa- Phosphotungstic acid (MeD-PTA). With a detection limit of 3.2×10-6 M and a Nernstian slope of 54.97 mV/decade, Electrode A exhibits a wide linear dynamic range to detected a concentration of MeD which was equals to 5.1×10^{-6} - 1.0×10^{-2} M. The limit of detection of 1.4×10^{-6} M and a Nernstian slope of 57.12 mV/decade, Electrode B showed linearity over the range of concentrations of 4.0×10-8 to 1.0×10^{-2} .Methyldopa (MeD) exhibited a good selectivity over a wide range of inorganic cations, starch, and glucose, according to selectivity coefficients calculated using the separate solution method (SSM). The MeD in tablet samples was ascertained using the calibration curve method and potentiometric measurement. using the suggested sensors, excellent percentage recovery was one of the outcomes, which were adequate and occasionally better than those from other standard assay procedures. Because of its appealing qualities, the CGE is more suited for commercialization.

***Keywords*— Graphite electrode, potentiometric technique, coated wire, methyldopa, selectivity.**

I. INTRODUCTION

Methyldopa's IUPAC name is (2S).(3, 4-dihydroxyphenyl)-2-methylpropanoic acid, or 2-Amino-3-. This medication is used to treat hypertension. Usually, A diuretic is often co-administered to enhance its effectiveness and reduce fluid retention. It has a molecular weight of 238.2 gm/mol. It is a powder with white to yellowish white color . It is moderately soluble in water and fully dissolves in alcohol.The drug's chemical structure is depicted in Figure 1[1].

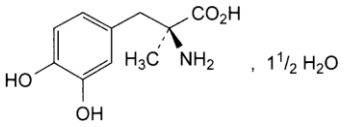

Fig.1: Methyldopa's Chemical Structure [2].

ISEs were found to be helpful in the study of pharmaceutical formulations because of their attractive features, which include their straightforward design, ease of fabrication, respectable selectivity, fast response time, application to turbid and colored solutions, and potential for interface with automated and computerized systems. [3,4].

Electrochemical potentiometric sensors are currently highly recommended as sensitive tools for the detection of a range of pharmaceuticals due to their non-toxicity, affordability, sustainability, and sensitive surfaces. Because of their inherent measuring qualities and ease of miniaturization, they also provide a superb green character. Coated graphite electrodes are regarded as the cutting edge of ion-selective electrode technology. Due to their many advantages over conventional membrane electrodes, including their long lifespan, stability, quick response, chemical inertness, lack of internal filling solution, simplicity in design, and ability to be customized for microfabrication and miniaturization, they have attracted a lot of attention. With a high sensitivity that can achieve low LOD, the analytical detection of anions, cations, metals, and pharmaceuticals is greatly aided by coated graphite electrodes [5].

According to the literature review, methyldopa was measured using analytical techniques such spectrophotometry, which has been documented for the quantification of MeD [6-8]. Injection of flow [9].HPLC stands for high performance liquid chromatography [10] and oxidation using electrocatalysis [11].

Methyldopa-molybdophosphori acid dissolved in mixture contain:plasticizers di butyl phthalate (DBP) and Tetra hydrofuran (THF) as a more appropriate solvent mediator for coated wire electrode(CWE) and coated graphite electrodes (CGE) were used to determination Methyldopa in pharmaceutical formulations was shown to be accurately determined by these electrodes.

II. EXPERIMENTAL PART

A. Reagents and solutions

In our experiment, we used distilled water . Samarra Pharmaceutical Industries (SDI) provided the methyldopa.

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We purchased 10 mg tablets of methyldopa (MeD) from nearby pharmacies. Sigma provided the molybdophosphoric acid(PMA).Tetrahydrofuran (THF), graphite powder, di butyl phthalate (DBP), and high relative molecular weight polyvinyl chloride (PVC) were acquired from the Aldrich chemical firm. Each of the following cations were synthesized in a 10^{-2} M solution of phosphate, sulfate, carbonate, nitrate, or chloride: Na^{+}, K^{+}, Ca^{2+}, Zn^{2+}, Al^{3+}, and Fe^{3+}. Additionally, Aldrich provided 10^{-2} M solutions of glucose and starch.

A. B. Apparatus

The following cell was used to do potential measurements:

Hg, Hg_2Cl_2(s), KCl(sat.)||sample solution | ISES electrodes.

A saturated calomel electrode was used as a reference, a digital millivoltmeter (SR-MUL-3800) and a digital pH meter (HANNA pH 211) were used to measure potential. The working electrodes are the ion-selective electrodes.

B. Preparation of the ion-pair

Methyldopa-molybdophosphoric acid (MeD-PM) was prepared as a 0.01 M solution. Next, 10.0 mL of 0.01 M molybdophosphoric acid (PM) was mixed with 10.0 mL of 0.01 M methyldopa (MeD) solution by using deionized water. Two days were allowed for the precipitation to fully coagulate at room temperature. Filtration process was used to separate the precipitate, which was then rinsed with distilled water and allowed to dry.

C. Preparation the stock solution of Methyldopa

The MeD drug standard solution was made by dissolving 0.2382 gram in deionized water in a 100 mL volumetric flask at a concentration of $10.\times10^{-2}$ mole/L^{-1}. Deionized water was then used to dilute the remaining standard solutions (1.0×10^{-2} -1.0×10^{-8}) M.

D. Preparation of the Electrodes

1. Coated Graphite Electrode (CGE)

To create the coated graphite electrode with a length of 5.5 cm , 8 mm diameter rod of pure carbon was encased in a tight polyethylene tube. To create a uniform mixture, the following components: 10% ion-pair (MeD-PMA), 30% poly vinyl chloride (PVC), and 60% plasticizer di butyl phthalate (DBP). Five times, for ten seconds each, were weighed, diluted in 10 milliliters of an organic solvent (THF), and stirred for ten minutesone centimeter of the uncoated graphite rod was immersed, separately for two to three minutes, and then allowed to dry at room temperature for an hour. After immersing the electrode in a 1×10^{-2} M MeD solution for different time, the other end of the coated carbon rod was connected to a potentiometer recorder via an insulated copper wire [12].

2. Coated Wire Electrode (CWE)

Copper wire was cleaned with HNO_3, rinsed with deionized distilled water, and then allowed to dry in an organic solvent called acetone. The copper wire should be 8 cm long, 2 mm in diameter, and tightly insulated. The wire was exposed and uninsulated about one centimeter from each end. The coating mixture, which was made by weighing 60% plasticizer di butyl phthalate (DBP), 30% poly vinyl chloride (PVC), and 10% ion-pair (MeD-PMA), was applied to one end of the wire and allowed to dry in the air after being dissolved in 10 mL of an organic solvent (THF) and stirred for 10 minutes to create a homogenous mixture. The other end of the copper wire was attached to a pH meter after the electrode was submerged in a 1.0 × 10-2M MeD solution. [13].

3. Effect of pH

The effect of the pH of the test solution on the electrode potential was examined in 0.1 mM MeD. The solution's pH was adjusted between 2.0 and 10.0 by adding 0.1 M or 1.0 M HCl and/or NaOH.

4. Interfering ions' effects

Common interferents, such as inorganic substances and some excipients included in medicinal formulations, were investigated for their effects on the ion selective electrod ISE. The electrodes' selectivity was evaluated using the separate solution method (SSM) [14]. To perform the SSM, the potential of a cell in MeD solution was measured. Selectivity coefficient values obtained from measured potential values generated at the summits of the peaks at the same drug concentrations were used to control the conditional factors. According to Table 2, most foreign cations showed very modest values for the selectivity coefficient, and all electrodes exhibited good agreement performances with indicated and insignificant interferences.

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التعليق [as2]:

III. Recommended Procedures

A. Calibration graph method

In this method, a set of solutions of known concentrations were made and their potentials measured, then a plot of the measured potentials versus the concentrations of the solutions were made. This is considered the calibration curve for analysis of an unknown sample from its measured potential using this plot. Pharmaceutical formulation (tablets) of methyldopa from different companies was determined by the calibration curve method. The results, shown in Table 1, indicate that electrodes may be dependently used for determination of methyldopa.

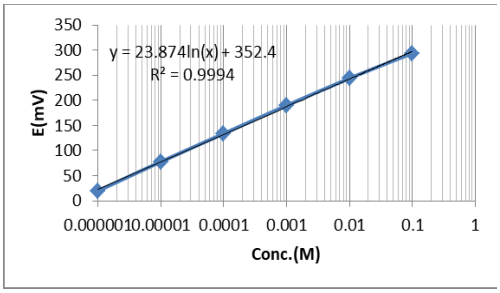

Fig. 2: Calibration curves of MeD-PMA-DBP Coated wire electrode

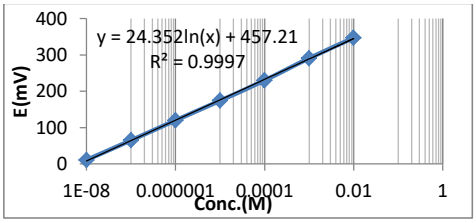

Fig. 3: Calibration curves of MeD-PMA-DBP Coated Graphite electrode

Table 1: Parameters of MeD-PMA-DBP Coated Wire and Coated Graphite Electrodes

Parameters	MeD-PMA-DBP Coated wire electrode	MeD-PMA-DBP Coated Graphite electrode
Slope (mV.decade	54.97	57.12
ercept(mV)	325.4	488.32
Regression equations	Y= (54.97) log [ATL] + 325.4	Y= (57.12) log [ATL] + 488.32
Correlations Coefficient(r)	0.9994	0.9993
Range of Conc. (mol.L^{-1})	5.1×10^{-6}-1.0×10^{-2}	4.0×10^{-8}-1.0×10^{-2}
LOD (mol.L^{-1})	3.2×10^{-6}	1.4×10^{-8}
Response time(s)	24	18
Range of PH	2.0-6.0	2.0-7.5
Life of time(day)	42	50

B. Effect of pH in the test solution

The impact of pH on the electrode potential at 25 °C was measured in 1.0×10-3 M MeD spanning the pH range of 2.0–10.0. Small volumes of 1.0 M or 0.1 M HCl/NaOH were added to adjust the pH of the test solutions. According to the findings gathered for the MeD electrode in Figure 4, the pH ranges for the MeD-PMA-DBP coated wire electrode and the MeD-PMA-DBP coated graphite electrode are 2.0 to 6.0 and 2.0 to 7.5, respectively. Proton interference and membrane surface penetration are shown by deviations below pH 2.0. Furthermore, Hydroxide ions react with methyldopa to form neutral species that cannot diffuse into the electrode membrane, leading to a gradual decline in potential at pH values above 6.0. Additionally, the measurements were impeded by the precipitate that formed in the solution. Figure 4 shows how the test solution's pH affects the A and B electrodes' potential response at 1.0 × 10^{-3} M.

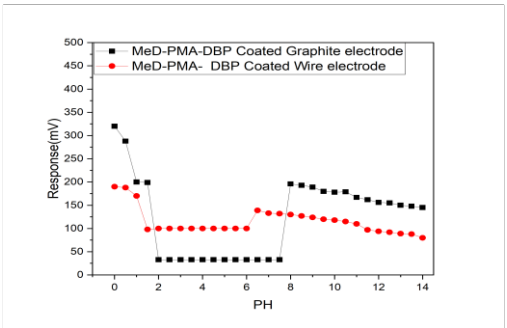

Fig.4: pH values of MeD-PMA-DBP Coated wire electrode and MD-PMA-DBP Coated graphite electrode

The most characteristic of an ion selective electrodeI(SE) that is dependent on the equilibrium between the electrode-sample solution interfaces is selectivity. Selectivity is impacted by other ions according to how closely their size and charge resemble the ion of interest that the electrode is measuring. The Nicolsky-Eisenman equation was used to determine the selectivity for the ions with the same charge [15–17]. The range of selectivity is 0 to less than 1. If an electrode's selectivity for all other ions is low, meaning they have little effect on it, then it is selective toward a given ion. These electrodes' selectivity for frequently occurring species was assessed, and the findings are reported in Table 2.

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Table2: Selectivity Coefficients of MeD-PMA-DBP Coated Wire and Graphite Electrodes for Various Interfering Ions

Ion interference	MeD-PMA- DBP Coated Wire electrode	MeD-PMA-DBP Coated Graphite electrode
K^{+1}	2.3053×10^{-2}	3.9759×10^{-2}
Na^{+1}	7.6791×10^{-2}	4.4870×10^{-2}
Mg^{+2}	3.1543×10^{-4}	6.0857×10^{-4}
Zn^{+2}	2.9008×10^{-4}	5.6143×10^{-4}
Al^{+3}	4.3059×10^{-5}	7.7850×10^{-6}
Fe^{+3}	3.9599×10^{-5}	6.7644×10^{-6}
Glucose	9.5536×10^{-4}	3.4167×10^{-4}
Starch	8.4255×10^{-4}	3.1520×10^{-4}

C. Analytical applications

The electrodes that are currently being manufactured share comparable characteristics, including reaction times, operating pH ranges, and linear concentration ranges. These results demonstrate that methyldopa in pharmaceutical preparations (tablets), as indicated in Table 3, may be successfully determined using the electrodes currently manufactured.

Table 3: Statistical Analysis of Methyldopa Determination Using MeD-PMA-DBP Coated Wire and Graphite Electrodes in Pure and Pharmaceutical Forms via Direct Approach

Samples	**MeD-PMA-BBP Coated wire electrode**			**MeD-PMA-DBP Coated graphite electrode**		
Pure Drug	**Taken MeD ($mol.L^{-1}$)**	**Found MeD ($mol.L^{-1}$)**	**%Rec**	**Taken MeD ($mol.L^{-1}$)**	**Found MeD ($mol.L^{-1}$)**	**%Rec**
	6.0	5.98	98.00	8.0	7.94	99.25
	5.0	4.99	95.20	7.0	6.96	99.42
	4.0	3.89	98.25	6.0	5.86	98.00
	3.0	2.93	99.00	5.0	4.97	95.20
	2.0	1.96	98.00	4.0	3.92	98.25
				3.0	2.99	99.00
				2.0	1.95	98.00
%Mean±SD	97.66±1.68			98.16±1.43		
N	5			7		
%RSD	1.72			1.45		
%RE	-2.34			-1.84		
Methyldopa 250/ mg	**Taken MeD ($mol.L^{-1}$)**	**Found MeD ($mol.L^{-1}$)**	**%Rec**	**Taken MeD ($mol.L^{-1}$)**	**Found MeD ($mol.L^{-1}$)**	**%Re**
	6.0	5.92	98.66	8.0	7.96	99.50
	5.0	4.93	98.60	7.0	6.95	99.28
	4.0	3.95	98.75	6.0	5.92	98.66
	3.0	2.89	96.33	5.0	4.93	98.60
	2. 0	1.95	97.50	4.0	3.95	98.75
				3.0	2.97	99.00
				2. 0	1.99	99.50
%Mean±SD	97.96±1.04			98.97±0.39		
N	5			5		
%RSD	0.10			0.39		
%RE	-2.04			-1.03		

Table 4: Statistical Analysis of the Standard Addition Method for Determining MeD Using MeD-PMA-DBP Coated Wire Electrode and MeD Coated Graphite Electrode in Bulk and Pharmaceutical Preparations

Samples	MeD-PMA-DBP Coated wire electrode			MeD-PMA-DBP Coated graphite electrode		
Pure Drug	Taken MeD($mol.L^{-1}$)	Found MeD ($mol.L^{-1}$)	%Rec	Taken MeD ($mol.L^{-1}$)	Found MeD ($mol.L^{-1}$)	%Rec
	3.0	2.90	96.70	3.0	2.91	97.11
		2.81	93.71		2.99	99.73
		2.85	96.51		2.87	95.97
		2.90	96.98		2.88	96.24
		2.95	98.49		2.99	99.89
%Mean±SD	96.47±1.73			97.78±1.89		
N	5			5		
%RSD	1.79			1.93		
%RE	-3.53			-2.22		
Methyldopa 250/ mg	Taken MeD ($mol.L^{-1}$)	Found MeD ($mol.L^{-1}$)	%Rec	Taken MeD ($mol.L^{-1}$)	Found MeD ($mol.L^{-1}$)	%Rec
	3.0	2.87	95.91	3.0	2.91	97.30
		2.82	94.08		2.97	99.01
		2.89	96.51		2.86	95.36
		2.88	96.27		2.95	98.64
		2.94	98.12		2.97	99.02
%Mean±SD N %RSD	96.17±1.44			98.86±1.56		
	5			5		
%RE	1.50			1.60		
	-3.83			-2.14		

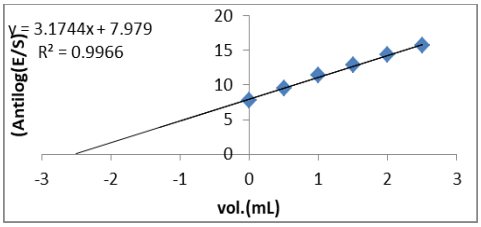

Fig.5: Antilog (E/S) Response of MeD-PMA-DBP Coated Wire Electrode for Methyldopa in its Pure Form at 1.0×10^{-3} mol.L^{-1}

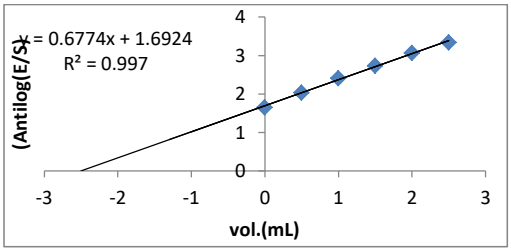

Fig. 6: Antilog (E/S) Response of MeD-PMA-DBP Coated Wire Electrode for Pharmaceutical Form of Methyldopa at 1.0×10^{-3} mol.L^{-1}

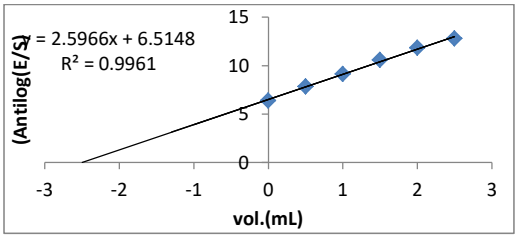

Fig. 7: Antilog (E/S) Response of MeD-PMA- DBP Coated Graphite Electrode for Methyldopa in its Pure Form at 1.0×10^{-3} mol.L^{-1}

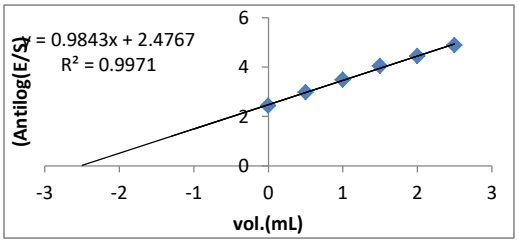

Fig. 8: Antilog (E/S) Response of MeD-PMA-DBP Coated Graphite Electrode for Pharmaceutical Form of Methyldopa at 1.0×10^{-3} mol.L^{-1}

V. CONCLUSION

A few CW, and CG ion-selective electrodes for the measurement of the drug methyldopa are shown in this paper. The drug methyldopa associates he electrode matrix with phosphotungstate is essential to makes the electrodes work. The electrodes features are rapid response time, low detection limits, and a wide range of usable concentrations. The electrodes have been successfully utilized to determine the specific medication in pharmaceutical preparations and urine samples that was tested with known concentrations of this drug. The CGE's appealing qualities-accuracy, speed, simplicity, and affordability—are expected to make it commercially preferred.

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CONFLICT OF INTEREST

Authors declare that they have no conflict of interest.

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