A Novel Coated Wire Electrode And Coated Graphite Electrode for Potentiometric Determination of Amitriptyline Hydrochloride in its pharmaceutical preparations, urine and blood plasma.

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Abstract. This paper uses the potentiometric method to evaluate (amitriptyline hydrochloride, AM) by creating selective electrodes for AM drugs with the active ingredient (Ammonium Reinackate, AR) using a plasticizer (Dibutyl phthalate, DBP). The results showed that for (Coated Wire Electrode (CWE)) and Coated Graphite Electrode (CGE) respectively, the Nernstian slope of the prepared Am-AR-DBP electrodes is (57.293, 58.803 mV / decade). With a pH range of (4-7) and a concentration range of 1 \times 10^{-6} - 1 \times 10^{-1} M for both electrodes, the upper and lower limit of detection for the Am-AR-DBP CGE is 0.2042M, 4.8 \times 10^{-7} M, and the upper and lower limit of detection for the Am-AR-DBP CWE electrode is 0.2051M, 4.91 \times 10^{-7} M, respectively. The response time ranges from 20-83 sec, 14-76 sec for CWE and CGE electrodes respectively. For the CWE electrode, the age of the electrodes is 26 days, and for the CGE electrode, 42 days. The research included calculating the selectivity with the presence of interferers of these electrodes where the $K_{i,j}^{pot}$ values for all ions were less than 1. In the estimation of the drug Amitriptyline Hydrochloride in the pharmaceutical preparation (Amitriptyline tablets), the manufactured electrodes were used by following the direct process, the standard method of additions, the possible titration method and the homogeneity of the material sample, as well as the drug was estimated in urine and blood plasma with a recovery of not less than 100.57 for urine and 99.46 for urine.

Keywords: Amitriptyline hydrochloride, Ion selective electrodes, Coated Wire Electrode; Coated Graphite Electrode, Ion pair.

I. Introduction:

Electrochemical sensors are one of the smallest chemical tools that can give instant and direct information when a specific compound or ion is present in complex samples. Among the different classes of chemical sensors, ion selective electrodes used in potential sensors are one of the most widely used. Potential detection by ion selective electrodes (ISEs) provide several advantages over other analysis methods such as speed, ease of operation, simple instrumentation, relatively fast response, wide dynamic range, reasonable selectivity, and low cost [1]. A selective electrode is generally known as a chemical sensor capable of converting the activity of a particular ion dissolved in a solution into an electrical potential that can be measured with a voltmeter or pH meter [2,3] The formula for amtriptyline hydrochloride is [4]
The molecular formula [4] is C_{20}H_{23}N, HCl, and its molecular weight is 313.9 g / mol, and the scientific name for the drug [5] is 3-(10,11-Dihydro-5H-dibenzo[a,d][7]annulen-5-ylidene)-N,Ndimethyl propan -1- amine hydrochloride. It is in the form of white powder or colorless crystals, easily dissolved in water, alcohol, and dichloromethane [6]. Amitriptyline hydrochloride is used to treat mental / mood problems such as depression. It may help improve mood and feelings of well-being, relieve anxiety and tension, aid in a better sleep, and increase the patient's energy level. This medication belongs to a class of drugs called tricyclic antidepressants [7]. Due to the medical importance of this drug, it has been determined by many different analytical methods, such as spectroscopy [8,9], HPLC [10,11], (RP-HPLC) [12], Voltmeter technology [13], and gas Liquid chromatography [14], capillary electrophoresis method [15], LC-MS technique [16], liquid chromatography [17], flow injection technique [18], thin-layer chromatography [19], fluorometry [20], and atomic absorption spectroscopy [21]. In this study, several selective electrodes were manufactured for the determination of Amitriptyline hydrochloride in its pure form, in its pharmaceutical preparations, and in biological fluids. Two types of electrodes were prepared (Coated Graphite Electrode (CGE) and Coated Wire Electrode (CWE).

2. Experimental Section

2.1. Apparatus
Jenway 3310 pH Meter, HANNA Instruments pH Meter 211, calomel electrode Swiss source, JENWAY Hot Plate with Stirrer-Germany, C.H.N Perkin Elmer USA 2400 Series II element analyzer.

2.2. Materials and Reagents
All chemicals used were of a high degree of purity and supplied by SDI, BDH, and Fluka 1. solution of Amitriptyline hydrochloride, AM 10^{-4} M. Prepared the standard solution of Amitriptyline hydrochloride at a concentration of 10^{-4} M by dissolving 3.1390 grams in deionized distilled water using a 100 mL volumetric flask and complete the volume with deionized distilled water to the mark and the other standard solutions (10^{-2}-10^{-6}) M were prepared by dilution With deionized distilled water.

2.3 Ammonium reinackate solution, AR 10^{-1} M. Prepared the solution by dissolving 3.5444 g of the substance in a 100 mL volumetric flask and complete the volume with deionized distilled water to the mark.

2.4 Hydrochloric acid at a concentration of approx 0.1 M. 0.8 mL of concentrated hydrochloric acid (12 N) was transferred by a graduated pipette to a 100 mL volumetric flask containing 50 mL deionized distilled water and the volume was completed with deionized distilled water to the mark.

2.5 Sodium hydroxide at a concentration of approx 0.1 M. Dissolved 0.4 g of the substance in a 100 mL volumetric flask and complete the volume with deionized distilled water to the mark.

2.6 Amitriptyline Tablets preparation solution 25 mg. Ten tablets containing 0.25 g of the basic substance Amitriptyline hydrochloride developed by the State Medicines and Medical Supplies Company of Samarra were crushed in an agate mortar and 1,025 grams was the average weight of one tablet. When 1,2867 g of the pharmaceutical preparation was taken and then dissolved with an ultrasonic system in deionized distilled water with Shake to ensure full dissolution and filtered with Whatman filter paper, the filtrate was then diluted in a 100 mL volumetric flask and the volume was
completed with deionized distilled water to the mark, so the result was a solution with a concentration of 10-2 M and a concentration of 100 mL.

2.7 Biological fluid solutions (urine, blood plasma) 0.01 M
In a stopper test tube, 4.5 mL of human plasma or urine were then added, 0.5 mL was added at a concentration of 0.1 M amtriptyline hydrochloride, and the tube was shaken for 1 minute. Other solutions of different concentrations were prepared by dilution with deionized distilled water.

2.8 Preparation of the ion-pair
The ion pair was prepared by combining 10 ml of AM drug solution at 10-1 M concentration with 10 ml of AR solution at 10-1 M concentration with stirring to form a light red AM-AR precipitate, then the precipitate was filtered and washed several times with deionized distilled water and left for two days at the temperature of the laboratory until dehydration and the precipitate was dehydrated and washed several times with deionized distilled water (1).

Table 1. Element Analysis for the AM-AR ion pair

| Element analysis | AM-AR | AM-AR |
|------------------|-------|-------|
|                  | %C    | %H    | %N    |
| Found            | 43.24 | 5.38  | 16.76 |
| Calculated       | 43.13 | 5.43  | 16.75 |
| Formula          | \([C_{20}H_{24}NCl][C_{4}H_{16}CrN_{7}S_{4}]\cdot H_2O\) |

2.9. Preparation of the Electrodes
2.9.1. Coated Graphite Electrode (CGE)
Through a series of preliminary experiments, the selective membrane was prepared by mixing its components according to weight ratios, which gave the best membranes in terms of the nature of the membrane and its response according to the following: The coated graphite electrode was prepared by encapsulating a pure carbon rod (5.5 cm in length, 8 mm in diameter) with a tight polyethylene tube. A mixture consisting of (10% AM-AR, 30% PVC, 60% DBP as plasticizer) was prepared. And then dissolve the mixture in (5 ml) of THF, which is considered a good solvent and adhesive, and then continue stirring until we get a thick solution at a volume of 2-3 ml of the mixture. 1cm of the uncoated graphite rod was immersed (5) times each immersion for 10 seconds, between each immersion and another (2-3) minutes, then left in the air for an hour to dry. The electrode was immersed in a 1 × 10⁻² M solution of amtriptyline hydrochloride for different periods, then the other end of the coated carbon rod was connected with an insulated copper wire and connected to a Potentiometer recorder [22].

2.9.2. Coated Wire Electrode (CWE)
Via a series of preliminary experiments, the selective membrane was prepared by mixing its components according to the weight ratios given by the best membranes in terms of the nature of the membrane and its reaction according to the following: when the silver wire was washed with nitric acid, rinsed with distilled water, dried with acetone, and then left to dry. The silver wire should be insulated well (8 cm long and 2 mm in diameter). We leave the silver wire 1 cm from both ends exposed and uninsulated. A mixture was prepared consisting of (10% AM-AR, 30% PVC, 60% DBP as plasticizer). And then dissolve the mixture into (5 ml) THF, which is known to be a strong solvent and adhesive, and then continue stirring until 2-3 ml of the mixture has a thick solution. 1 cm of unwrapped silver wire (5) was submerged every 10 seconds between each dip and another (2-3) minutes, then left in the air to dry for an hour. For different times, the electrode was submerged in an amtriptyline hydrochloride solution of 1 ?? 10⁻¹⁻² M, then the other end of the silver wire was attached to the potentiometer recorder[23].
3. Results and Discussion

3.1. Study the optimal components of (CWE, CGE)

In a 50 ml glass beaker, the AM-AR electrode (CWE, CGE) was immersed with a calomel electrode, and the potential difference was recorded for the pharmaceutical solutions at concentrations of $10^{-8}$ - $10^{-1}$ M and a corresponding graph of (-) the logarithm of the solutions concentration and the results are shown in Table (2). Solutions concentrations that are less than $1 \times 10^{-6}$ M did not show a linear response in the (CWE, CGE) electrodes and were therefore neglected in the subsequent experiments. Two types of electrodes were prepared, CWE and CGE, with different proportions. The electrode (No. 1) is the best AM-AR-DBP CGE electrode, with the Nernst slope being about 58.62 mV.decade^{-1}, and the electrode (No. 4) the best AM-AR-DBP CWE electrode, where the Nernst slope gives about 56.85 mV.decade^{-1}. This can be seen from Table (2). The properties and specifications of these selective electrodes that are manufactured for the medicinal substance have been studied according to the following Table (2):

| Electrode No. | PVC (%) | Plasticizer (%) | Am-AR (%) | Slope mV/decade | Linear range M | $R^2$ |
|---------------|---------|-----------------|-----------|-----------------|----------------|-------|
| AM-AR-DBP, CGE |         |                 |           |                 |                |       |
| 1             | 30      | 60              | 10        | 58.62           | $1 \times 10^{-4}$ - $1 \times 10^{-1}$ | 0.9998 |
| 2             | 30      | 63              | 7         | 53.29           | $1 \times 10^{-6}$ - $1 \times 10^{-1}$ | 0.9951 |
| 3             | 30      | 65              | 5         | 52.22           | $1 \times 10^{-6}$ - $1 \times 10^{-1}$ | 0.9876 |
| AM-AR-DBP, CWE |         |                 |           |                 |                |       |
| 10            | 30      | 60              | 10        | 56.85           | $1 \times 10^{-4}$ - $1 \times 10^{-1}$ | 0.9996 |
| 11            | 30      | 63              | 7         | 54.66           | $1 \times 10^{-6}$ - $1 \times 10^{-1}$ | 0.9991 |
| 12            | 30      | 65              | 5         | 53.91           | $1 \times 10^{-6}$ - $1 \times 10^{-1}$ | 0.9993 |

3.2 Effect of pH

In order to research the effect of the pH on the electrode's potential response, the potential was determined by adding NaOH or HCl to a constant concentration of $1 \times 10^{-4}$ M of amtriptyline hydrochloride solution and to different pH values ranging from (1-10). As a function of pH in Fig., the potential shift was plotted. 1. The results indicated that the potential of the electrode is constant between the pH (4-7). In this range, no interference from hydrogen ions or hydroxyl ions was observed. Fluctuations in the potential value at a pH of more than 7 can be due to the formation of soluble and insoluble complexes with hydroxyl ions in the solution of the medication amtriptyline hydrochloride. As for the fluctuations at a pH below 4, it is likely to be due to the partial protonation of the formed complex. The results of this research are shown in Figure 5 (1).
3.3. Effect of Temperature
The potential change was measured by changing the temperature of the solution from (5-85) °C for a concentration of $1 \times 10^{-4}$ M, and the relationship between the temperature and the measured potential difference was plotted, and it was found that the best temperature range in which the electrodes would operate is between (10-50) °C for (CWE, CGE) electrodes, which was used in the subsequent experiments, and the results are shown in Fig. 2. It shows a significant increase in the potential difference values at higher temperatures, which can be attributed to the increase in the movement of drug solution particles inside and outside the electrode. The temperature that is less than 5 °C was neglected due to the freezing of the solution, as the phenomenon of water anomalies occurs at a temperature of 4 °C, so the surface of the solution becomes freezing, preventing the electrode from performing its work, which makes measuring the potential difference of the solution at a temperature less than 5 °C is not possible.

![Figure 2. Effect of Temperature on the potential response of AM-AR-DBP Electrodes](image)

3.4. Effect of electrode immersion time on electrode performance
The effect of submerging the AM-AR-DBP electrodes in a $1 \times 10^{-2}$ M solution of Amitriptyline hydrochloride was studied for different periods by measuring and following the slope values until the readings stabilized and the highest value of the Nernstian slope was obtained. The slope values reached their maximum values for the prepared AM-AR-DBP electrodes (58.62, 56.85) mV / (decade) after continuous immersion for (12, 24 hours) CWE and CGE electrodes respectively.

3.5. Calibration Curve and Detection limit
After determining the optimal conditions of the pH and temperature in several experiments, a calibration curve was drawn, and it is evident in Figure 3 how linear the calibration curve is. The upper and lower detection limit of the prepared AM-AR-DBP electrodes were calculated and the upper and lower detection limit of the CGE electrode was 0.2042M, $4.8 \times 10^{-7}$ M respectively, and the upper and lower detection limit of the CWE electrode was 0.2051M, $4.91 \times 10^{-7}$ M respectively.

![Figure 3. calibration curve of AM-AR-DBP Electrodes](image)
3.6. Precision and accuracy

After drawing the calibration curve for the AM-AR-DBP electrodes, precision and accuracy were studied by calculating the potential of different drug concentrations to be tested within the linear range of the calibration curve for (7) consecutive readings and at the optimal selected conditions, and the results are shown in the Table (3).

Table 3. Precision and accuracy of results for AM-AR-DBP electrodes

| Sample | Taken [AM] M | Found [AM] M | %Recovery | %RE  |
|--------|--------------|--------------|-----------|------|
| CGE    | 1 × 10^{-1} | 1.0095 × 10^{-1} | 100.95 | 0.95 |
|        | 1 × 10^{-2} | 1.0018 × 10^{-2} | 100.18 | 0.18 |
|        | 1 × 10^{-3} | 9.941 × 10^{-4} | 99.41 | -0.59 |
|        | 1 × 10^{-4} | 1.0258 × 10^{-4} | 102.58 | 2.58 |
|        | 1 × 10^{-5} | 9.788 × 10^{-6} | 97.88 | -2.12 |
|        | 1 × 10^{-6} | 9.71 × 10^{-7} | 97.10 | -2.90 |
| %Mean ± SD | 99.683 ± 2.0120 | 6 | 4.0483 | -1.9 |
| %RSD   | 2.0183 |

In addition to good recovery and relative error values, Table (3) shows a value for the relative standard deviation of the AM-AR-DBP electrodes which are 2.0183% and 1.1473% for the CGE and CWE electrodes respectively for the concentrations selected from the calibration curve. These results indicate that the prepared electrodes can be used. To estimate the drug with high accuracy and Precision.

3.7. Response Time

The Response Time of the electrodes was studied by immersing the electrode in the solution of the drug to be analyzed at concentrations of 10^{-6}-10^{-1} M and measuring the potential difference for each solution and determining the response time and the results are shown in Figure (4) and it is clear that the response time of the prepared AM-AR-DBP electrodes ranges between 20-83 seconds, 14-76 seconds for CWE and CGE electrodes respectively.
3.8. Study the life time of the Electrode

The lifetime of the AM-AR-DBP electrode was calculated by repeating the calibration two or three times a week for each prepared electrode, with Nernst slope follow-up values, as no deviation or decrease in Nernst slope was observed for 26 days, 42 for CWE and CGE electrodes, respectively. After that, a negative deflection was shown by the electrodes. In general, the explanation for the end of the electrode's existence could be due to the leakage of the electrode material (the active substance).

3.9. Selectivity

The electrodes showed high selectivity in the direction of the drug without the potential being affected by the interfering ions selected through the selectivity coefficient values that are less than one and shown in Table (4). The selectivity was measured by the separate solutions method \(^{(24)}\), where the potential of the drug solution was measured at a concentration of \(1 \times 10^{-3} \text{ M}\) without adding the interfering ion \((E_i)\), then the potential of the interfering ion solution was measured at a concentration of \(1 \times 10^{-3} \text{ M}\) Alone \((E_j)\).

### Table 4. Selectivity coefficient values

| the interfering ion \(1 \times 10^{-3} \text{ M}\) | Selectivity coefficient values \(K_{ij}^{\text{tot}}\) | AM-AR-DBP |
|---------------------------------------------|-------------------------------------------------|-----------|
| \(Na^{+}\) | 5.001 \times 10^{-1} | 4.444 \times 10^{-1} |
| \(K^{+}\) | 4.878 \times 10^{-1} | 4.100 \times 10^{-1} |
| \(NH_4^{+}\) | 4.099 \times 10^{-1} | 3.911 \times 10^{-1} |
| \(Ba^{2+}\) | 4.111 \times 10^{-3} | 5.998 \times 10^{-3} |
| \(Ca^{2+}\) | 9.0012 \times 10^{-3} | 60333 \times 10^{-3} |
| \(Mg^{2+}\) | 4.111 \times 10^{-3} | 7.321 \times 10^{-3} |
| \(Cl^{-}\) | 9.679 \times 10^{-2} | 8.008 \times 10^{-2} |
| \(Br^{-}\) | 6.321 \times 10^{-2} | 7.191 \times 10^{-2} |
| \(I^{-}\) | 3.665 \times 10^{-2} | 2.900 \times 10^{-2} |
| \(NO_3^{-}\) | 2.988 \times 10^{-2} | 3.434 \times 10^{-2} |
| \(CO_3^{2-}\) | 4.432 \times 10^{-2} | 8.801 \times 10^{-2} |
| \(SO_4^{2-}\) | 2.200 \times 10^{-2} | 3.120 \times 10^{-2} |
| Glucose | 1.922 \times 10^{-3} | 2.222 \times 10^{-3} |
| Fructose | 8.004 \times 10^{-3} | 6.990 \times 10^{-3} |
| Starch | 7.777 \times 10^{-3} | 5.000 \times 10^{-3} |

3.10. Robustness and Ruggedness

The robustness of the analytical method used for the AM-AR-DBP electrodes prepared for both types CWE and CGE was examined by using ethanol as a solvent instead of water in the preparation of drug solutions for the concentration range \(1 \times 10^{-6} - 1 \times 10^{-3} \text{ M}\). As for the rigidity of the method, it was studied by using another Potentiometer recorder (HANNA Instruments 211 pH Meter) with changing the laboratory used, and the results are shown in Table (5).
Table 5. Robustness and Ruggedness of the analytical method used for AM-AR-DBP electrodes

| Parameter | Robustness | Ruggedness |
|-----------|------------|------------|
|           | CGE        | CWE        |
| %Mean ± SD| 101.015 ± 2.3942 | 101.2466 ± 2.0018 |
| n         | 6          | 6          |
| Variance  | 5.7324     | 4.0072     |
| %RE       | 1.0150     | 1.2466     |
| %RSD      | 2.3701     | 1.9771     |
|           | CGE        | CWE        |
| %Mean ± SD| 100.01 ± 1.6865 | 99.800 ± 1.6015 |
| n         | 6          | 6          |
| Variance  | 2.8445     | 2.5648     |
| %RE       | 0.0100     | -0.2000    |
| %RSD      | 1.6863     | 1.6047     |

3.11. Applications of drug Amitriptyline hydrochloride in pharmaceutical preparations
3.11.1. The direct method

The drug was estimated in the pharmaceutical formulation, Amitriptyline tablets, using the prepared AM-AR-DBP electrodes, and the results are shown in Table (6).

Table 6. Estimating the drug by the direct method

| Sample AM-AR-DBP | Taken [AM] M | Found [AM] M | %Recovery | %RE | %RSD |
|------------------|--------------|--------------|-----------|-----|------|
| CWE              | 5 x 10^{-2}  | 5.0261 x 10^{-2} | 100.522 | 0.522 | 0.2548 |
|                  | 5 x 10^{-3}  | 5.0857 x 10^{-3} | 101.71  | 1.714 | 0.3042 |
| CGE              | 5 x 10^{-2}  | 4.9891 x 10^{-2} | 99.7827 | -0.217 | 0.1565 |
|                  | 5 x 10^{-3}  | 4.9508 x 10^{-3} | 99.0160 | -0.984 | 0.3175 |

The good recovery values using the prepared AM-AR-DBP electrodes and the relative standard deviation values for the CWE, CGE electrodes confirm that the estimation using these electrodes is of high Precision and accuracy.

3.11.2. Standard Additions Method

The calibration curves for the standard additions method of AM on the pharmaceutical preparation Amitriptyline tablets of the prepared AM-AR-DBP electrodes are shown in Fig. (5). Depending on the straight-line equation and when y = 0, x = -2.0064 for the CWE electrode and x = -2.0247 for the CGE electrode, it represents the volume of the standard solution Vs with a concentration of 1 x 10^{-3}M, and using the relationship:

C V = -V, X

Since C = concentration of the pharmaceutical preparation solution (required), V = volume of Amitriptyline tablet preparation solution = 10 ml, X = standard solution concentration of the pure drug additive = 1 x 10^{-3}M, Vs = volume of standard solution Of the drug.
Figure 5. Standard Additions Curves for Estimation of AM in (Amitriptyline Tablet) using the prepared AM-AR-DBP electrodes.

Table 7. Estimating the drug by the Standard Additions method

| Sample AM-AR-DBP | Taken [AM] M | Found [AM] M | %Recovery | %RE |
|------------------|--------------|--------------|-----------|-----|
| CWE              | $2 \times 10^{-4}$ | $2.0064 \times 10^{-4}$ | 100.32    | 0.32 |
| CGE              | $2 \times 10^{-4}$ | $2.0247 \times 10^{-4}$ | 101.23    | 1.23 |

The recovery values of the amitriptyline hydrochloride concentration using AM-AR-DBP electrodes prepared after application for the pharmaceutical preparation of amitriptyline tablets are shown in Table (7). We infer from these good results of recovery values and relative error that the electrodes developed and used in the determination of amitriptyline hydrochloride in the amitriptyline tablet pharmaceutical preparation are electrodes that give good precision results.

3.11.3. potentiometric titration method

The drug was estimated in the pharmaceutical preparation amitriptyline tablets using the prepared AM-AR-DBP electrodes and the results are shown in Table (8) after the graph of the values of the potential of the solution AM, its concentration $1 \times 10^{-3}$ M and its volume of 10 ml against the titrant solution AR. Its concentration is $1 \times 10^{-3}$ M, and the end point is defined as a bisection of the steeply sloping portion of the curve which is analogous to the inverse of the letter S.

Table 8. Estimating the drug by the potentiometric titration method

| Sample AM-AR-DBP | Taken [AM] M | Found [AM] M | %Mean* ± SD | %Recovery | %RE | %RSD |
|------------------|--------------|--------------|-------------|-----------|-----|------|
| CWE              | $1 \times 10^{-3}$ | $1.0083 \times 10^{-3}$ | 100.83 ±2.5000 | 100.83 | 0.83 | 2.4794 |
| CGE              | $1 \times 10^{-3}$ | $1.0027 \times 10^{-3}$ | 100.27 ± 2.6352 | 100.27 | 0.27 | 2.6281 |

Average of nine potential readings *
3.11.4. Study the homogeneity of content

The drug was measured using the prepared AM-AR-DBP electrodes in the pharmaceutical formulation, amitriptyline tablets, and the results are shown in the table (9). After a series of bakers had been prepared and one tablet was dissolved in 100 ml of deionized distilled water in each baker, then the potential was measured and the concentration of the solution was determined by the calibration curve.

**Table 9.** Estimating the drug by the homogeneity of content method

| Sample AM-AR-DBP | Taken [AM] M | Found [AM] M | %Recovery* | %RE  |
|------------------|--------------|--------------|------------|------|
| CWE              | 7.9643 × 10⁻⁴ | 7.8595 × 10⁻⁴ | 98.6800    | -1.32|
| CGE              | 7.9643 × 10⁻⁴ | 8.0068 × 10⁻⁴ | 100.5341   | 0.5341|

Average of six potential readings*

3.11.5. Determination of drug in urine and blood plasma

Amitriptyline hydrochloride was estimated in urine and blood plasma in the pharmaceutical formulation Amitriptyline tablets using AM-AR-DBP electrodes prepared and the results are shown in Table (10).

**Table 10.** Estimating the drug in urine and blood plasma

| Sample Urine AM-AR-DBP | Taken [AM] M | Found* [AM] M | %Recovery | %RE  |
|------------------------|--------------|---------------|-----------|------|
| CWE                    | 2 × 10⁻³     | 2.0179 × 10⁻³ | 100.89    | 0.89 |
| CGE                    | 2 × 10⁻³     | 2.0115 × 10⁻³ | 100.57    | 0.57 |

Average of seven potential readings*

4. Conclusion

In the presence of DBP as a plasticizer, Ion-selective electrodes consisting of an electrically active material resulting from the interaction of AM with AR were produced. A linear response range (10⁻⁶-10⁻¹ M) with a slope equal to (57.293, 58.803 mV / decade) was achieved by the prepared AM-AR-DBP electrodes. The CGE electrode's upper and lower detection limit was 0.2042M, 4.8 × 10⁻⁷ M, and the CWE electrode's upper and lower detection limit was 0.2051M, 4.91 × 10⁻⁷ M. For both CWE and CGE electrodes, the lifetime of the electrodes was (26 days, 42 days). This new technique has been shown to be highly accurate and successfully applied to pharmaceutical preparation (Amitriptyline tablets), urine and plasma blood.
References

[1] Bagotsky V S 2006 *Fundamentals of Electrochemistry*, 2nd Ed., John Wiley and Sons, New Jersey, 694,402.
[2] Zdrachek E and Bakker E 2019, *Anal. Chem.*, 91, 2.
[3] Mikhailson., 2010, *J. Anal. Chem.*, 65, 112.
[4] U.S. pharmacopoeia on CD-ROM, 1965, 2013 36th ed. NF 25, system simulation ltd. The stationary office, America.
[5] British pharmacopoeia in CD-ROM, 1827, 2013, 7th ed., by system simulation ltd., The stationary office, London.
[6] Moffat A C , Ossleton M D and Widdop B 2011 *Clarke's Analysis of Drugs and Poisons*, 4th ed. (Pharmaceutical Press, London UK).
[7] Sweetman S C , Martindale 2014 *The complete drug reference*, 38th ed. (Pharmaceutical Press. London).
[8] Susmitha K , Thirumalachary M , Singh T C and Venkateshwarlu G 2014 *J. Chil. Chem. Soc.*, 59, 2265.
[9] Reddy T V B, Ramu G and Rambabu C 2014, *J. Pharm. Sin.*, 5, 9.
[10] Farag R S , Darwish M Z , Fathy W M and Hammad H A 2013, *Int. J. Chemical and Anal. Sci.*, 4, 120.
[11] Mosavian M T H , Es'haghi Z , Razavi N and Banihashemi S  2012, *J. Pharma. Anal.*, 2, 361.
[12] Thejaswini C G and Gurupadayya B  2014, *J. Pharma. Res.*, 4, 3597.
[13] Beitollahi H , Nejad F G , Tajik S , Jahani S and Biparva P  2017, *Int. J. Nano Dimens.*, 8, 197.
[14] Ulrich S, Isensee T and Pester U, 1996, *J. Chroma. B: Biomedical Scie. and Appl.*, 685, 81.
[15] Wu S M , Wu H L , Ko W K and Chen S H 2000, *Anal. Chim. Acta.*, 413, 125.
[16] Shen Y , Zhu R H , Li H D , Liu Y W and Xu P 2010, *J. Pharma. and Biomed.*, 53, 735.
[17] Karpinska J and Starczewska B 2002, *J. Pharma. and Biomed. Anal.*, 29, 519.
[18] El-Nashar R M , Abdel Ghani N T and Bioamy A A 2004, *J. Microchem.*, 78, 107.
[19] Patel S.K. and N.J. Patel. 2009, *Chroma.*, 69, 393.
[20] Kaur K and Malik A K 2013, *J. Fluoresce.*, 23, 533.
[21] Elnennia E M , El Zawawy F M and Hassan S S M 1993, *Microchimica. Acta.*, 110, 79.
[22] Khalil M M , Issab Y M and Mostafa S M  2015, *Int. J. Eng. Res. and Gen. Sci.*, 3, 1191.
[23] Abdallah N A 2016, *Sens. Mater.*, 28, 797.
[24] Bakker E and Pretsch E 2007, *J. Angew. Chem. Int. Ed.* 46, 5660.