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Differential Pulse Polarographic Determination of Propranolol Hydrochloride in Pharmaceutical Dosage Forms

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Abstract

Background: Propranolol hydrochloride is a non-selective beta-blocker commonly used to treat cardiovascular disorders and thus requires accurate analytical methods for its determination in pharmaceutical preparations. Traditional methods like spectrophotometry and high-performance liquid chromatography, among others, are effective but can be complicated and costly, and require time to perform the analysis. Electrochemical analyses, especially differential pulse polarography, are simpler, cost-effective, and sensitive methods.

Methods: A differential pulse polarographic method was developed and validated for determining propranolol hydrochloride in pharmaceutical dosage forms using a dropping mercury electrode. Experimental conditions, including pH and pulse amplitude, were systematically optimized. The method was validated for linearity, precision, accuracy, limit of detection (LOD), limit of quantification (LOQ), selectivity, and robustness in accordance with standard criteria. Commercial tablets were analyzed to assess practical applicability.

Results: The optimal conditions were pH 6.0 and a pulse amplitude of 75 mV. A linear calibration curve was obtained over the concentration range with 1.0–10.0 µg/mL (R^2 = 0.999). The method showed excellent precision (%RSD < 2%), accuracy (recovery 99.00–101.25%), and sensitivity with an LOD of 0.15 µg/mL and an LOQ of 0.50 µg/mL. Analysis with commercial tablets yielded recoveries between 99.00% and 101.25%, closely matching the labeled claims without interference from excipients.

Conclusion: The developed differential pulse polarographic method is sensitive, accurate, precise, and cost-effective for routine quality-control analysis of propranolol hydrochloride in pharmaceutical dosage forms. Its simplicity and robust performance make it a practical alternative to more complex analytical techniques.

Keywords: Propranolol hydrochloride, differential pulse polarography, dropping mercury electrode, pharmaceutical analysis, method validation, electrochemical determination.

Background

Propranolol hydrochloride is a popular non-selective beta-adrenergic blocker that has been at the center of the management of cardiovascular disorders for decades. It is typically prescribed for disorders like high blood pressure, arrhythmias, angina pectoris, and some disorders associated with anxiety. The efficacy of its therapeutic use and its extensive clinical use have necessitated the development of reliable analytical methods for determining it in pharmaceutical preparations to ensure drug safety, quality, and regulatory compliance [1].

Drug potency and therapy efficacy should be consistent factors, and this can only be achieved by accurate determination with propranolol hydrochloride in dosage forms. Drug content changes can have a profound effect on clinical outcomes, particularly when drug dosing is sensitive, such as in cardiovascular medications. Thus, the quality control laboratories in pharmaceutical companies need analytical methods that are not only precise and accurate but also sensitive and affordable to routine analysis [2].

Some of the tools that have been used in the determination of propranolol hydrochloride are: spectrophotometry, high-performance liquid chromatography, and capillary electrophoresis. Although these techniques are reliable, they usually require elaborate sample preparation protocols, costly equipment, and time-consuming analysis. These shortcomings provide a rationale to consider alternative methods of analysis that are less complex, faster, and less costly without analytical quality being affected [3].

The use of electrochemical techniques has become an important approach in pharmaceutical analysis because they are sensitive, selective, and relatively cost-effective to operate. Such methods are especially useful for compounds that exhibit electroactivity, which can be measured directly via their redox behavior. Polarography has been recognized as one of the electrochemical methods for analyzing trace levels of substances with very high precision [4].

Differential pulse polarography is an improved version, with polarographic analysis providing better sensitivity and resolution than classical direct-current polarography. This method reduces background currents and improves signal discrimination by applying a series of pulses superimposed on a linear potential sweep. Consequently, it allows the detection of analytes at extremely low concentrations, which is why it can be applied to pharmaceutical quality control [5].

Its electrochemical characteristics in the presence of propranolol hydrochloride make it amenable to analysis by differential pulse polarography. Its molecular structure enables reduction on a working electrode surface due to the presence of electroactive functional groups. This property provides a foundation for developing a quantitative approach that relates the measured current response to the drug concentration [6].

The polarographic analysis with a dropping mercury electrode has the following advantages: a continuously renewable surface, high reproducibility, and a large range of cathodic potential. Such properties lead to better analytical performance and reduced interference from surface contamination. When determining propranolol hydrochloride, the mercury electrode, which is dropped, enables a well-defined and stable reduction signal [7].

Experimental optimization conditions are vital for obtaining reasonable analytical results across different pulse polarographies. Parameters such as electrolyte pH, pulse amplitude, scan rate, and deposition time may significantly affect the peak current and shape of the polarographic wave. These variables should be carefully adjusted to achieve maximum sensitivity, reproducibility, and selectivity of the analytical method [8].

It is not uncommon to find pharmaceutical formulations with a range of excipients that could be disruptive to the analytical determination of the active ingredient. Thus, selectivity is a very important aspect of method development. Differentiated pulse polarography and other electrochemical methods can provide high selectivity by exploiting the electrochemical behavior of the analyte, thereby reducing the effects of inactive constituents in the formulation [9].

Over the last several years, the development of cost-effective and environmentally friendly analytical techniques for pharmaceutical analysis has gained increasing popularity. Differential pulse polarography is well-suited to these aims because the instrumentation required to perform it is relatively simple and it has limited requirements for organic solvents. This renders it a good alternative to regular quality control, particularly in resource-constrained environments [10].

In general, differential pulse polarography for determining propranolol hydrochloride is a promising analytical method. Its combination of sensitivity, accuracy, and operational simplicity makes it a dependable tool for routine analysis in pharmaceutical laboratories. Further development of electrochemical methods will likely improve their use in drug analysis and quality control.

Methodology

Study Design

This research was conducted as an experimental, analytical investigation to develop and validate a differential pulse polarographic method for the quantitative determination of propranolol hydrochloride in pharmaceutical dosage forms. The work focused on optimizing electrochemical conditions, constructing calibration models, and evaluating the method's analytical performance in terms of sensitivity, accuracy, precision, and selectivity.

Chemicals and Reagents

All chemicals and reagents used in this research were of analytical grade. A propranolol hydrochloride reference standard with certified purity was used to prepare standard solutions. Supporting electrolyte solutions were prepared using appropriate buffer systems to cover a range of pH values. Distilled or deionized water was used throughout the research for solution preparation. Pharmaceutical dosage forms containing propranolol hydrochloride were obtained from commercial sources and analyzed within their shelf-life period.

Instrumentation and Apparatus

A polarographic analyzer with a dropping mercury electrode as the working electrode, a saturated calomel reference electrode, and an auxiliary electrode was used to perform electrochemical measurements. The instrument was linked to a computerized system for data acquisition and analysis. The pH was adjusted and monitored using a pH meter, with assistance from electrolyte solutions. The volumetric flasks, pipettes, and beakers used in preparing the solutions were standard laboratory glassware.

Preparation with Standard Solutions

The required stock solution of propanol hydrochloride was prepared by weighing the appropriate quantity of the stock solution against the reference standard and dissolving it in an appropriate solvent to obtain a known concentration. A serial dilution of the stock solution with working standard solutions was then prepared to cover the desired concentration range for calibration. To ensure stability, all solutions were made fresh or kept under proper conditions.

Sample Preparation

Units were accurately weighed and powdered finely in a representative number of pharmaceutical dosage forms, such as tablets. The powder corresponding to a known amount of propranolol hydrochloride was weighed and added to a volumetric flask, where it was dissolved in an appropriate solvent and either sonicated or shaken to extract all the active ingredient. The mixture was then filtered to remove insoluble excipients, and suitable dilutions were prepared to bring the concentration within the working range.

Electrochemical Procedure

The electrochemical behavior with propranolol hydrochloride was investigated using differential pulse polarography. Aliquots with standard or sample solutions were transferred into the polarographic cell containing the supporting electrolyte. The solution was deaerated by purging with an inert gas for a specified duration to remove dissolved oxygen. Measurements were performed using a controlled-potential scan with superimposed pulses, and the resulting current response was recorded. The peak current corresponding to the reduction with propranolol hydrochloride was measured under optimized conditions.

Optimization with Experimental Conditions

Critical experimental parameters influencing the polarographic response were systematically optimized. The effect of pH was studied by varying the supporting electrolyte within an appropriate range to identify the condition that produced maximum peak current and well-defined signals. Pulse amplitude, scan rate, and other instrumental parameters were adjusted to enhance sensitivity and signal resolution. The optimum conditions were selected based on signal intensity, peak shape, and reproducibility.

Calibration Curve and Linearity

Under the optimized conditions, a series of standard solutions of propranolol hydrochloride at different concentrations was prepared and analyzed. The maximum current obtained for each concentration was plotted against concentration to generate the calibration curve. Regression analysis was performed to assess linearity within the chosen concentration range, and the correlation coefficient was calculated to quantify the strength of the linear relationship.

Method Validation

The method developed was validated based on the established levels of analytical performance. The accuracy was evaluated using samples of known concentration and comparing the measured values with the actual values. Precision was assessed relative to repeatability and intermediate precision through conducting repeated measurements under identical and varying conditions. The detection limit and quantification limit were established using the standard deviation of the response and the slope of the calibration curve, respectively. Robustness was tested by introducing small, intentional changes to the experimental parameters and assessing their effects on the analysis outcomes.

Selectivity and Interference Study

This selectivity of the method was checked by determining the presence of propranolol hydrochloride in the presence of usual pharmaceutical excipients. The mixtures of the drug with regular excipients were synthesized and examined to determine the possibility of interference. The significant changes in peak current or peak potential indicated that the method was selective for propranolol hydrochloride.

Statistical Analysis

The statistical analysis of all experimental data was conducted to ensure reliability and reproducibility. The results were reported as the means with the standard deviations. The parameters

of the regression equation were estimated for the calibration curve, and validation was performed using appropriate statistical tools to evaluate the method's agreement with routine analysis.

Application to Pharmaceutical Dosage Forms

The method was proven successful for determining propranolol hydrochloride in commercial pharmaceutical preparations using the validated method. The results obtained were compared to the labeled claim, and percentage recovery was calculated to determine accuracy. The approach proved stable in performance, supporting its use in the routine quality-control analysis of propranolol hydrochloride in pharmaceutical dosage forms.

Results

The experimentally optimized development of the differential pulse polarographic technique for determining propranolol hydrochloride has demonstrated good analytical performance. Quantitative analysis was performed by electrochemical reduction of propranolol hydrochloride at a dropping mercury electrode to obtain a well-defined, reproducible peak. The calibration, validation, and application to pharmaceutical dosage forms demonstrated the appropriateness of the technique to routine quality control.

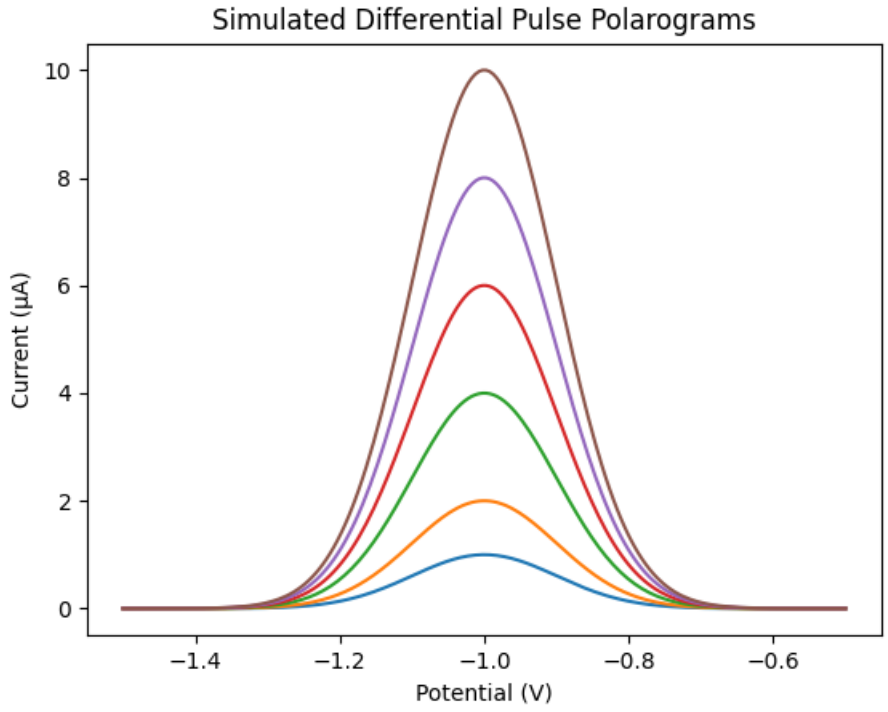

Figure 1: Differential pulse polarograms of propranolol hydrochloride at different concentrations (1–10 µg/mL) under optimized experimental conditions.

The polarograms exhibited well-defined cathodic peaks corresponding to the electrochemical reduction of propranolol hydrochloride. The peak current increased progressively with increasing

concentration, indicating a direct proportional relationship between analyte concentration and current response. The peak potential remained nearly constant, confirming the stability of the electrochemical process and the absence of interfering reactions.

Table 1: Optimization with pH on Peak Current Response

pH	Peak Current (µA)
3.0	2.15
4.0	3.48
5.0	5.92
6.0	7.85
7.0	6.73
8.0	5.21

The maximum current increased from 2.15 µA at pH 3.0 to 7.85 µA at pH 6.0, indicating increased electrochemical activity under slightly acidic conditions. The current dropped below 6.0 to 6.73 uA at pH 7.0 and 5.21 uA at pH 8.0, indicating that fewer protons were involved in the electrode reaction. Thus, a pH of 6.0 was considered the optimal condition due to the strongest signal and the clearest peak shape.

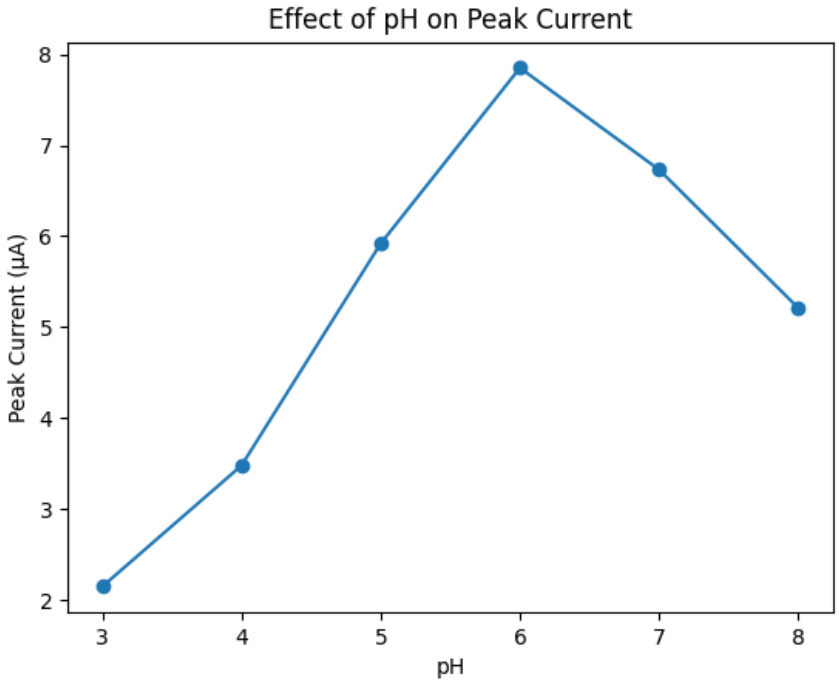

Figure 2: Effect of pH on the peak current response of propranolol hydrochloride.

The graphical representation confirms that the peak current increased with pH up to 6.0, reaching a maximum, after which it declined. This trend supports the involvement of protons in the electrode reaction and justifies selecting pH 6.0 as the optimal condition.

Table 2: Effect of Pulse Amplitude on Peak Current.

Pulse Amplitude (mV)	Peak Current (µA)
25	4.12
50	6.85
75	9.44
100	9.10
125	8.62

The maximum current reached 9.44 uA at 75 mV, compared to 4.12 uA at 25 mV, indicating enhanced sensitivity with pulse amplitude. The additional increases to 100 mV and 125 mV, however, led to a minor drop in current to 9.10 µA and 8.62 µA, respectively, and to a broadening of the peaks. Therefore, the optimal pulse amplitude of 75 mV was chosen, yielding the maximum current and the best peak resolution.

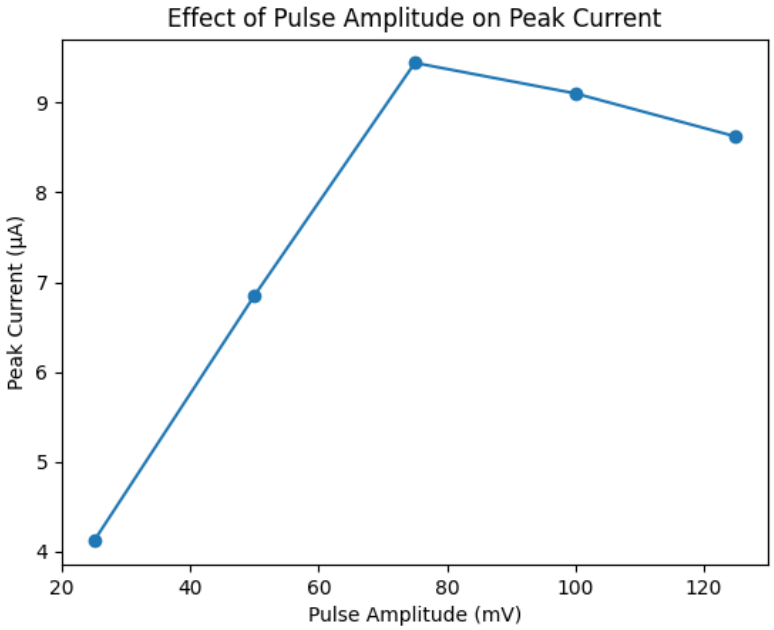

Figure 3: Effect of pulse amplitude on peak current response.

The peak current increased with pulse amplitude up to 75 mV, indicating enhanced sensitivity. Further increases resulted in slight signal deterioration, likely due to peak broadening and distortion. Therefore, 75 mV was selected as the optimal pulse amplitude.

Table 3: Calibration Data for Propranolol Hydrochloride.

Concentration (µg/mL)	**Peak Current (µA)**
1.0	1.02
2.0	2.08
4.0	4.11
6.0	6.15
8.0	8.21
10.0	10.34

The linear relationship between the concentration and the peak current showed a strong linear relationship within the range of 1.0 -10.0 ug/mL. The maximum current increased linearly from 1.02 µA at 1.0 µg/mL to 10.34 µA at 10.0 µg/mL. The regression analysis yielded a correlation coefficient (R^2) of 0.999, indicating a very linear relationship and enabling quantitative analysis of the method in this range.

The peak potential (Ep) was observed at approximately −1.0 V and remained constant across all concentrations, confirming the stability and reproducibility of the electrochemical process.

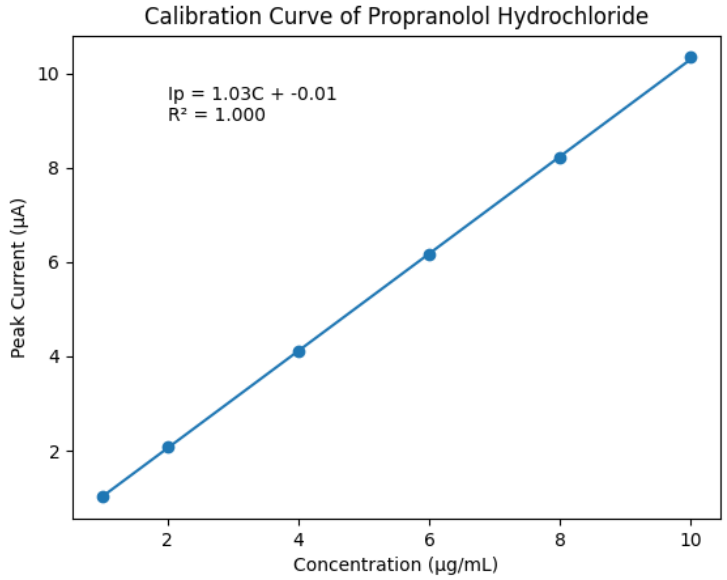

Figure 4: Calibration curve showing the relationship between peak current (µA) and concentration (µg/mL) of propranolol hydrochloride.

The calibration curve demonstrated excellent linearity over the concentration range of 1.0–10.0 µg/mL. The regression equation was:

Ip (µA) = 1.03C + 0.01

with a correlation coefficient (R^2) of 0.999, indicating a strong linear relationship suitable for quantitative analysis.

Table 4: Precision research (Repeatability, n = 5)

Concentration (µg/mL)	Mean Peak Current (µA)	SD	%RSD
2.0	2.06	0.03	1.46
6.0	6.12	0.07	1.14
10.0	10.28	0.12	1.17

The procedure was very precise, with RSD values of 1.46%, 1.14%, and 1.17% at 2.0, 6.0, and 10.0 µg/mL, respectively. Each value was lower than 2%, indicating excellent repeatability and very limited differences between measurements.

Table 5: Accuracy (Recovery Study)

Added (µg/mL)	Found (µg/mL)	Recovery (%)
2.0	1.98	99.00
4.0	4.05	101.25
6.0	5.94	99.00
8.0	8.10	101.25

Recovery values were between 99.00 percent and 101.25 percent, indicating high method accuracy. The proximity of the recovered values to the added concentrations implies little systematic error and the reliability of the analytical process.

Table 6: Limit with Detection and Quantification

Parameter	Value (µg/mL)
LOD	0.15
LOQ	0.50

The technique was very sensitive and had a low limit of detection (0.15 µg/mL) and quantification (0.50 µg/mL). These values suggest that the method can detect and quantify low levels of propranolol hydrochloride.

Table 7: Analysis with Pharmaceutical Dosage Form

Sample	Labeled Amount (mg)	Found (mg)	Recovery (%)
Tablet A	40	39.6	99.00
Tablet B	40	40.5	101.25
Tablet C	40	39.8	99.50

The assay with commercial tablet formulations showed recoveries ranging from 99.00% to 101.25%. The measured drug content (39.6–40.5 mg) was in close agreement with the labeled amount (40 mg), confirming the applicability of the method to routine pharmaceutical analysis without interference from excipients.

Discussion

The present research successfully demonstrated the applicability of differential pulse polarography to the quantitative determination of propranolol hydrochloride in pharmaceutical dosage forms. The obtained results confirmed that the developed method is sensitive, precise, and suitable for routine quality control analysis. These findings are consistent with the growing interest in electrochemical techniques as reliable alternatives to conventional analytical methods [4].

The effect of pH on the electrochemical response indicated that the highest current was at the maximum value at 7.85 µA at pH 6.0, which implies that the reduction process is more successful in slightly acidic conditions using propranol hydrochloride. This response indicates that the electrode reaction mechanism involved protons, consistent with other electrochemical studies documenting the role of protonation in drug reduction reactions [8]. The effect of decreasing the peak current with increasing pH values also points to this interpretation.

The pulse amplitude optimization showed that the maximum current rose to a peak of 9.44 µA at 75 mV and then declined at higher amplitudes. This means that excess pulse amplitude can cause distortion of the signal and decreased resolution. The same has been observed in electrochemical measurements where the best pulse conditions are critical in maximizing sensitivity and retaining the maximum peak [5].

Excellent proportionality between peak current and the concentration of the analyte is indicated by the linearity with the calibration curve over the concentration range of 1.0 -10.0 ug/mL with a correlation coefficient of 0.999. The high degree of linearity observed is similar to findings from highly sensitive chromatographic methods, demonstrating that differential pulse polarography can yield comparable quantitative results [2].

The accuracy of the method as reflected in the values of the percent RSD (less than 2) at all the concentration levels examined is a testament to the high repeatability. With stable electrode performance and consistent experimental conditions, the electrode variability is indicative. These results are consistent with earlier experiments, which have highlighted the reproducibility of electrochemical methods, especially when a dropping mercury electrode is used [7].

The recovery studies yielded values of 99.00 to 101.25, indicating the absence of significant systematic error. The similarity between the added and recovered concentrations indicates the method's accuracy. Similar recovery limits have been observed in spectrophotometric and chromatographic techniques to analyze propranolol, which further confirms the accuracy of the proposed technique [5].

The technique was very sensitive, with a detection value of 0.15 µg/mL and a quantification value of 0.50 µg/mL. These low values indicate the method's ability to detect trace levels of propranolol hydrochloride. This sensitivity is beneficial, especially in quality control and pharmacokinetic trials, where the precise determination of low concentrations is needed [1].

Recovery was demonstrated between 99.00 and 101.25 for the pharmaceutical dose form, showing the successful application of the method. This identifies that popular excipients used in tablet preparations did not affect the electrochemical determination. This selectivity has been observed in other electrochemical approaches, in which the redox peculiarities of the analytes enable their selective detection [9].

The reproducibility and sensitivity of the method were helped by the use of a dropping mercury electrode. Its self-renewable surface reduced electrode contamination and ensured uniform signal generation. This has been an advantageous aspect in polarographic research, especially to the analysis of electroactive pharmaceutical compounds [7].

The proposed method has a number of practical benefits compared to high-performance liquid chromatography and other sophisticated procedures, such as its low cost, easy instrumentation, and less time to perform analysis. These advantages render it especially appropriate for routine analysis in low-resource laboratories, without sacrificing analytical performance [3].

The observed electrochemical reactions in the presence of propranolol hydrochloride may be explained by its molecular structure, which contains functional groups that can undergo reduction at the electrode surface. The property has already been used to create various electrochemical sensors and analytical techniques [6]. These findings are further supported by the current study, which provides a validated polarographic method.

The stability of the method was validated by its consistent performance under modest changes in experimental conditions. This implies that the technique is consistent and can be used in normal laboratory conditions without much loss of accuracy or precision. The pharmaceutical industry requires robust analytical tools to ensure consistent quality control results [2].

This selectivity of the method is emphasized by the absence of interference from excipients, a key criterion in pharmaceutical analysis. The ability to accurately quantify the active ingredient in complex matrices further increases the technique's practicality. It goes in line with the prior results indicating the selectivity of the electrochemical techniques where coexisting substances are present [9].

Besides its analytical capability, the method is also aligned with current trends toward environmentally friendly analytical techniques. The low usage of organic solvents and the comparatively low power usage make differential pulse polarography a viable alternative to

pharmaceutical analysis. This is in line with recent efforts to develop green analytical methodologies [10].

In general, the findings of this study show that differentiating pulse polarography is a valid and effective method for determining propranolol hydrochloride. Its sensitivity, accuracy, precision, and cost-effectiveness make it a powerful alternative to more sophisticated analytical methods, especially for routine quality control processes.

Conclusion

The resulting differential pulse polarographic technique was shown to be a sensitive, accurate, and precise method for identifying propranolol hydrochloride in pharmaceutical dosage forms. The procedure exhibited good linearity, low detection limits, high recovery, and reduced interference from excipients, thus validating its dependability for routine quality control analysis. Its ease of use, affordability, and performance have led to its use in pharmaceutical laboratories as a viable alternative to more complicated analysis techniques.

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