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Determination of Irbesartan in Pharmaceutical Preparations by Polarographic Methods

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Abstract: In this study, the polarographic behavior of irbesartan was investigated using the cyclic polarographic method. A mercury drop electrode was used to quantify the peak currents in comparison to Ag/AgCl at 0.10 V/s. Additionally, quick and easy square wave and differential pulse polarographic methods were developed and validated to determine irbesartan in pharmaceutical preparations. For both methods, the calibration curves were linear at concentrations between 5 and 70 µg/mL. The precision was given by relative standard deviation and was less than 2.61%. Accuracy was given with relative error and did not exceed 1.24%. The suggested methods are extremely accurate and precise. No interference was found under the chosen experimental conditions. In pharmaceutical preparations, irbesartan had an average recovery of 99.8%. Therefore, the methods are applicable to the determination of irbesartan in pharmaceutical preparations.

Keywords: Irbesartan, Polarography, Validation, Tablet.

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1. INTRODUCTION

Cardiovascular disease is responsible for 17.9 million annual deaths, or about 30% of all fatalities globally (1). At least 45% of heart disease deaths can be attributed to hypertension. Numerous medications, such as beta-blockers, diuretics, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and calcium channel blockers, have been used to treat hypertension (2). Irbesartan (Figure 1) is a medication that lowers blood pressure (3). In the past, it was also used to treat chronic renal failure, congestive heart failure, and hypertension.

Several analytical techniques, such as UV-spectrophotometry (4-10), spectrofluorimetry (11), capillary electrophoresis (12), LC-MS (13-16), and HPLC (17-25), have been reported for the detection of irbesartan.

When using these techniques, various issues arise. Methods for measuring spectrum have poor sensitivity. Chromatographic techniques necessitate derivatization or drawn-out extraction processes, and they are generally sluggish and expensive.

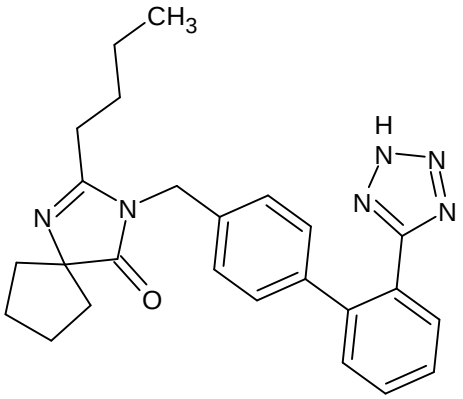

Figure 1: Chemical structure of irbesartan.

Bozal et al. (26) has reported voltammetric methods with differential pulse (DP) and square wave (SW) for the analysis of irbesartan in the pharmaceutical tablet formulations and in human serum samples. The calibration curve of voltammetric methods was linear for irbesartan in the range 8×10^{-6}-1×10^{-4} M. Intra- and inter-day precision values were lower than 1.72%. The minimum and maximum recovery of irbesartan was 95.02 and 99.21%, respectively.

The LOQ values of methods were found as 2.56×10^{-6} and 2.01×10^{-6}. In addition, validation parameters, such as accuracy, reproducibility and recovery were evaluated.

As a result, using simpler, quicker, and less expensive electrochemical techniques that are nonetheless sensitive can be thought of as a beneficial alternative. Comparing the polarographic approaches to many other analytical methods, several advantages are apparent. The spectrum of viable applications for polarography has expanded thanks to advancements in pulse techniques that make it possible to identify electroactive substances even at low concentrations. The polarographic processes have a number of benefits over chromatography, including low cost and a quick turnaround time for analysis. As opposed to HPLC, which frequently can disturb equilibria in the reaction mixture, electroanalytical approaches are significantly more useful for kinetic and equilibria research.

It is crucial to develope a new technique for figuring out how much medication is present in pharmaceutical solutions or biological fluids. With the advantages that, in the majority of cases, derivatization is not required and that these techniques are less sensitive to matrix effects than other analytical techniques, a wide range of pharmacological compounds have been determined using electroanalytical techniques. The identification of electrode mechanism is another electrochemistry application. Drugs' redox characteristics can provide information about their pharmacological efficacy, in vivo redox activities, or metabolic destiny. Despite the analytical significance of irbesartan's electrochemical behavior and reduction process, no research on the polarographic analysis of its electrochemical reduction in pharmaceuticals has been published.

Therefore, this work introduced novel polarographic techniques that allow for the direct detection of irbesartan in pharmaceutical preparations without the need for time-consuming extraction or evaporation steps before drug analysis. This article covers square wave (SW) and differential pulse (DP) polarography at mercury drop electrode as completely proven, quick, simple, and effective methods for irbesartan detection.

2. EXPERIMENTAL SECTION

2.1. Chemicals

Irbesartan was purchased from Sigma-Aldrich in Germany. We bought Karvea tablets at the neighborhood pharmacy in Erzurum, Turkey.

2.2. Electrochemical Instrumentation

On a Gamry Potentiostat Interface 1000, electrochemical experiments were conducted. A platinum-wire auxiliary electrode, a mercury drop working electrode (area of HMDE 0.026 cm^2) and an Ag/AgCl (KCl, 3M) electrode acting as the reference electrode were selected for the three electrode cell arrangement. The pulse width is 50 ms, the scan rate is 20 mV/s, drop size 0.38 mm^2, the amplitude of the square wave pulse is 25 mV, and the amplitude of the differential pulse is 50 mV. These parameters are used for analytical applications.

2.3. Preparation of Standard Solutions

Irbesartan (100 µg/mL) stock standard solution was made in 0.5 M sulfuric acid. This stock solution was used to build working standard solutions. The concentration of the standard solutions was 5, 10, 20, 30, 40, 50, 60 and 70 µg/mL. 7.5, 37.5, and 67.5 µg/mL were the concentrations at which the QC solutions were obtained.

2.4. Statistical Analysis

With the use of a computer program, SPSS 15.0 was used for the statistical analyses. The irbesartan standard line and calculations were made using regression analyses. The results' mean and standard deviation were given.

3. RESULTS AND DISCUSSION

3.1. Development and Optimization of the Method

At the mercury drop electrode, the electrochemical behavior of irbesartan was studied. The supporting electrolyte for the cyclic voltammetric technique was 0.5 M sulfuric acid. A typical cyclic voltammograms for 100 µg/mL irbesartan at 0.1 V/s scan rate are shown in Figure 2. At -1.055 V, the decrease peak was observed in the cathodic sweep.

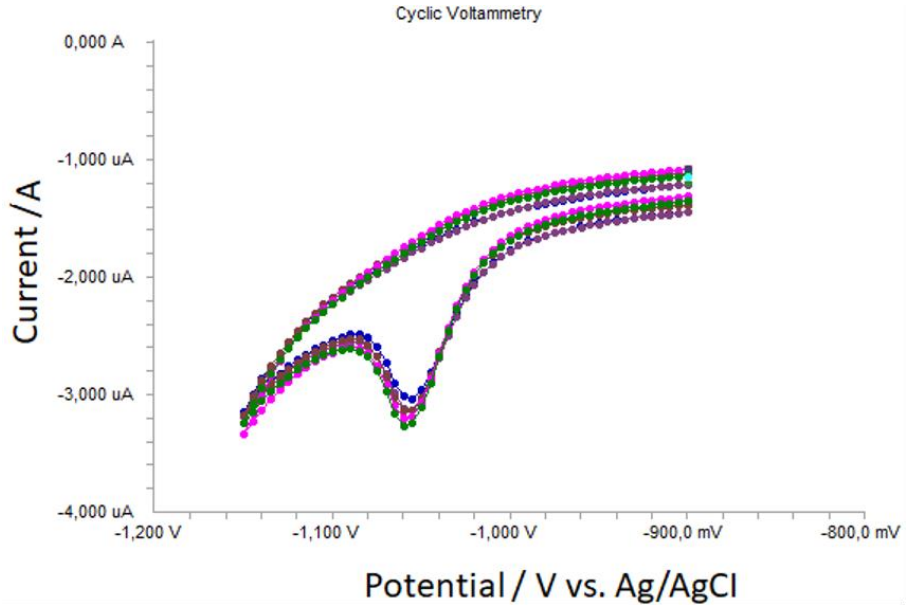

Figure 2: Cyclic voltammograms of 100 µg/mL irbesartan solution.

Moreover, research was done on how scan rate affected cathodic peak currents and peak potentials within the potential scan rate range of 0.005-1.0 V/s. Figure 3 shows the 20 µg/mL irbesartan linear sweep voltammograms as a function of scan rate.

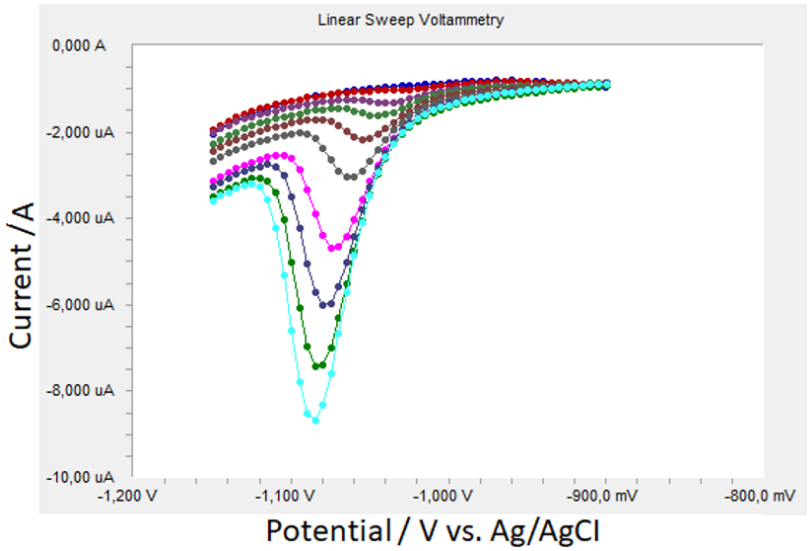

Figure 3: Linear sweep voltammograms of 20 µg/mL irbesartan as a function of scan rate.

The linear sweep voltammograms for irbesartan as a function of scan rate are displayed in Figures 4a, 4b. The logarithm of peak currents against the logarithm of scan rates graphs, however, show straight lines with a slope of 0.56 at irbesartan concentrations of 20 µg/mL (Figure 4c). This value is near to the projected value of 0.5 expected for a perfect diffusion-controlled electrode process (23).

A diffusional process for the peak should be taken into account since this should be done utilizing the log I-log v curve. According to these results, the redox species rapidly diffuse from the solution rather than precipitate onto the electrode surface. The solubility of the intermediate species in 0.5 M sulfuric acid or a lack of product adherence to the electrode surface, respectively, can cause this phenomena (24,25).

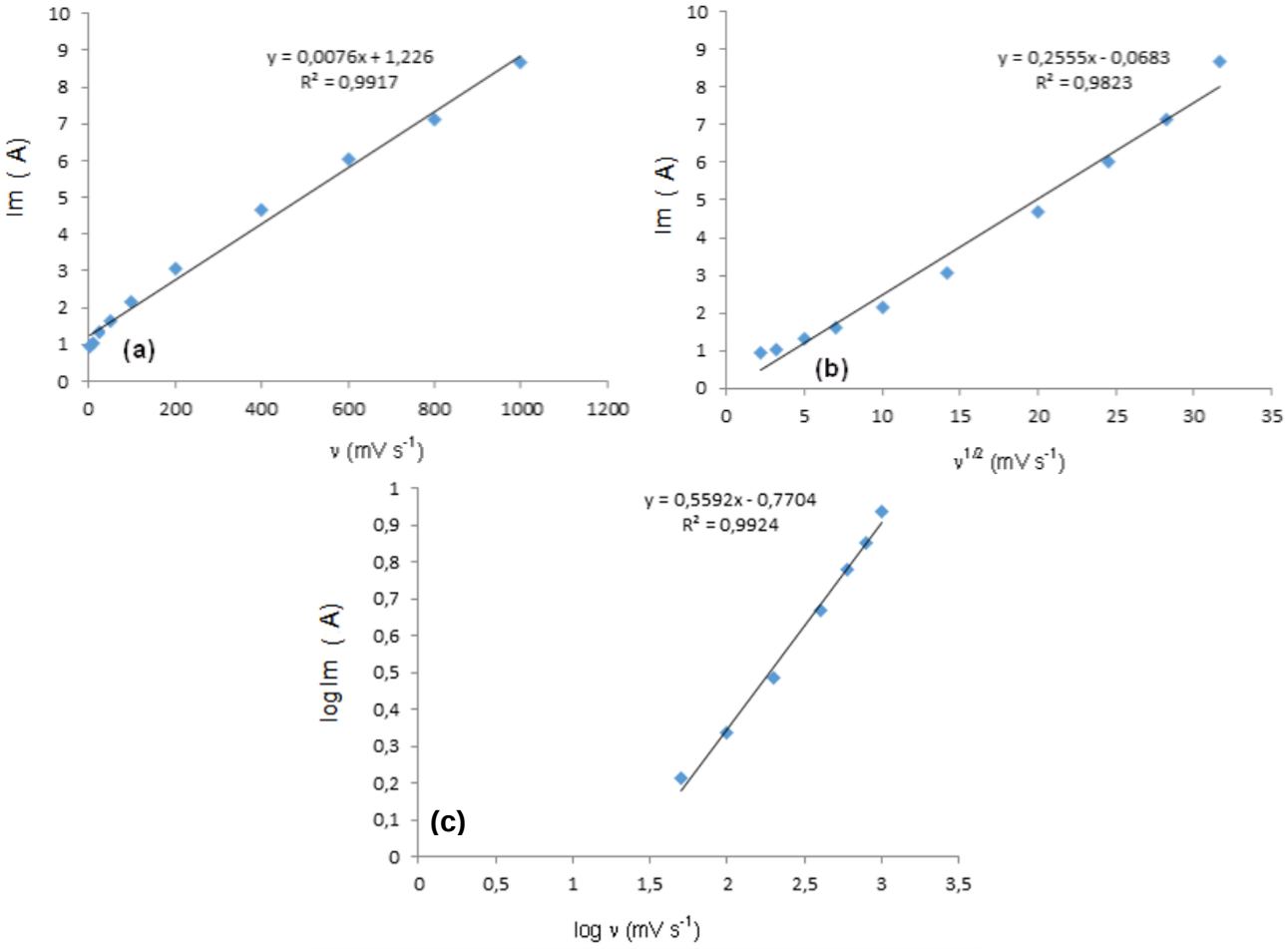

Figure 4(a-c): Dependence of peak current on scan rate (20 µg/mL).

3.2. Validation of the Method

While establishing the validation parameters, ICH Q2B guidelines were adhered to. Stability, ruggedness, limit of detection (LOD), limit of quantification (LOQ), specificity, linearity, precision, accuracy, and recovery are some of these requirements (27).

3.2.1. Specificity

In this study, common excipients and additives were investigated for potential interferences. After preparation, the QC samples were inspected. There is no indication that these substances are interfering at the amounts found in dose formulations. This formulation used an excipient that is most commonly used in the pharmaceutical sector. The specificity of the method was examined by keeping an eye out for any interference from common tablet ingredients such as titanium dioxide, cellulose, silicon dioxide and magnesium stearate. The recommended approach was unaffected negatively by these deviations. Depending on the analysis's conclusions, the process may be particular.

3.2.2. Linearity

Standard solutions were prepared as 5-70 µg/mL for both SWP and DPP. The development of calibration curves for the irbesartan standard was made possible by plotting the compound concentration vs peak current responses (Figures 5 and 6). The calibration curves' correlation coefficients were utilized to evaluate them. The linear regression equations were obtained and are presented in Table 1 using the Microsoft Excel® tool and the least squares method.

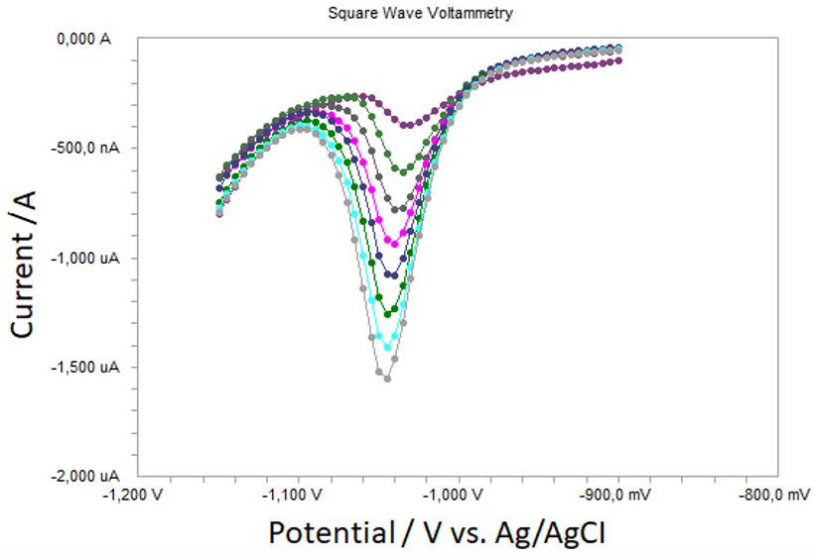

Figure 5: SW voltammograms of irbesartan (5-70 µg/mL).

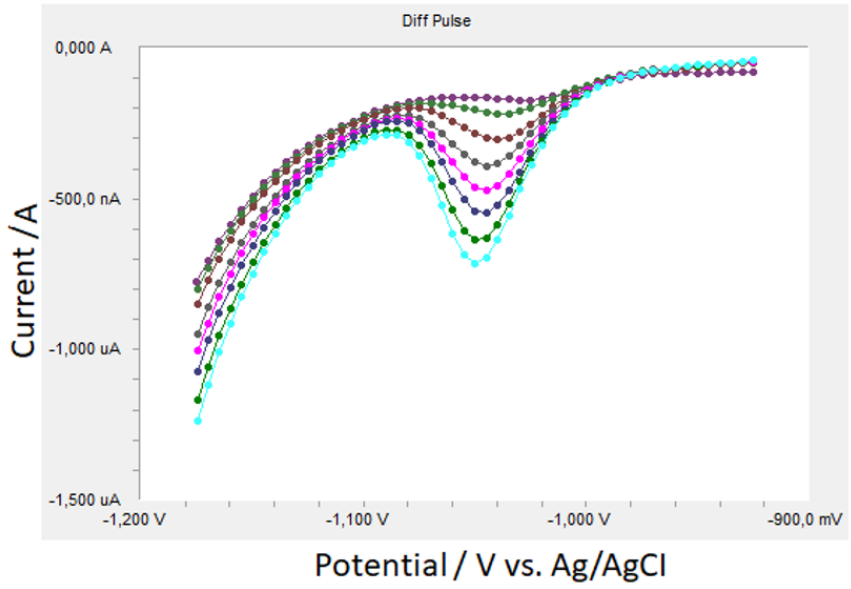

Figure 6: DP voltammograms of irbesartan (5-70 µg/mL).

Table 1: Regression information for the irbesartan calibration lines (n=6).

Parameters	SWP	DPP
Linearity (µg/mL)	5-70	5-70
Slope	0.0172	0.0083
Intercept	0.3849	0.1355
Coefficient of correlation	0.992	0.999
LOD (µg/mL)	0.50	0.40
LOQ (µg/mL)	1.50	1.20
Precision (RSD%)	2.61	2.34
Accuracy (% relative error)	-1.24	1.17
Precision of peak current (RSD%)	1.12	1.07
Accuracy of peak potential (RSD%)	1.24	1.31

3.2.3. Accuracy and precision

Using the QC samples, the SWV and DPV techniques' precision and accuracy were assessed for intra-day and inter-day use. The QC samples' same-day analysis was used to evaluate the accuracy and precision of intra-day measurements. By comparing the assays conducted on two different days, it was able to evaluate the precision and accuracy between those dates. The precision ranged from 0.87% to 2.61%, whereas the intra-day accuracy ranged from

1.09% to 1.24% (Table 1). The data clearly show that this procedure has good precision and accuracy.

3.2.4. Limits of detection (LOD) and quantification (LOQ)

Using calibration standards, the LOD and LOQ values of the recommended techniques were calculated. LOD and LOQ values were calculated as 3.3 σ/S and 10 σ/S, respectively, where S is the slope of the calibration curve and σ is the standard deviation of y-intercept of regression equation (n=6) (30). Table 1 provides a summary of the findings.

3.2.5. Ruggedness

In this experiment, a different analyst used the same instrument and standard to calculate the SW and DP voltammograms of irbesartan. The results showed no statistically significant differences across the operators, demonstrating the resilience of the suggested method.

3.2.6. Stability

For a minimum of 72 hours, the stability of the irbesartan stock solution was investigated. Additionally, at both room temperature and refrigeration temperatures of 4 and -20 °C, irbesartan standard solutions demonstrated 72-hour stability. The recommended range for irbesartan accuracy is 90-110%. In these cases, there are no significant irbesartan breakdown products.

3.2.7. Recovery

To evaluate the effects of formulation interference, the recovery was investigated at three different concentrations. The recoveries were done by combining irbesartan tablet samples that had already undergone analysis with a known quantity of pure medications. The amounts recovered from the spiked samples were compared to the actual added concentrations to determine the recoveries. The results are presented in Table 2.

Table 2: Recovery of irbesartan in tablet (n=6).

Pharmaceutical preparation	Added (µg/mL)	SWP			DPP		
		Found ± SD	Recovery (%)	RSD[a] (%)	Found ± SD	Recovery (%)	RSD[a] (%)
Karvea (25 µg/mL)	5	4.9 ± 0.17	98.0	3.46	5.1 ± 0.13	102.0	2.54
	15	14.5 ± 0.29	96.7	2.00	14.8 ± 0.25	98.7	1.69
	35	35.6 ± 1.12	101.7	3.14	35.2 ± 1.67	100.6	4.74

[a]RSD: Relative standard deviation

3.3. Procedure for Pharmaceutical Preparations

The 300 mg irbesartan-containing Karvea tablet was carefully weighed and finely ground. The right amount of powder was dissolved in 50 milliliters of 0.5 M sulfuric acid. Next, a balloon flask was filled to the ultimate capacity of 100 mL. After the tablet solutions were appropriately diluted, a Whatman filter was employed to filter them in order to provide a final concentration that fell between the linearity limitations of the SWP and DPP procedures (Figures 7 and 8). The calibration curve was used to determine the drug concentration for irbesartan.

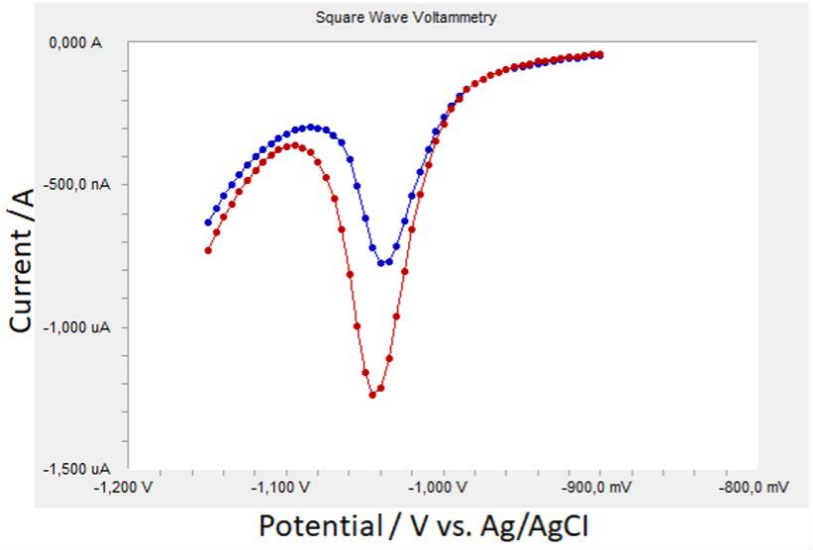

Figure 7: The SW voltammograms of Karvea tablet containing irbesartan (30 and 60 µg/mL).

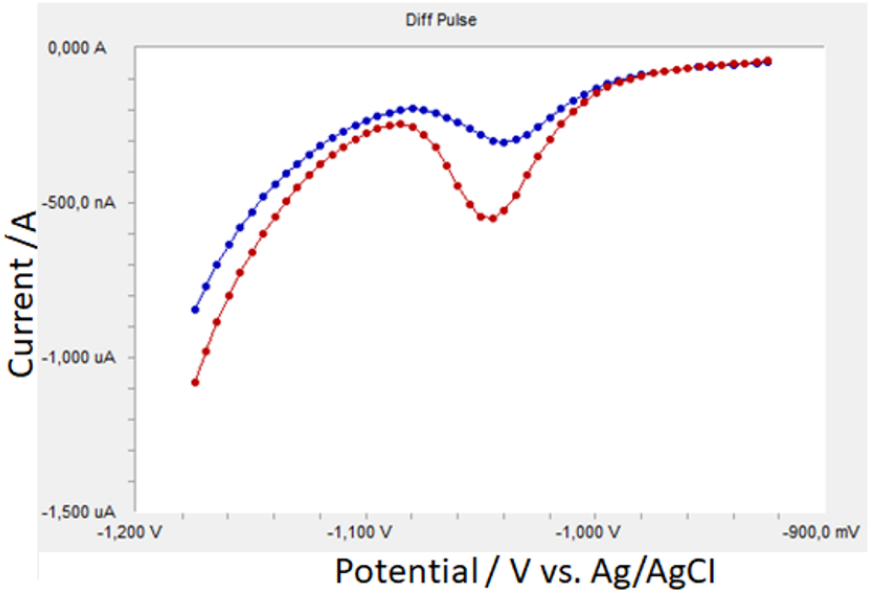

Figure 8: The DP voltammograms of Karvea tablet containing irbesartan (30 and 60 µg/mL).

3.4. Comparison of the Methods

Voltammetry is a potentially novel analytical method that has been proposed recently for the electrochemical detection of pharmaceuticals. Because of their exceptional price, user-friendliness, and quick analysis durations, voltammetric techniques are essential for pharmaceutical analysis (28,29).

The commercial tablets were identified using SW and DP techniques (Table 2). The findings demonstrate the excellent reproducibility and dependability of the two techniques. The t-test was used to compare the best outcomes statistically. The calculated t-values do not surpass the theoretical values at a 95% confidence level (Table 3).

Consequently, the differences between SW and DP voltammetric techniques are minimal. Using the suggested procedures, the %RSD for the polarographic analysis of irbesartan tablets was 1.07%. The recovery of standard additives further confirmed the validity of the proposed methods used on irbesartan tablet. A mean recovery rate of 99.8% was attained. The outcomes of the drug analysis obtained using the suggested techniques closely match the value asserted.

The proposed methods' results were contrasted with those of the official (30) and reference methods (8). The student t- and F-values, which were calculated with a 95% level of confidence, revealed no appreciable variations in performance between the official or reference procedures and the recommended methods (Table 3).

Table 3: Comparison of the proposed and reported methods of irbesartan.

Parameters	SWP	DPP	Official method (30)	Reported method (8)
Mean (recovery %)	99.2	100.4	100.04	99.63
SD	0.621	1.074	-	-
% RSD	0.626	1.069	0.260	0.362
Variance	0.386	1.153	-	-
SE	0.253	0.438	-	-
t-test (2.228)[a]	0.897		-	-
F- test (5.1)[a]	3.74		-	-

SE: Standard error, No statistically significant difference between the four approaches exists, $F_t > F_c$: Ho hypothesis is accepted ($P > 0.05$), [a]Theoretical values, Theoretical values at P=0.05.

4. CONCLUSION

There are two new electro-analytical techniques that combine DP and SW to estimate the irbesartan content in pharmaceutical formulations. The efficacy and simplicity of the SW and DP procedures for the quantitative determination of irbesartan were shown. The main advantage of this method is that the concentration of the active ingredient may be measured directly from the irbesartan formulations without any additional processing, such as time-consuming or derivatization. The methodologies mentioned above can be effectively used to perform routine analyses of irbesartan in both its pure form and its formulations.

5. CONFLICT OF INTEREST

According to the writers, there was no conflict of interest.

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