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Research Article

Analytical Comparison of Cefadroxil Determination by Square Wave Adsorptive Stripping Voltammetric and Spectrophotometric Methods

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Abstract

The goal of this research is to verify the proposed nano-silver amalgam paste electrode (Ag-nano-SPE) method to compare with a spectrophotometric technique based on derivatization with potassium periodate (KIO_4), 2,4-dinitrophenyl hydrazine (DNP) and sodium hydroxide (NaOH) for the estimation of cefadroxil (CFDL) by square wave adsorptive stripping voltammetry (SWAV). The different parameters of both methods were optimized in detail separately and then compared their efficiency, selectivity, sensitivity and applications. The SWAV produced a reduction peak with a precise definition at -0.160 V while measuring CFDL in 0.04 $molL^{-1}$ Britton–Robinson buffer at pH 4, accumulation potential (0.5 V), accumulation time (10 sec), and with stirring rate of 200 rpm. Whereas, the CFDL was measured at 515 nm (λ_{max}) by UV-Visible spectrophotometer after the derivatization by using 1.5 mL of 0.5 mM DNP, 1.5 mL of 6.52 mM KIO_4 and 0.5 mL of 10 M NaOH solution at room temperature. The linear response for CFDL was found using the SWAV and spectrophotometric techniques along a linear dynamic range from 0.033 - 0.304 and 0.051 - 1.376 µM, respectively. However, the precision, detection limit and quantification limit of SWAV for CFDL in the samples and standards significantly lower ($p < 0.01$) as compared to spectrophotometric method. This indicates that the SWAV is more sensitive and selective than the spectrophotometric technique for regular CFDL analysis.

Keywords: Cefadroxil; Silver nano amalgam paste electrode; Square-wave adsorptive stripping voltammetry; Spectrophotometric

Introduction

An antibiotic is a class of antimicrobial medicine, which is active against the infections of microorganism, prevention and treatment of bacterial infections [1]. These drugs are used to either kill or inhibit the growth of infective microorganisms in order to stop them from spreading throughout the body [2]. Penicillin is the first synthetic medicine invented by Alexander Fleming in 1928 for successful prevention and treatment of microbial infections [3]. Antibiotics are used to treat and prevent a variety of microbiological infections. Cephalosporins, is an effective class of antibiotics that have action against both gram-positive and gram-negative bacteria [4]. Cefadroxil (CFDL) is a first-generation cephalosporin semi-synthetic β-lactam drug [5,6]. The in vitro studied indicated that its activity was very similar to cephalexin. The chemical structure of CFDL (Figure 1). It is effectively used for several infections triggered by micro-organisms including infections of central nervous system, genitourinary, gynecology, upper respiratory tract, urinary, post-surgical and skin [6,7]. It is frequently prescribed by doctors for the bacterial infections and readily available in market in different trade names in the forms of capsules, tablets, and powder for suspension. It is rapidly absorbed into the body fluids after its oral application (approximately within three hours) [8]. It is noticed that 10 to 20% of CFDL administrative dosage can be accumulated by the body fluids while rest of its dose excreted through urine [9]. The quality prevalence of CFDL for the sales and administration is highly considerable because of its composition which may have a great impact on its quality. The obtained data has a great importance for the composition of drug material and the development of analytical methods [10].

Several analytical methods such as high performance liquid chromatography (HPLC) [7,11,12], liquid chromatography mass spectrometry (LC-MS) [13], electro chromatography [14,15], capillary zone electrophoresis [16-19], chemiluminescence [20-22], spectrophotometry [23-25] and electroanalytical techniques [26,27] were reported in the literature for the quantification and detection of the CFDL. Among them, spectrophotometry and electrochemical methods are preferable because ease of use, ecofriendly, and cost-effective techniques for routine analysis of CFDL in complex matrices. However, the direct determination of CFDL was observed at 264 nm by spectrophotometer but it was semi quantitative [28]. Thus, different chemical reagents like 4-amino anti-pyrene, N-bromosuccinide and tetracyanoquinoid-methane were used to enhance the selective and sensitive determination of CFDL by spectrophotometry [29-31]. However, 2,4-dinitrophenylhydrazine (DNP) is most effective derivatizing agent for the quantitative analysis of different drugs [32-34]. Thus, it is selected for current study to develop an accurate spectroscopic method for CFDL analysis which depends on a simple one single step reaction using DNP.

Electroanalytical techniques are the best choice for routine analysis

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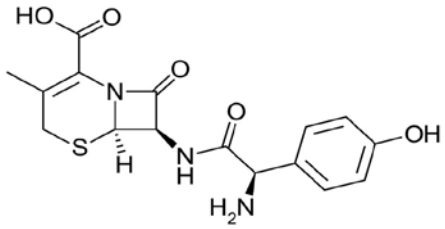

Figure 1: Chemical structure of cefadroxil.

of CFDL. It's due to their ease of use, repeatability, great sensitivity, and quick analytical results [35]. Cefadroxil has electroactive groups that can be readily reduced on the surface of mercury drop electrodes and hanging mercury drop electrodes [36,37]. These electrodes reduced hydrogen overvoltage and reduced analyte repeatability. Furthermore, they have the potential to release significant levels of mercury into the environment. The paste electrodes are attractive sensing materials to analytical scientists for the determination of the pharmaceutical drugs. It's due of their ease of use, inertness, affordability, environmental friendliness, robustness, low resistance, steady response, effective detection, and broad applications. Due to comparable chemical properties and minimal toxicity, amalgam paste electrodes are the ideal alternative to mercury electrodes [38,39]. There are several types of metal solid amalgam paste electrodes made from the prosperous metals such as silver (Ag), gold (Au), iridium (Ir), copper (Cu) and bismuth (Bi) and a suitable amount of mercury (Hg) for targeted analytes [40]. Some chemical substances, bio-macromolecules, pharmaceutical medicines, and medicinal supplements are determined by using these electrodes [41]. The goal of this research was to compare the analytical capabilities of square wave adsorptive stripping voltammetry (SWAV) and UV-visible spectrophotometry methods for determining cefadroxil (CFDL) using sodium hydroxide (NaOH), 2,4-dinitrophenyl hydrazine (DNP) and potassium periodate (KIO_4).

Materials and Methods

Instruments

The CHI 15.07 version software, Windows 7 electrochemical Analyzer (Tennison Hill Drive, Austin, USA) was used to conduct voltammetric investigations. There are three electrodes used as a working electrodes, reference and auxiliary electrode electrochemical cells containing nano-silver amalgam paste electrode (Ag-nano-SPE) silver/silver chloride and platinum wire. A UV-2600 double-beam UV-Visible spectrophotometer (Shimadzu, Japan) was used to examine CFDL. Spectral absorption scanning of CFDL standards and pharmaceutical formulations was carried out in quartz cells (1.0 cm) at room temperature with spectra management UV-Pro software.

Materials and reagents

All of the chemicals utilized were of the highest analytical quality. Cefadroxil was purchased from MP Biomedicals (Kaysersberg, France). The supporting analytes were phosphate and acetate, as well as Britton–Robinson buffer (BRB). Mili-Q water produced by a Milli-Q water purifying system (Millipore, USA). The Ag-nano-SPE (working electrode) fabricated from Ag nanoparticle (size < 100 nm) purchased from Sigma-Aldrich (Louis, USA). The pH ion meter of Thermo Fisher Scientific (Massachusetts, United States) is used to check pH. Other analytical grade chemicals purchased from Fluka (Bush, Switzerland). The (KIO_4) potassium periodate and (DNP) 2, 4-dinitrophenyl hydrazine were produced by Sigma-Aldrich (Louis, USA). CFDL national and international pharmaceutical formulas were acquired from a local pharmacy in Hyderabad, Sindh.

Electrochemical determination method

The suitable volume of BRB-associated to acceptable CFDL standard solution was determined in an electrochemical cell with a three-electrode system. Different voltammetry modes, such as differential pulse, square wave and cyclic stripping voltammetry, were investigated to find the best mode for measuring potentials between 1.0 and 1.0 V. The other parameters, such as deposition duration, deposition potential, frequency, stirring rate, potential increase, quiet time, cleaning potential, and equilibrium time, were optimized as well. CFDL reduction peak potential was measured at 0.16 V in the quantitative study. Each scan is followed by a wash of the electrodes with Milli-Q water to remove any CFDL deposits. The same technique was used to record the voltammetric readings of each set of standard solution, medication, and biological sample.

Spectrophotometric procedure and samples preparations

1.5 mL duplicate six samples of standard solution (0.7 mM) and pharmaceutical samples of CFDL (0.025 g of each tablet and capsule diluted in 100 mL deionized water) were collected in the 10 mL volumetric flasks. 1.5 mL of (1.74 to 10.8 mM) KIO_4, (0.015 to 10 mM) DNP and 0.5 mL of (5.0 to 15 M) NaOH solution added in each volumetric flask with deionized water up to 10 mL. The impact of temperature on the chromogen production process was investigated at temperatures ranging from 25 to 60 °C. The absorbance of each sample was checked against a reagent blank at a maximum λ_{max} of 515 nm.

Sample preparation of pharmaceutical preparation for voltammetric method

Each tablet and capsule contains around 500 mg of CFDL (5 samples for each) according to the label. After weighing properly on a physical balance, each CFDL pharmaceutical formulation's homogenous fine powder is produced in a mortar and pestle. Each pharmaceutical formulation 0.1 mg powder was rapidly dissolved in volumetric flasks containing 50 mL milli-Q water. The resulting solutions were sonicated in an ultrasonic water bath for 10 minutes and then keep at room temperature for 30 minutes. To avoid any photochemical reactions, the final solution was prepared to a volume of 100 mL using milli-Q water and stored in the dark. Then, according to the electrochemical technique, the produced pharmaceutical formulation was evaluated by voltammetry.

Results and Discussion

Optimization of electrochemical method

Amalgam paste electrode is the finest replacement for hanging dropping mercury electrodes and dropping mercury electrodes (HDME and DME) for the regular examinations of pharmaceutical substances like CFDL. The sensitive square wave adsorptive stripping voltammetry (SWAV), Differential pulse (DPV), and cyclic voltammetry (CV) methods performed at pH 4.0 in the BRB system produced a quantifiable diffusion current from the electrochemical reduction of CFDL at the Ag-nano-SPE. There

Table 1: Response of optimization study of voltammetric and spectrophotometric parameters for cefadroxil.

Voltammetry			Spectrophotometry		
Parameters	**Values in Range**	**Optimized Value**	**Parameters**	**Values in Range**	**Optimized Value**
Buffer pH	2-12	4	DNP concentration (mM)	0.015-10	5
Buffer Volume (mL)	1-8	5	Volume of 0.1mM DNP solution (mL)	0.50-2.5	1.5
Frequency (Hz)	10-40	25	PPI concentration (mM)	1.74-10.8	0.15
Stirring rate (rpm)	50-350	200	Volume of 0.15mM PPI solution mL	0.50-2.5	1.5
Deposition Potential (V)	0.1-0.5	0.5	NaOH concentration (molarity)	15-May	10
Deposition time (sec)	5 to 10	5	Volume of 10M NaOH (mL)	0.20-2.0	0.5
			Temperature (°C)	25-60	25
			Measuring wavelength (nm)	300-700	515
Analytical Characteristics					
Dynamic Range (µM)	0.033-0.304			0.051-1.376	
R^2	0.9966			0.9925	
LOD (µM)	0.011			0.044	
LOQ (µM)	0.033			0.132	

Table 2: Recovery of Cefadroxil by the Proposed Methods voltammetry and spectrophotometry.

	Voltammetry			Spectrophotometry		
	Added (µM)	**Observed (µM)**	**%Recovery**	**Added (µM)**	**Observed (µM)**	**% Recovery**
CPS-1		2.64	--		2.36	--
	0.08	2.722	102.5	0.16	2.521	100.5
	0.2	2.839	99.5	0.32	2.676	98.6
	0.32	2.96	100	0.48	2.837	99.4
TPS-1		4.22	--		4.18	--
	0.08	4.302	102.6	0.16	4.342	101.3
	0.2	4.423	101.7	0.32	4.503	100.8
	0.32	4.539	99.6	0.48	4.652	98.4

CPS: Capsule Pharmaceutical Sample; TPS: Tablets Pharmaceutical Sample.

was not a significant current response of CFDL found by DPV. On the other hand, SWAV is very sensitive, resulting in a strong and noticeable decrease peak for CFDL. Thus, ideal instrumental settings of The SWAV were investigated, including buffer volume, buffer systems, pH, accumulation potential (E_{acc}), accumulation time (t_{acc}), and stirring rate. To determine the response of CFDL on CPE, GC, and Ag-nano-SPE in BRB solutions (0.04 M), preliminary tests were done to characterise the main features. In the case of Ag-nano-SPE, a noticeable and strong peak was produced (Table 1). The inclusion of mercury or silver Nano-powder combination with prosperous structure, which offered a wide surface area for CFDL to interact, might explain the substantial decrease of CFDL achieved by nano-Ag-PE.

The pH of the solution, as well as the composition of the supporting electrolytes, had a significant influence on the SWAV to the targeted analyte. As a result, at pH 4, Britton-Robinson buffer, acetate and phosphate were studied as supportive electrolytes. CFDL reduction peaks were seen in all buffers between - 0.14 and - 0.20 V (Table 1). When compared to phosphate, the greatest reduction response was achieved in the BRB and acetate buffer combination. In the case of the acetate buffer system, the response was not substantial due to significant acetate ion deposition on the electrode. In the BRB system, greater peak current and improved peak shape were attained. As a result, the BRB system was chosen for further study optimization.

The effect of solution pH on the CFDL reduction response on Ag-nano-SPE observed in the BRB system varied from 2 to 8. The maximum decrease in the peak was recorded at pH = 4.0 (Table 1). With an increase in pH, the electrode potential (Ep) shifted to the negative side, indicating that SWAV significantly reduced CFDL on the surface of Ag-nano-SPE. The peak intensity or peak current was firstly slightly increased up to pH 4 than decreased with increased in pH because of the decreased in the protonation. Furthermore, it has been observed that the CFDL may provide a highly defined reduction peak in acidic aqueous solution, which is related to C=O unsaturation in this electrochemical technique. Similar, the reduction of unsaturation of C=C and C=N in cefixime were also reported in literature [42]. At pH 4.0, CFDL revealed a significant reduction peak on the selected electrode. As a result, it has been decided to be discriminating in future research.

The influence of accumulation time (t_{acc}) on the response of 0.25 M CFDL reduction on nano-Ag-APME was investigated. The change of t_{acc} in the 5 to 15 s time period with accumulation potential of 0.1 V. The peak current increased with t_{acc} up to 10 s. Because of its vast surface area, the rise in peak current with increasing t_{acc} showed CFDL

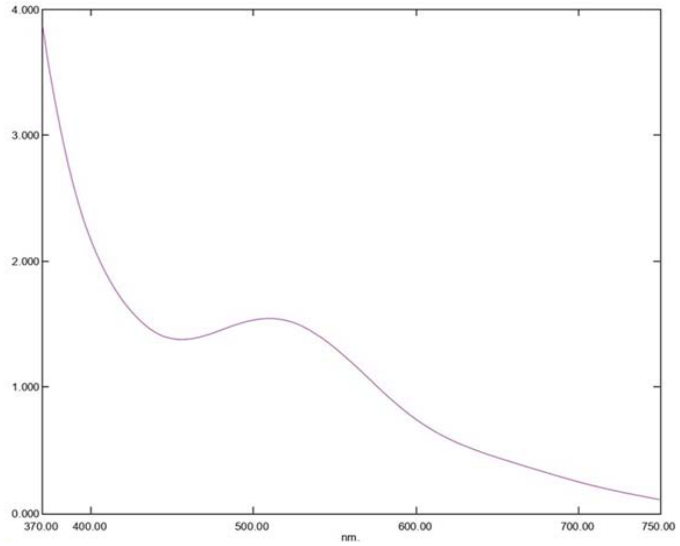

Figure 2: Absorption spectra of colored chromogen of CFDL against blank.

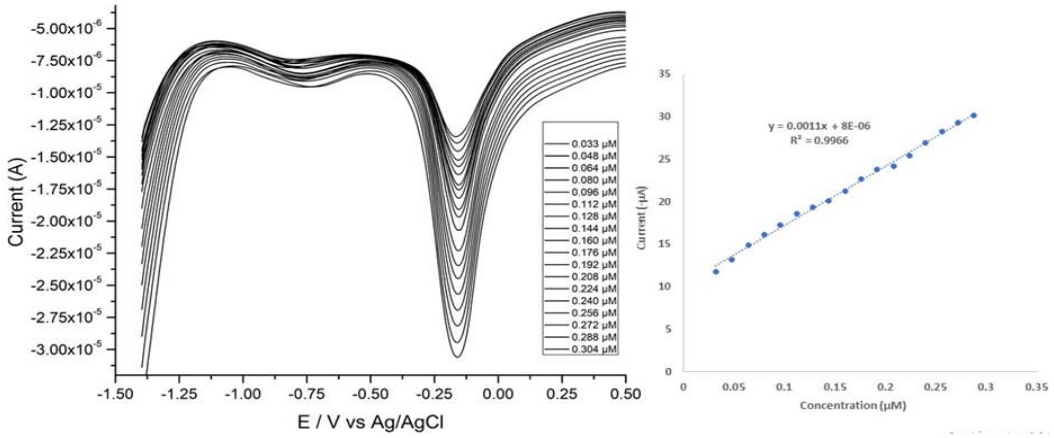

Figure 3: SW-AdS voltammograms and calibration graph of CFDL on nano-Ag-APE in 0.04 mol/L BRB solution at pH 4.0.

deposition on the surface of Ag-nano- SPE. It suggests that CFDL can be effectively adsorbed by Ag-nano-SPE. It was then reduced due to CFDL saturation on the suggested electrode. As a consequence, throughout the rest of the trial, the t_{acc} of 10 s was selected. The impact of the accumulation potential (E_{acc}) on the intensity of peak current was also investigated for 0.25 M CFDL after a 10 s t_{acc} across a voltage range of 0.1 to 0.5 V (Table 1). The reactions of CFDL reduction by accumulation potential did not differ significantly. The lack of influence of E_{acc} on the electrode for CFDL was intriguing. It may be demonstrated that the surface of the suggested Ag-nano-SPE is adsorptive in nature, allowing CFDL to accumulate. This might assist to reduce the amount of energy needed for deposition. As a result, it is a cost-effective electrochemical method for detecting CFDL. When the adsorption potential on Ag-nano-SPE was 0.5 V *vs.* Ag/AgCl as the reference electrode, the peak intensity was the best. For additional optimization and experimental data, the optimum E_{acc} was set to 0.5 V at Ag-nano-SPE against Ag/AgCl. The stirring rate for strong CFDL reaction on Ag-nano-SPE was investigated between 150 and 400 rpm as listed in (Table 1). Via increasing the stirring rate to 200 rpm, the strength of the peak current for CFDL by SWAV was enhanced. Following then, the CFDL reaction to Ag-nano-SPE began to deteriorate. The variance in peak current response, on the other hand, was not significant ($p > 0.05$). As a result, for subsequent optimization experiments, 200 rpm was chosen as the best stirring rate.

Optimization of spectrophotometric method

The spectrophotometric technique was also investigated for comparison purposes. This technique uses potassium periodate (KIO_4), 2, 4-dinitrophenyl hydrazine (DNP) and sodium hydroxide (NaOH) to derivative CFDL. The concentrations of KIO4, DNP, and NaOH, as well as their volume, reaction time, temperature, and spectrophotometric wavelength selection for the suggested chromogen, were all thoroughly investigated. In general, direct spectrophotometric measurement of pharmaceutical preparations is sensitive owing to possible interference that might affect CFDL absorption. The use of selective reagents for chemical derivatization of a target drug, on the other hand, might improve the selectivity and sensitivity of a spectrophotometric analysis [33]. By attaching a diazonium cation under basic conditions (NaOH solution) and

Table 3: Recovery of Cefadroxil by the Proposed Methods voltammetry and spectrophotometry from pharmaceutical preparations.

Samples	Expected Value (mg)	Voltammetry		Spectrophotometry	
		Observed Value	% Recovery	Observed Value (mg)	% Recovery
CPS 1	500	480	96	478	95.7
CPS 2	500	453	90.6	451	90.2
CPS 3	500	398	79.7	393	78.5
TPS 1	500	431	86.2	401	80.1
TPS 2	500	476	95.3	451	90.1
TPS 3	500	503	101	493	98.7
TPS 4	500	493	98.5	486	97.2

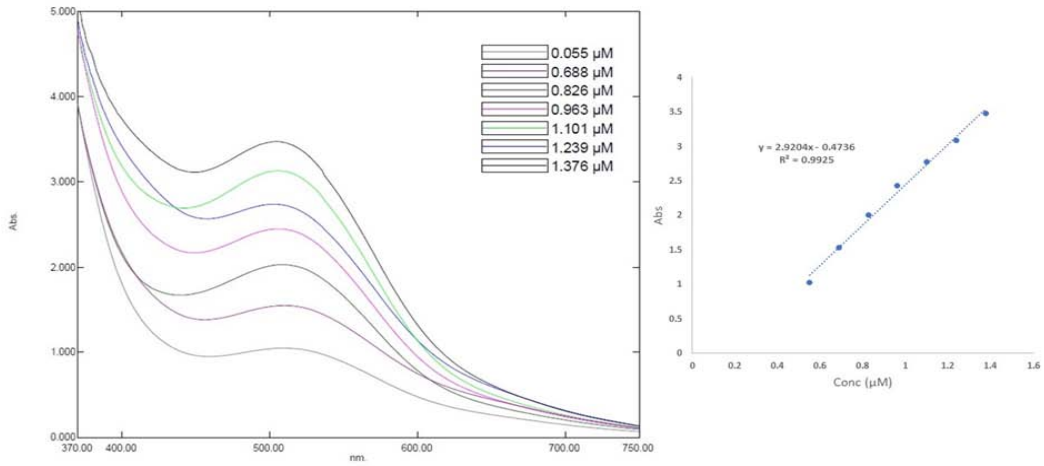

Figure 4: Absorption spectra and calibration graph of CFDL using DNP, KIO_4 and NaOH.

bathochromic shift to generate coloured chromogen, the phenolic ring of CFDL may be converted to an azo derivative (Figure 2) [7]. At around 515 nm, the maximum absorption (max) was found as reported elsewhere [25]. As a result, this wavelength was chosen for quantifiable absorbance in aqueous solution for the suggested derivative. The optimization of appropriate conditions for the chromogenic reaction of DNP with CFDL was investigated for the current work in order to acquire considerable sensitivity.

DNP, KIO_4, and NaOH concentrations were measured in the ranges of 0.015 - 10 mM, 1.74 - 10.8 mM, and 5 - 15 M, respectively, while DNP, KIO_4, and NaOH volumes were measured in the ranges of 0.50 - 2.5, 0.50 - 2.5, and 0.20 - 2.0 mL, respectively (Table 1). 1.5 mL DNP (0.5 mM), 1.5 mL KIO_4 (6.52 mM), and 0.50 mL (10 M) NaOH exhibited the highest peak intensity. The influence of temperature on the chromogen production process was investigated at temperatures ranging from 25 to 60 °C. The temperature research was conducted out in a thermostatic water bath. However, the best results were obtained at room temperature (25 °C). This meant that the chromogen reaction was finished as soon as the right amounts of DNP, KIO_4, and NaOH were added to CFDL at room temperature. The response took less than a second to complete. As a result, a considerable response time is not required.

Comparison of electrochemical and spectrophotometric methods

In this study, the SWAV and spectrophotometric techniques were used to detect CFDL in pharmaceutical products. The SWAV method relies on a decrease in CFDL at the surface of Ag-nano-SPE in acidic solution (pH = 4). Similarly, following derivatization by DNP, KIO_4, and NaOH, the reaction of the azo derivative colored chromogen of CFDL was examined using spectrophotometry. Electrochemical approaches had a significant advantage over spectrophotometric methods in that they could measure CFDL without any pretreatment or derivatization, saving time, cost, and interference [43]. Meanwhile, the proposed SWAV method for regular CFDL examination is one of the most ecologically friendly and easiest to use. The calibration curve of linear dynamic range for CFDL using the SWAV technique was 0.033 - 0.304 M (Figure 3) and 0.051 - 1.376 M using the spectrophotometric approach (Figure 4), respectively. SWAV and UV-Visible methods had co-efficient of determination (R^2) of 0.9966 and 0.9925, respectively. LOD = 3 sm-1 and LOQ = 10 sm-1 were used to calculate the detection and quantification limits, respectively, where "s" stands for the standard deviation of ten measurements of the lowest standard (whose response was close to baseline) and "m" stands for the slope of the calibration curve. SWAV and spectrophotometric techniques had LODs of 0.011 and 0.044 M, respectively, and LOQs of 0.033 and 0.132 M. As a result, the SWAV technique is more sensitive than the spectrophotometric method.

Using the conventional addition procedure, the accuracy of both analytical methods was evaluated. Three recognized standards were mixed into a diluted solution of one tablet and capsule of pharmaceutical preparation for this purpose. The standard addition

method's percentage recovery (% R) was calculated using the formula below

$$\%R = \frac{(C_{Obtained} - C_{Sample})}{C_{Added}} \times 100$$

The letter "*C*" indicates for concentration in this case. The percent R of CFDL determined by SWAV and spectrophotometry using the standard addition technique were 99.5-102.6 and 98.4-101.3 %, respectively (Table 2). The % recovery of additional known concentrations of CFDL, on the other hand, does not change much. However, when the relative standard deviation (% RSD) of six independent analyses of the same sample was compared, the SWAV approach (RSD = 1.80 %) was shown to be more precise than the spectrophotometric method (RSD = 2.80 %).

On the surface of three different Ag-nano-SPEs with the same composition that had just been freshly manufactured, the repeatability of voltammetric studies was examined. To ensure that the peak current response is repeatable, at subsequently produced Ag-nano-SPE electrodes, eleven consecutive measurements at pH 4.0 in the BRB system were performed. The peak currents recorded on the three Ag-nano-SPE electrodes examined exhibited a high degree of similarity, with RSD of less than 1.8 %. The substantial similarity of CFDL reaction on each freshly produced Ag-nano-SPE was confirmed by these findings. As a result, no reverse potential or activation of the suggested electrodes is required. The suggested chromogen's stability was measured using a UV-Visible spectrophotometer at intervals of five minutes to three hours. The reaction solution's λ_{max} was steady for two hours. Later, the chromogen's colour disappeared entirely, and the chromogen's λ_{max} was considerably moved to a lower wavelength, indicating that the chromogen's stability was too short. Seven different reaction solutions were produced in the same way as the azo derivative chromogen production technique. Each prepared chromogen's acquired response has an RSD of less than 3.0 %. The SWAV is considerably more stable and produces consistent results, according to the stability and reproducibility investigation.

Interfering substances such as lactose, sucrose, cellulose, starch, and magnesium stearate, which may be present as a binder or drug carrier in pharmaceutical formulations, were examined using the recommended SWAV and spectrophotometric procedures. The interference influence of each substance was studied using a 1:1 ratio of CFDL and the interfering specie. The CFDL reaction in the absence of interfering chemicals (%) was compared to the CFDL response in the presence of interfering substances (%). The highest interference was found to be – 3.50 % for SWAV and - 4.90 % for spectrophotometric techniques, respectively. However, interference remained considerably below the permissible level of 5% in all situations. Both techniques found that the examined interfering compounds had little influence on CFDL. As a result, both techniques found no significant interference for the examined co-existing drugs at the 95 % confidence level ($p > 0.05$). As a consequence, the suitability of both methods for quantitative detection of CFDL in pharmaceutical samples in the presence of the drugs under investigation has been confirmed. The SWAV technique, on the other hand, was much more sensitive than the spectrophotometric method for the selective assessment of CFDL in real samples. SWAV and spectrophotometric analysis were used to determine the mean concentration of CFDL in pharmaceutical samples CPS-1, CPS-2, CPS-3, and TPS-1, TPS-2, TPS-3, and TPS-4 as listed in [Table 3]. According to the findings, there is no significant difference in % recoveries. However, for the CFDL in pharmaceutical formulations, the SWAV technique has a low RSD of 3.5 %, whereas the spectrophotometric method has a % RSD of > 4.5 %. CPS-1 had the maximum printed quantity of CFDL in capsule samples, whereas CPS-3 had the lowest (Table 3). TPS-3, TPS-4, and TPS-5 have quantifiable CFDL contents in tablet samples, but TPS-1 had the smallest quantity (500 mg) on the cover.

Conclusion

The current study compared the analysis of CFDL using a nano silver amalgam paste electrode (Ag-nano-SPE) and derivatization related to the method of UV-visible spectrophotometric by using potassium periodate (KIO_4), 2,4-dinitrophenyl hydrazine (DNP), and sodium hydroxide (NaOH) applying square wave adsorptive stripping voltammetry (SWAV). After derivatization with DNP, KIO4, and NaOH at room temperature, spectrophotometric measurement of CFDL was performed at 515 nm (max). For assessing CFDL in pharmaceutical formulations, the SWAV method was shown to be more precise, accurate, and selective. Although there was no significant difference in % recoveries of CFDL in preparations between the SWAV and spectrophotometric methods, when compared to the UV-Visible spectrophotometric method, the percent relative standard deviation (% RSD) for the determination of CFDL by the SWAV method was significantly lower (RSD 2.0 %). It might be concluded that the SWAV approach was relatively novel for CFDL matrix analysis in pharmaceutical formulations, and that it was superior to the spectrophotometric method.

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