

Full Paper

A Novel Potentiometric Method for the Determination of Atenolol in Pure and Commercial Products

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Abstract- To ascertain the amount of atenolol present in pharmaceutical and pure samples, two distinct kinds of ion selective electrodes were developed: coated graphite electrodes (CGE) and coated wire electrodes (CWE). At the range 6.2×10^{-6} - 1.0×10^{-2} and 4.5×10^{-8} - 1.0×10^{-2} mol.L⁻¹ with a slope of 52.95, and 56.23 mV/decade with a low limit of detection 1.8×10^{-6} and 1.3×10^{-8} mol.L⁻¹, the electrodes adhered to the Nernst equation for CGE and CWE electrodes, respectively. Additionally, the CWE and CGE electrodes had response times of 38 and 26 seconds and life times of 34 and 41 days, respectively. Moreover, the recommended sensors showed long-term stability and functioned after preparation with negligible variations in the potential or slope values. In this study, the ATL drug's high selectivity over a number of inorganic cations was demonstrated by the ATL sensors that were made for the drug formulation samples. The sensors being studied allow for the direct determination of ATL in specific Commercial Products.

Keywords- Atenolol; ISEs; Direct method; Nernstian response; Selectivity; Coated wire and graphite electrode

1. INTRODUCTION

The chemical name for atenolol (ATL), Figure 1, [1] is 4-(2-hydroxy-3-[(1-methylethyl) amino] propoxy) benzeneacetamide. Atenolol is a member of the beta-blocker class. Cardiovascular conditions like hypertension, chronic stable angina pectoris, and cardiac arrhythmias can be effectively managed with this drug. Additionally, it lowers the risk of death and non-fatal re-infarction in people who have survived an acute myocardial infarction [1].

This powder is white or nearly white, has a molecular weight of 266.3 g/mole, is soluble in anhydrous ethanol, sparingly soluble in water, and slightly soluble in methylene chloride [2]. Figure 1 depicts the chemical structure of atenolol.

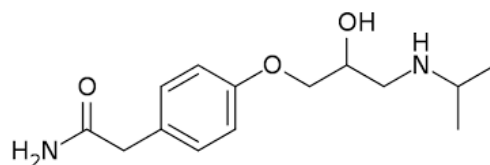


Figure1. Chemical structure of atenolol [3]

The scientific community has continued to pay close attention to potentiometric sensors that use ion-selective electrodes. These sensors have been used in a variety of fields, such as pharmaceutical drug analysis, industry, agriculture, forensic analysis, environmental assessment, and medicine. These sensors do, in fact, have a number of benefits, including ease of design, manufacture, and manipulation; quick reaction time; high selectivity; suitability for turbid and colored solutions; and potential for interface with automated and computerized systems. However, from a medical perspective, the monitoring of therapeutic medications and the detection of pharmaceutical substances in their formulations and biological samples hold significant importance, especially for drugs that have a narrow therapeutic index. Interestingly, one of the most significant electrochemical methods for pharmaceutical drug analysis has been widely used: potentiometric sensors. Moreover, regarding various performance indicators such as sensitivity, specificity, minimal detection threshold, and affordability, potentiometric sensors utilizing ion-selective electrodes (ISEs) surpass other documented methods for analyzing pharmaceutical drugs [4].

Numerous techniques have been used to determine atenolol, including High Performance Liquid Chromatography [5,6] and spectrophotometric methods [7,8]. A voltammetric sensing apparatus utilizing glassy carbon electrodes enhanced with composites of polyarylenephthalide and chiral amino acid complexes of Cu(II) and Zn(II)–glycine-l-alaninate and glycine-l-argininate Cu(II), bis-l-phenylalaninate Zn(II) has been created [9]. A new atenolol ion-sensitive electrode has been developed, characterized, and employed in pharmaceutical evaluations. This electrode features a PVC membrane containing an atenolol-tetrakis(p-chlorophenyl) borate ion-pair complex. A novel atenolol ion-selective sensor has been developed, characterized, and applied in the analysis of pharmaceuticals. This sensor features a PVC membrane integrated with an atenolol-tetrakis(p-chlorophenyl) borate ion-pair complex. The sensor demonstrates a Nernstian response for atenolol, with a slope registered at 56.5 ± 0.8 mV per decade. Furthermore, it displays strong selectivity towards atenolol in the presence of various common inorganic and organic substances. It is functional across a broad pH spectrum ranging from 3.0 to 9.0 [10]. A membrane electrode designed for the drug atenolol

has been developed by integrating the atenolol-phosphotungstate ion within a PVC-coated membrane, using acetophenone as a plasticizing agent. This drug electrode demonstrated Nernstian behavior across a concentration span of 5×10^{-7} – 1×10^{-2} mol.L⁻¹ and exhibited remarkable selectivity, accuracy, and functionality within a pH range of 3.0–6.0. The sensor was characterized by a rapid response time of approximately 8 seconds and a minimal detection threshold of 1×10^{-7} mol.L⁻¹ [11]. In this study, the concentration of atenolol was determined by using a direct method and a standard addition method using coated wire electrodes and coated graphite electrodes, which have a low detection limit and a wide concentration range. It is essential to enhance and create a new system sensor with superior efficiency characteristics compared to earlier models, such as shorter time responses and higher selectivity. The goal of this work was to develop two novel ion-selective electrodes for assessing ATL in pharmaceutical and bulk samples. This was accomplished by using a fabrication electrode with acceptable Nernstian responses to prepare two ion-selective electrodes in straightforward and precise steps.

2. EXPERIMENTAL SECTION

2.1. Chemicals and reagents

The stock solutions were made with deionized water. Tetra hydrofuran (THF) (BDH), phosphotungstic acid (PTA) (BDH), graphite rod (Sony Corporation), *o*-nitro phenyl octyl ether (NPOE) (Fluka), and atenolol (ATL) (SDI, Samara-Iraq) were among the chemical materials used in the work. Local pharmacies provided pharmaceutical samples, such as tablets of Almadet 250 mg.

2.2. Apparatus

Calomel electrode Swiss source, Jenway 3310 pH meter, HANNA Instruments pH meter 211, and JENWAY Hot Plate with Stirrer-Germany.

2.3. Preparation of the ion-pair

50 ml of ATL drug solution at 1.0×10^{-2} mol.L⁻¹ concentration and 50 ml of PTA solution at 1.0×10^{-2} mol.L⁻¹ concentration were combined with stirring to create an ATL-PTA precipitate, which was filtered and repeatedly cleaned with distilled water before being allowed to dehydrate at room temperature [12].

2.4. Preparation of the stock solution of Atenolol

Using a 100 mL volumetric flask, 0.2663 g was dissolved in deionized water to create the ATL drug standard solution at a concentration of 1.0×10^{-2} mole.L⁻¹. The remaining standard solutions (1.0×10^{-2} - 1.0×10^{-8} mol.L⁻¹) were then made by diluting them with deionized water.

2.5. Stock Solutions of Interfering Ions

Solutions of 1.0×10^{-3} mol.L⁻¹ were made by dissolving the proper amounts of KCl, NaCl, MgSO₄, ZnCl₂, FeCl₃, AlCl₃, glucose, and starch in 100 milliliters of deionized water in volumetric flasks.

2.6. Preparation of the Electrodes

2.6.1. Coated Graphite Electrode (CGE)

To fabricate the graphite electrode with a coating, a snug polyethylene tube was utilized to encase a pristine carbon rod that was 5.5 cm long and 8 mm wide. A mixture comprising 60% plasticizing agent *o*-Nitro phenyl octyl ether (NPOE), 30% poly vinyl chloride (PVC), and 10% ion-pair (ATL-PTA) was measured, dissolved in 10 mL of an organic solvent (THF), and stirred for 10 minutes to achieve a uniform blend. Following the immersion of 1 cm of the bare graphite rod five times for 10 seconds each, with pauses of two to three minutes in between, it was permitted to air dry for an hour. Subsequent to dipping the electrode in a 1×10^{-2} M atenolol solution for various durations, the opposite end of the coated carbon rod was linked to a potentiometer recorder through an insulated copper wire [13].

2.6.2. Coated Wire Electrode (CWE)

To produce CWE, copper wire was treated with HNO₃, rinsed with deionized distilled water, dried using acetone, an organic solvent, and then set aside to air dry. The copper wire should measure 8 cm in length and have a diameter of 2 mm, encompassing tight insulation. The wire was left uncoated and bare for 1 cm at both ends. The coating solution, composed of 60% plasticizer *o*-Nitro phenyl octyl ether (NPOE), 30% poly vinyl chloride (PVC), and 10% ion-pair (ATLPTA), was applied to one end of the wire and then allowed to dry naturally after being dissolved in 10 mL of an organic solvent (THF) and stirred for 10 minutes to achieve a uniform mixture. The electrode was subsequently immersed in a 1.0×10^{-2} mol.L⁻¹ ATL solution, and a pH meter was connected to the opposite end of the copper wire [14].

3. RESULTS AND DISCUSSION

3.1. Potentiometric response

To verify that the prepared electrodes are accurate and appropriate probes for determining the various sample concentrations. For every prepared electrode, a Nernstian equation had to be used. As seen in Figures 2 and 3, this was effectively described using the two construction electrodes: the ALT-PTA-NPOE coated graphite electrode and the ATL-PTA-NPOE coated wire electrode. It was evident from the demonstration data that the electrochemical sensors' individual measurements were in various drug forms in order to comply with the IUPAC

recommendation for selective membranes incorporating ion associates under static conditions [15,16].

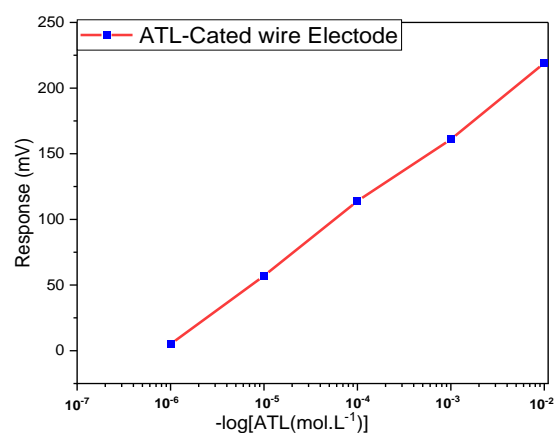


Figure 2. Calibration curves of ATL-PTA-NPOE Coated wire electrode

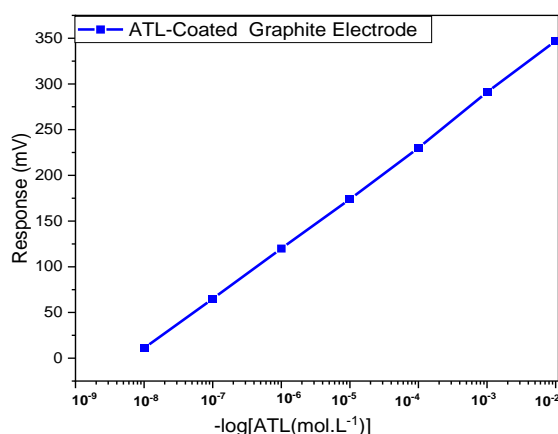


Figure 3. Calibration curves of ATL-PTA-NPOE Coated Graphite electrode

Table 1. The Parameters of ATL-PTA-NPOE Coated wire electrode and ATL-PTA-NPOE Coated Graphite electrode

Parameters	ATL-PTA-NPOE Coated wire electrode	ATL-PTA-NPOE Coated Graphite electrode
Slope (mV.decade ⁻¹)	52.95	56.23
Intercept(mV)	322.80	458.14
Regression equations	$Y = (52.95) \log [\text{ATL}] + 322.80$	$Y = (56.23) \log [\text{ATL}] + 458.14$
Correlations Coefficient(r)	0.9995	0.9998
Range of Conc. (mol.L ⁻¹)	$6.2 \times 10^{-6} - 1.0 \times 10^{-2}$	$4.5 \times 10^{-8} - 1.0 \times 10^{-2}$
LOD (mol.L ⁻¹)	1.8×10^{-6}	1.3×10^{-8}
Range of pH	3.0-7.0	2.5-9.0
Life of time (day)	34	41

The ATL-PTA-NPOE Coated wire electrode and ATL-PTA-NPOE Coated graphite electrode were found to have near-Nernstian slopes of 52.95 and 56.23 mV decade⁻¹, respectively, with the lowest detection limits being 1.8×10^{-6} and 1.3×10^{-8} mol.L⁻¹. The ATL-PTA-NPOE Coated wire electrode had a response time of 38 and 26 seconds, and the ATL-PTA-NPOE Coated graphite electrode had a lifetime of 34 and 41 days. The preparation ATL electrodes' analytical parameters were described. As demonstrated by the data in Table 1, this distinctly demonstrated that the ATL-PTA-NPOE Coated Graphite electrode performed better than the ATL-PTA-NPOE Coated wire electrode.

3.2. Influences of pH

An important consideration in potentiometric reactions is the measurement of proton transfer in electrochemical electrodes. The potentiometric measurements' pH for the ATL-PTA-NPOE coated wire electrode is shown in this section, Graphite electrodes coated with ATL-PTA-NPOE were tested for standard 1×10^{-3} mol.L⁻¹ of ATL solutions in various pH ranges (2.0-8.0). Controlling the optimal series of chemical reagent samples that could be tested was the rationale behind this. The pH samples were treated with solutions of hydrochloric acid or sodium hydroxide at known concentrations. Two groups of pH ranges of 3.0-7.0 and 2.5-9.0 at 1×10^{-3} mol.L⁻¹ ATL reagents were shown by the results in Figure 4. The ATL-PTA-NPOE Coated wire electrode and the ATL-PTA-NPOE Coated graphite electrode were found to have no discernible effects on the probe's performance. Because of the progressive precipitation of the free interim base, the potential measurements for all probes were largely ignored, with negative drift at higher pH, H₃O⁺ molecules had a major effect on the sensor's performance at pH values below 2 [17]. Figure 5 shows the Influences of pH for ATL electrodes.

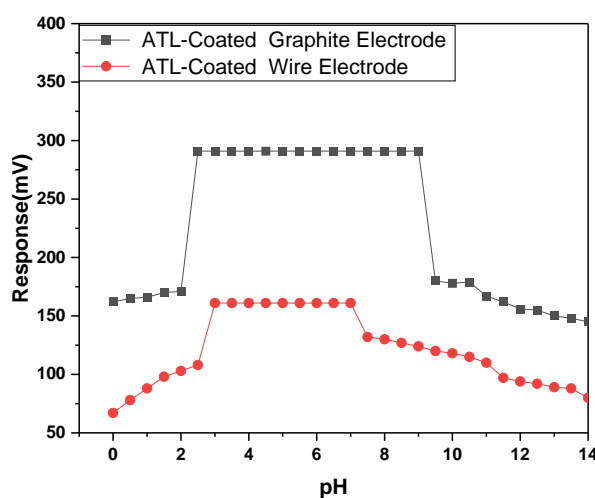


Figure 4. pH values of ATL-PTA-NPOE Coated wire electrode and ATL-PTA-NPOE Coated graphite electrode

3.3. Selectivity

The presence of foreign cations primarily affected the ISEs probes' performances. The matched potential method (MPM) was applied to all constructed probes in the presence of various interfering foreign anions to guarantee that the ion-selective electrodes were precise sensors with trustworthy measurements. When measuring potentiometric selectivity coefficients, the MPM is primarily helpful in avoiding the drawbacks of the corresponding methods that rely on the Nicolsky–Eisenman equation. [18-20]. These restrictions include the inequality of charges of any primary interfering ion and non-Nernstian functions of interfering ions. The variations in the ions' size, permeability, and mobility were unaffected by the inorganic cations. Selectivity coefficient values based on measured potential values generated at the tops of the peaks in the same drug concentrations governed the conditional factors. Table 2 shows that all electrodes reported good agreement performances with indicated and negligible interferences, and the majority of foreign cations displayed slight values for the selectivity coefficient.

Table 2. The Values of selectivity coefficient for ATL-PTA-NPOE Coated Graphite electrode and ATL-PTA- NPOE Coated Wire electrode

Ion interference	ATL-PTA-NPOE Coated Wire electrode	ATL-PTA-NPOE Coated Graphite electrode
K ⁺	2.38106×10^{-3}	4.09354×10^{-1}
Na ⁺	5.66945×10^{-2}	2.40794×10^{-2}
Mg ²⁺	7.70464×10^{-2}	4.68039×10^{-4}
Zn ²⁺	5.31721×10^{-3}	6.23406×10^{-4}
Al ³⁺	7.20916×10^{-3}	7.37824×10^{-3}
Fe ³⁺	1.20955×10^{-4}	7.08221×10^{-5}
Glucose	2.70109×10^{-3}	3.84992×10^{-4}
Starch	2.47609×10^{-3}	3.01125×10^{-4}

3.4. Potentiometric Analysis

Another study was carried out using potentiometric measurements of ATL in pure form and tablets in order to make sure that the current method is applicable in various sample types in the same way and with constructed electrodes. As indicated in Table 3, various samples were subjected to the direct, standard addition method. The suggested method was used to analyze atenolol tablets (250 mg) in pharmaceutical dosage forms; Table 4 shows the outcomes of the two approaches.

Table 3. The Statistical treatment of data for the determination of ATL in bulk and pharmaceutical preparations by direct method for ATL-PTA-NPOE Coated wire electrode and ATL-PTA-NPOE Coated graphite electrode

Samples	ATL-PTA-NPOE Coated wire electrode			ATL-PTA-NPOE Coated graphite electrode		
	Taken ATL (mol.L ⁻¹)	Found ATL (mol.L ⁻¹)	%Rec	Taken ATL (mol.L ⁻¹)	Found ATL (mol.L ⁻¹)	%Rec
Pure Drug	6.0	5.88	98.00	8.0	7.99	99.87
	5.0	4.76	95.20	7.0	6.96	99.42
	4.0	3.93	98.25	6.0	5.98	99.66
	3.0	2.97	99.00	5.0	4.90	98.00
	2.0	1.96	98.00	4.0	3.89	97.25
				3.0	2.93	97.66
			2.0	1.96	98.00	
%Mean±SD	97.69±0.72			98.55±1.13		
N	5			7		
%RSD	0.74			1.15		
%RE	-2.31			-1.45		
Aldomet 250/ mg	Taken ATL(mol.L ⁻¹)	Found ATL(mol.L ⁻¹)	%Rec	Taken ATL(mol.L ⁻¹)	Found ATL(mol.L ⁻¹)	%Re
	6.0	5.93	98.83	8.0	7.93	99.12
	5.0	4.77	95.40	7.0	6.95	99.28
	4.0	3.44	98.50	6.0	5.91	98.50
	3.0	2.95	98.33	5.0	4.73	94.00
	2.0	1.99	99.50	4.0	3.91	97.75
				3.0	2.97	99.00
				2.0	1.95	97.50
%Mean±SD	98.01±0.89			97.87±1.1		
N	5			7		
%RSD	0.90			1.17		
%RE	-1.98			-2.13		

Table 4. The Statistical treatment of data for the determination of ATL in bulk and pharmaceutical preparations by the standard addition method for ATL-PTA-NPOE Coated wire electrode and ATL-PTA-NPOE Coated graphite electrode

Samples	ATL-PTA-NPOE Coated wire electrode			ATL-PTA-NPOE Coated graphite electrode		
	Taken ATL (mol.L ⁻¹)	Found ATL (mol.L ⁻¹)	%Rec	Taken ATL (mol.L ⁻¹)	Found ATL (mol.L ⁻¹)	%Rec
Pure Drug	3.0	2.92	97.43	3.0	2.98	99.33
		2.99	99.90		2.97	99.00
		2.98	99.50		2.98	99.33
		2.99	99.83		2.98	99.33
		2.99	99.98		2.96	98.66
%Mean±SD	99.32±0.87			98.17±0.79		
N	5			5		
%RSD	0.87			0.80		
%RE	-0.68			-1.82		
Aldomet 250/ mg	Taken ATL (mol.L ⁻¹)	Found ATL (mol.L ⁻¹)	%Rec	Taken ATL (mol.L ⁻¹)	Found ATL (mol.L ⁻¹)	%Re
	3.0	2.92	97.33	3.0	2.98	98.78
		2.92	97.33		2.97	97.71
		2.99	99.66		2.98	98.78
		2.97	99.00		2.98	98.85
		2.99	99.96		2.99	99.46
%Mean±SD	98.65±0.88			98.71±0.31		
N	5			5		
%RSD	0.89			0.31		
%RE	-1.35			-1.28		

There were no appreciable variations in accuracy or reproducibility in the computation of the ATL recovery and concentration (found). It was previously demonstrated that the standard addition method produced the best results with the fewest errors for various samples. In contrast to the response to ATL, which recorded a wider pH range of roughly 2.5-9.0, the electrode displayed a minimal response to all the species tested. In certain unique situations, this might enhance the use of atenolol-coated electrodes.

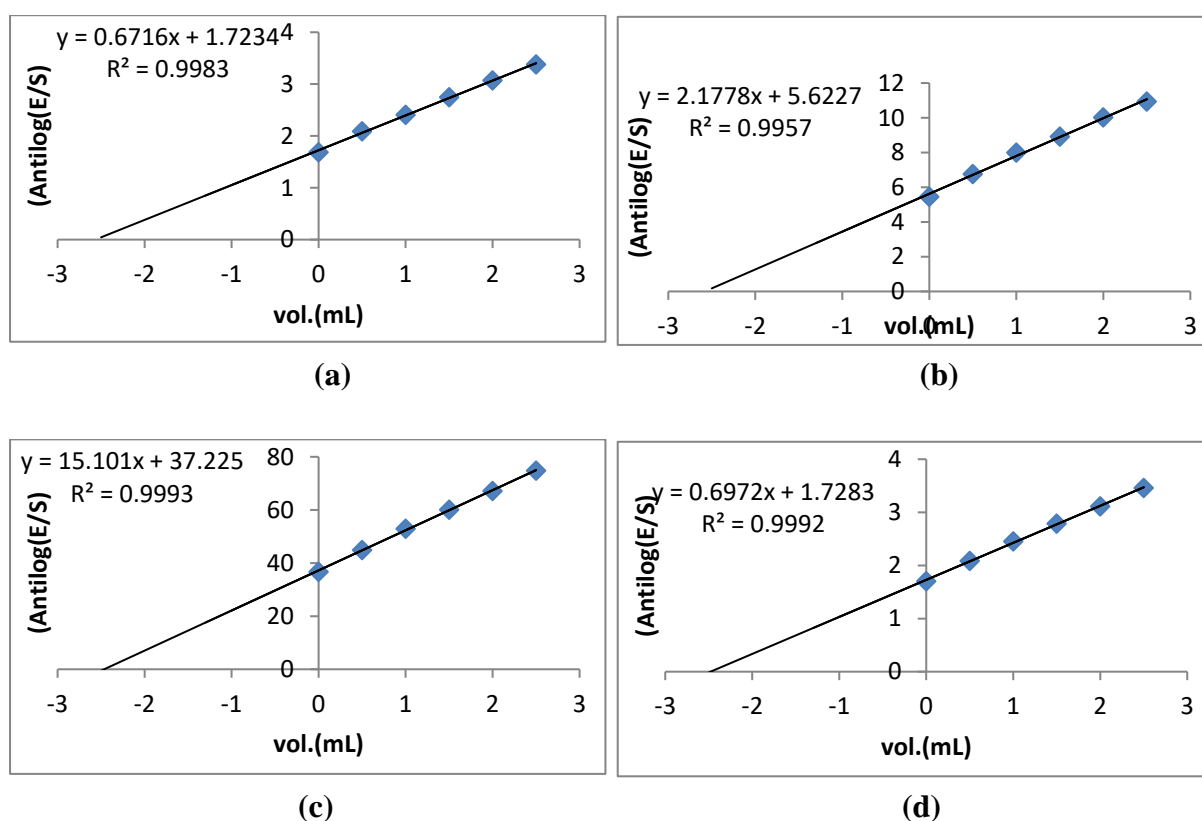


Figure 5. **a** and **b** Antilog (E/S) of ATL-PTA-NPOE coated wire electrode at $1.0 \times 10^{-3} \text{ mol.L}^{-1}$ for pure form of atenolol and for pharmaceutical form of atenolol, **c** and **d** Antilog (E/S) of ATL-PTA-NPOE Coated graphite electrode at $1.0 \times 10^{-3} \text{ mol.L}^{-1}$ for pure form of Atenolol and for pharmaceutical form of Atenolol.

The new technique has been demonstrated to be highly accurate and successfully applied to pharmaceutical preparation of Aldomet 250/mg, as shown in Tables 2 and 3 with Figure 5.

4. CONCLUSION

The creation, verification, and use of two new ATL-PTA-NPOE Coated wire electrodes and ATL-PTA-NPOE Coated graphite electrodes were detailed in this study. Phosphotungstic acid was used as an elector of atenolol (ATL) in pharmaceuticals. ATL was successfully quantified in the current study in quantities with a broad linear range in a highly selective and

accurate manner. Low detection limits and good agreement values were displayed by the Nernstian response. Using all built-in sensors, the pH test yielded a broad range of roughly 2.0 to 9.0. This might be helpful, indicating the benefits of using electrodes to confirm pharmaceutical samples in direct measurements, like those in ATL medications.

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Declarations of interest

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

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