Int. J. Electrochem. Sci., 16 **(2021)** Article ID: 210651, doi: 10.20964/2021.06.25

International Journal of
ELECTROCHEMICAL
SCIENCE
www.electrochemsci.org

Electrochemical Behavior and Voltammetric Determination of Albendazole Using Carbon Paste Electrode

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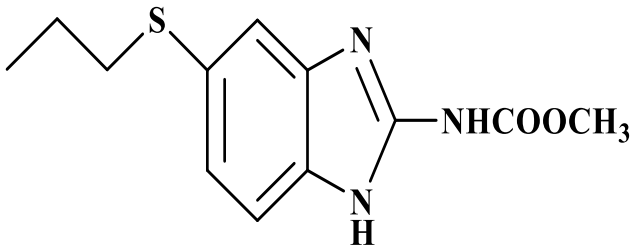
Received: 8 February 2021 / *Accepted:* 30 March 2021 / *Published:* 30 April 2021

Cyclic voltammetry (CV) and differential pulse voltammetry (DPV) techniques were used to study the electrochemical activity of albendazole (ABZ) in carbon paste electrodes (CPE). Using Britton-Robinson (BR) buffer (pH 4.01) ABZ, only one oxidation peak (Ep = 0.873 V) was observed, suggesting that the irreversible oxidation mechanism and this process are regulated by adsorption. The various experimental parameters for oxidation of ABZ have been customized. The oxidation peak current is proportional to the concentrations of ABZ within the range from 0.0265 to 0.1855 µg/ml under optimum conditions. The limits of detection and quantification obtained are 0.015 and 0.048 µg/mL. This approach was used in drug products and human urine samples for the voltammetric detection of ABZ.

Keywords: Albendazole (ABZ), DPV, CPE, pharmaceutical formulations, urine.

1. INTRODUCTION

Albendazole (ABZ) is a wide spectrum anthelmintic used against many helminthes. It is used in the treatment of threadworm, hookworm and tapeworm. It has low bioavailability due to its first metabolism [1-3]. ABZ is a standard antiparasitic agent with a wide spectrum [4] and was accepted for human usage in 1982. ABZ, one of the benzimidazole compounds and chemically referred to as methyl (5-propolythio-1H-benzimidazole-2-yl)carbamate, Scheme 1.



Scheme 1 Chemical structure of ABZ.

Several analytical methods, including high-performance chromatographic liquid methods, were reported for determining ABZ (HPLC) [5-12], spectrophotometry [13-17], capillary electrophoresis [18-19], titrimetric methods [20-23]. Electroanalytical methods (such as voltammetry) were also used for the determination of ABZ on the basis of the oxidation of the drug on the surface of hanging mercury drop electrode [24], glassy carbon electrode [25] and glassy carbon-rotating disk electrode [26, 27] and catholically pretreated boron-doped diamond (BDD) electrode [28]. This research focused on the electrochemical behavior of ABZ with the CPE. The objective is to optimize the most important conditions for developing DPV anodic methods to measure drugs in bulk solutions, pharmaceutical doses and spiked urine samples from humans without time-consuming and extraction steps before analysis.

2. MATERIALS AND METHODS

Chemicals

Chemicals used were of highly pure grade level. ABZ and the pharmaceuticals, Bendax tablets (200 mg) were supplied by Sigma Pharmaceutical Industries, Quesna Menoufia, Egypt. Graphite powder (1-2 μm) was from Aldrich and paraffin oil was from BDH. Sodium acetate, potassium chloride, Sodium citrate, sodium phosphate and sodium perchlorate has been obtained from Aldrich. BR buffer with a pH from 1.8-11.0 was prepared by using 0.04 M from each of phosphoric, boric and acetic acids. pH values were adjusted by 0.5 M sodium hydroxide.

Instruments

For CV and DPV measurements, the Metrohm 797Va Computrace (Herisau, Sweden) with Metrohm VA694 stand. The electrochemical cell is composed of three electrodes: the working electrode is a CPE, Ag/AgCl as a reference and platinum wire as an auxiliary electrode. The pH values were adjusted using Hanna pH 211-microprocessor pH meter.

The cyclic voltammetry was recorded using ABZ in 0.04 M BR buffer pH 4.01. The effect of accumulation time was studied from 0.0 s to 300 s, the effect of accumulation potential was studied from 0.0 V to +0.7 V, pulse amplitude was studied from 10 mV to 100 mV while scan rate was studied from 10 mV/s to 100 mV/s.

Preparation of CPE

The CPE was prepared as previously mentioned [28, 30]. The carbon paste was produced by combining the 0.5 g graphite powder into a mortar with 0.18 mL paraffin oil. With a volume of 1 ml, the carbon paste had been carefully pressed into the micropipette tip and a thin rod of stainless steel with a diameter of 2 mm. A piece of clean paper smoothed the CPE surface until it had a brilliant appearance.

Preparation of the ABZ solution from tablets

Ten tablets have been carefully measured and ground in mortar (200 mg of ABZ per tablet). In 30 ml methanol, the measured volume of tablet powder was dissolved. The solution was filtered and the residue washed by methanol 3 times and methanol labelled to give the solution $5x110^{-5}$ ABZ.

0.0133 g of ABZ was dissolved in methanol for spiked urine preparation, and transferred in a flask measuring 50 ml. 2.5 ml of healthy adult urine was added and then completed to the desired volume by methanol to prepare 1×10^{-3} M ABZ in urine sample. Then 5×10^{-5} M solution was prepared by dilution.

3. RESULTS AND DISCUSSION

3.1. Voltammetric behaviour

CV has been used as a powerful tool to study the electrochemical behavior of ABZ at CPE. Fig.1 show the cyclic voltammogram for 1.0×10^{-7} M ABZ in 0.04 M BR buffer pH 4.01 using a potential range from 0.0. to 1.4 V, accumulation time 60 s and scan rate of 60 mV. Oxidation anodic peak for ABZ was appeared at 0.873 V. The anodic peak due to the oxidation of the sulphur atom in the ABZ molecule [31, 32], and no peaks was observed in the cathodic direction, which indicates that irreversible process. The proposed mechanism for the oxidation of the sulphur atom may be as described by Lourencao et al [28] (Scheme 2).

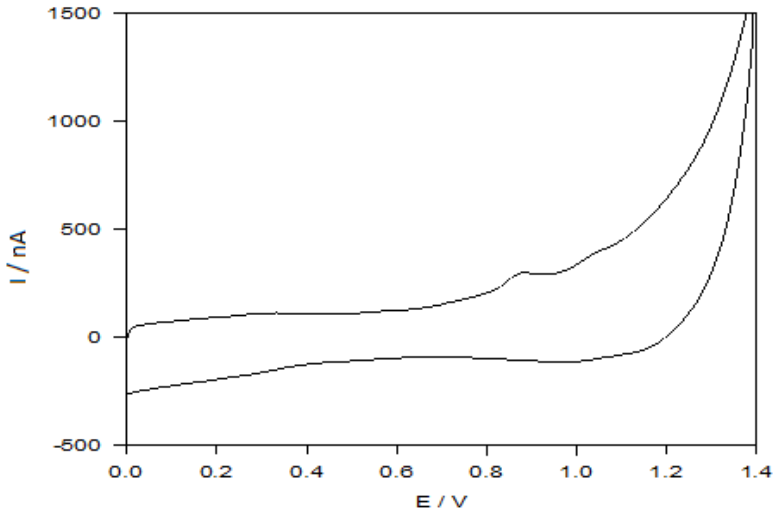
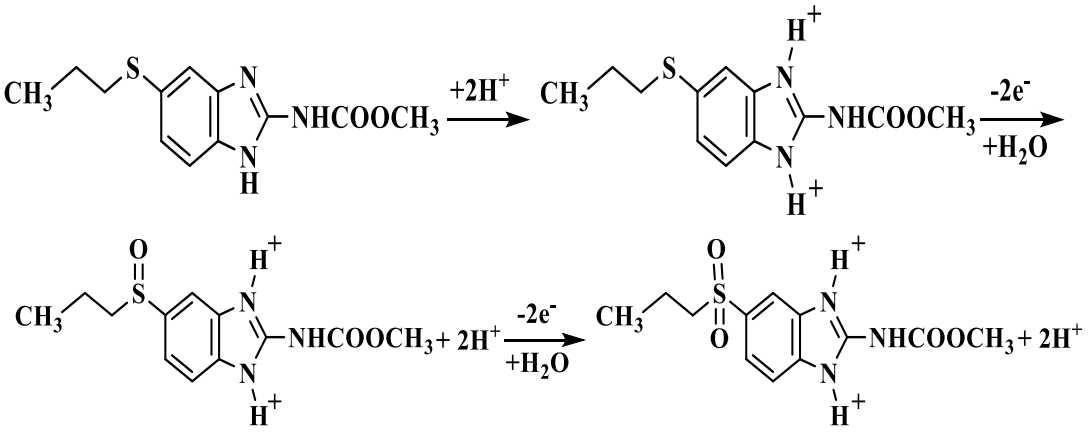


Figure 1 Cyclic voltammogram for 1.0×10^{-7} M ABZ in 0.04 M BR pH 4.01 at accumulation potential 0.1 V and accumulation time 60 s.



Scheme 2. Oxidation of ABZ.

The influence of the scan rate values on the oxidation peak currents and peak potentials for ABZ was studied from 10-100 mVs^{-1}. The oxidation peak current for ABZ increased by increasing the scan rate values. By plotting the peak current logarithm versus the scan rate logarithm (Fig. 2), a straight-line relationship with a slope of 0.90 was developed, which is close to the theoretically predicted value (1.0) for the ideal surface species response [33].

ABZ peak potential moves to more positive values by increasing scan rate values, which prove the irreversible behavior of the electrochemical method. Therefore, ABZ oxidation on CPE is an irreversible method of adsorption.

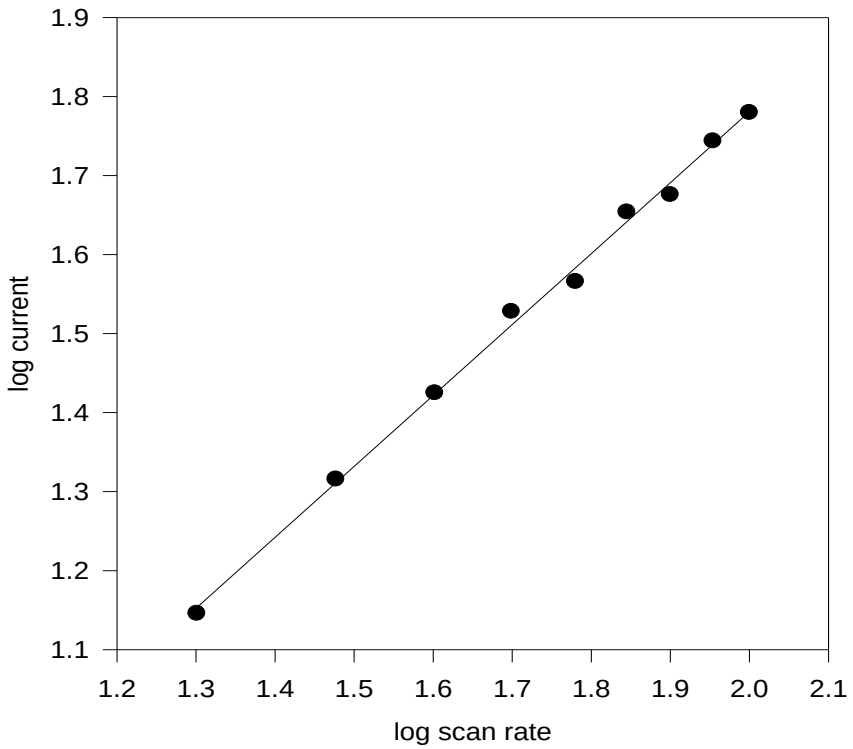


Figure 2. The linear dependence of log anodic peak current *Vs.* log scan rate for $1x10^{-7}$ M ABZ using cyclic voltammetry, the experimental data as mentioned in Figure 1.

3.2. Effect of different electrolytes and pH

Different electrolytes such as BR, acetate, potassium chloride, citrate, phthalate and sodium perchlorate buffers, were examined. BR buffer was selected as a supporting electrolyte because it provides the maximum peak current and the best peak form, so BR buffer was selected for further investigations. Influence of pH on peak oxidation current and potential was investigated in the range 20-110 (Fig. 3). The anodic peak current reach the optimum value at pH value of 4.01. The potential is moved to more negative values, indicating that protons actively participate in the mechanism of electrode reaction.

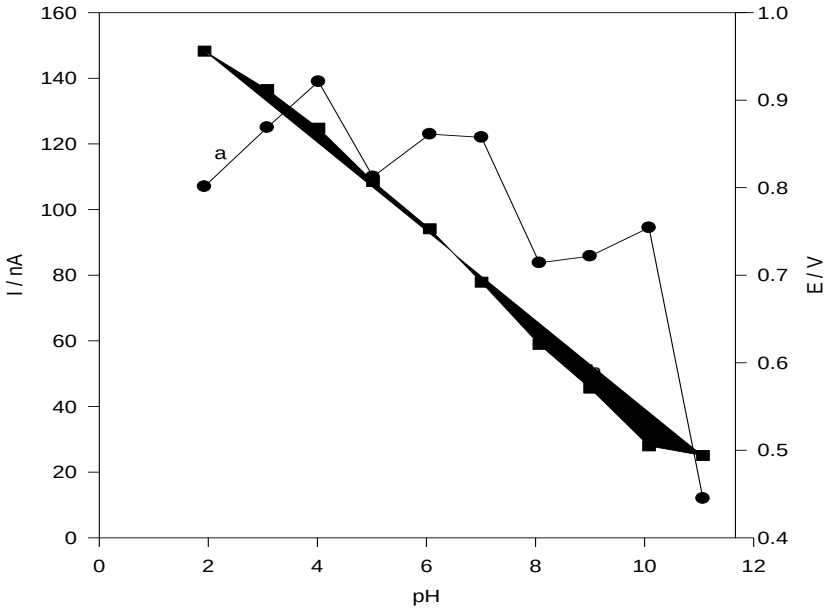


Figure 3. The effect of pH on the anodic peak current (a), and peak potential (b) for 2×10^{-6} M ABZ in BR buffer using accumulation potential 0.0 V, accumulation time 30s, and scan rate 50 mVs^{-1}.

3.3. Accumulation potential

The effect of accumulation potential on DP anodic peak current was tested for $9.98x10^{-8}$ M ABZ using 30 s accumulation time, 50 mV pulse amplitude and 50 mVs^{-1} scan rate. The height of oxidation current increased from 0.0 to 0.1 V, then remains nearly constant on increasing accumulation potential to 100 mV Fig. 4, thus 0.1V accumulation potential was chosen for further work.

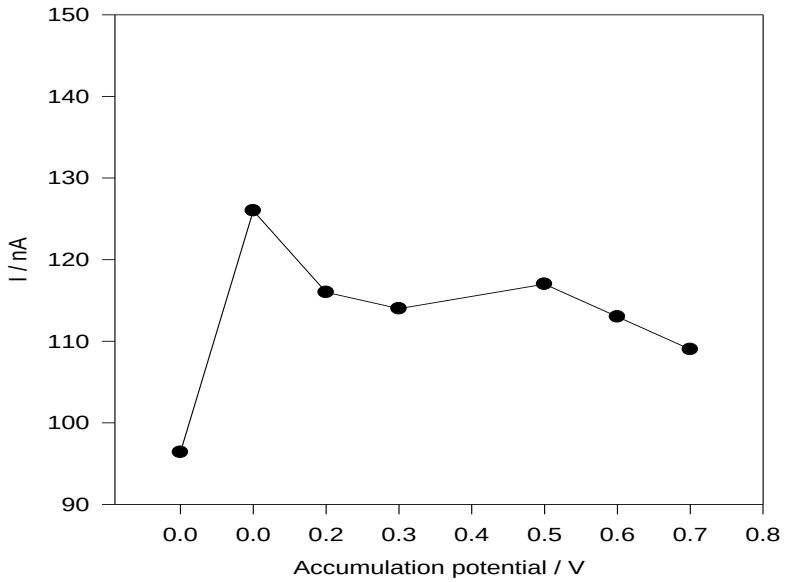


Figure 4. The influence of accumulation potential on the height of anodic peak current for 9.98×10^{-8} M ABZ by using 50 mV pulse amplitude,30 s accumulation time and 50 mVs^{-1} scan rate.

3.4. Accumulation time

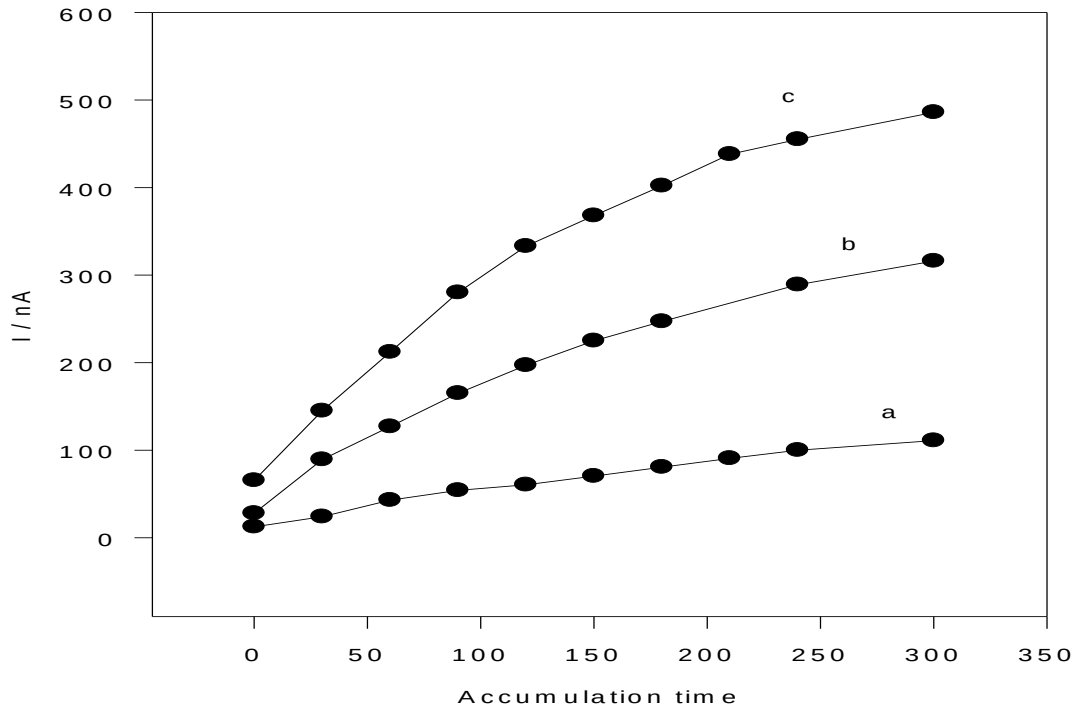


Figure 5. Dependence of anodic peak current on accumulation time for a) $5x10^{-8}$ M, b)1×10^{-7} M, and c) 2×10^{-7} M ABZ in BR buffer pH 4.01 at accumulation potential 0.1 V, scan rate 50 mVs^{-1}, and pulse amplitude 50 mV.

The effect of accumulation time on ABZ oxidation peak current has been investigated using different concentrations, 5×10^{-8}, 1×10^{-7} and 2×10^{-7} M (Fig. 5). With the rising the period of accumulation a liner increase in oxidation current was observed. This means that the drug concentration on the surface of CPE increases at a higher accumulation time, thereby increasing the peak current. Therefore, 90s accumulation time was commonly used for later studies.

3.5. Influence of different instrumental parameters

The dependence of the anodic peak current height of 1×10^{-7} M ABZ on the pulse amplitude was studied over the range 10-100 mV using differential pulse technique. The peak current increased by raising pulse amplitude from 10 to 60 mV and after that the peak current remains nearly constant Fig. 6, so a pulse amplitude of 60 mV was chosen for additional studies.

The effect of a peak current of 1×10^{-7} M ABZ with a variation in the scan rate over a range of 10-80 mVs^{-1} was studied using a differential pulse technique. The peak current increased from 10 to 80 mVs^{-1} (Fig. 7). The scan rate of 70 mVs^{-1} was chosen for further work, this scan rate provides the best current and shape.

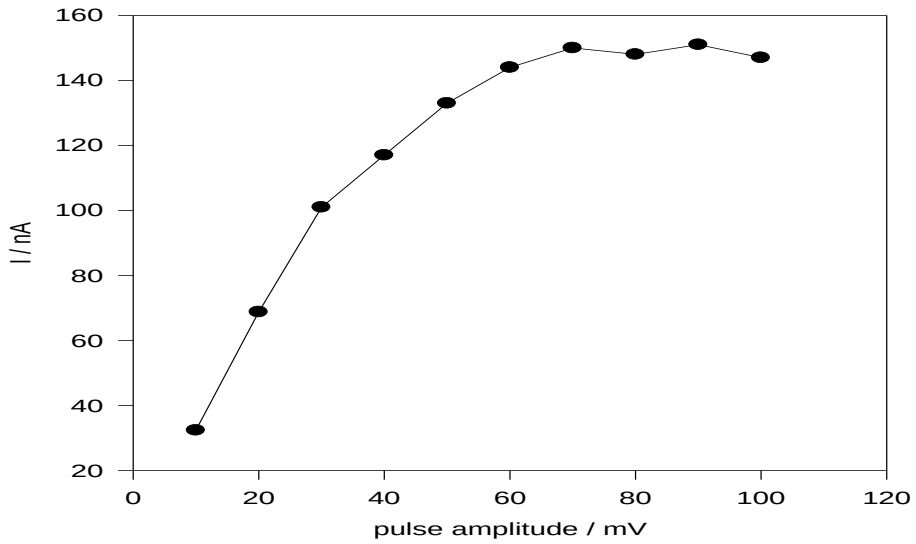


Figure 6. Influence of pulse amplitude on the oxidation current for 1×10^{-7} M ABZ in BR buffer pH 4.0 using accumulation potential 0.1 V, accumulation time 90 s, and scan rate 50 mVs^{-1}.

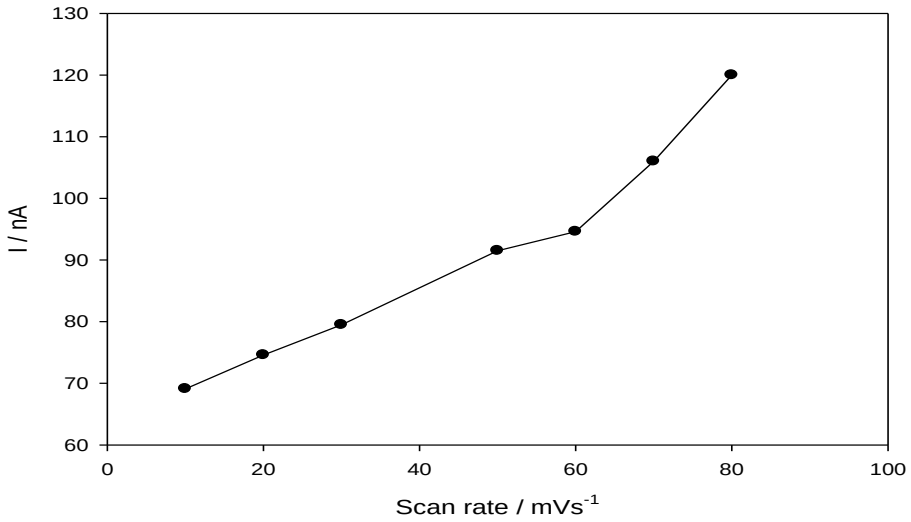


Figure 7. Influence of scan rate on the oxidation peak current height for 1×10^{-7} M ABZ in 0.04 M BR buffer pH 4.01 using accumulation potential 0.1 V, accumulation time 90 s, and pulse amplitude 60 mV.

3.6. Calibration plot

ABZ was detected using CPE under the optimum conditions mentioned in Fig. 7, using DPV. The effect of ABZ concentrations was studied from 0.0265 to0.1855 µg/ml. Fig. 8a represents the DPV using standard addition method. The linear regression equation obtained:

I (nA) = 128.14 + 6123.99 C

Where C is ABZ concentration (µg/ml), with a correlation coefficient of 0.9959 (Fig. 8b). The limit of detection and limit of quantitation were calculated as reported before [34] and were found to be 0.015 and .048 µg/ml ABZ, respectively. The parameters obtained from the linear relationship are shown in (Table 1). The detection limit was 0.015 µg/ml was obtained; this value was compared with the data obtained from literature and summarized in Table 2.

Table 1. The calibration graph parameter for ABZ determination using the DPV method.

Results	***Parameter***
0.0265-0.1855	*Linear range ($\mu g ml^{-1}$)*
6123.143	*Slope*
128.1429	*Intercept*
0.995	*Correlation coefficient (r)*
0.015	*LOD ($\mu g ml^{-1}$)*
0.048	*LOQ ($\mu g ml^{-1}$)*

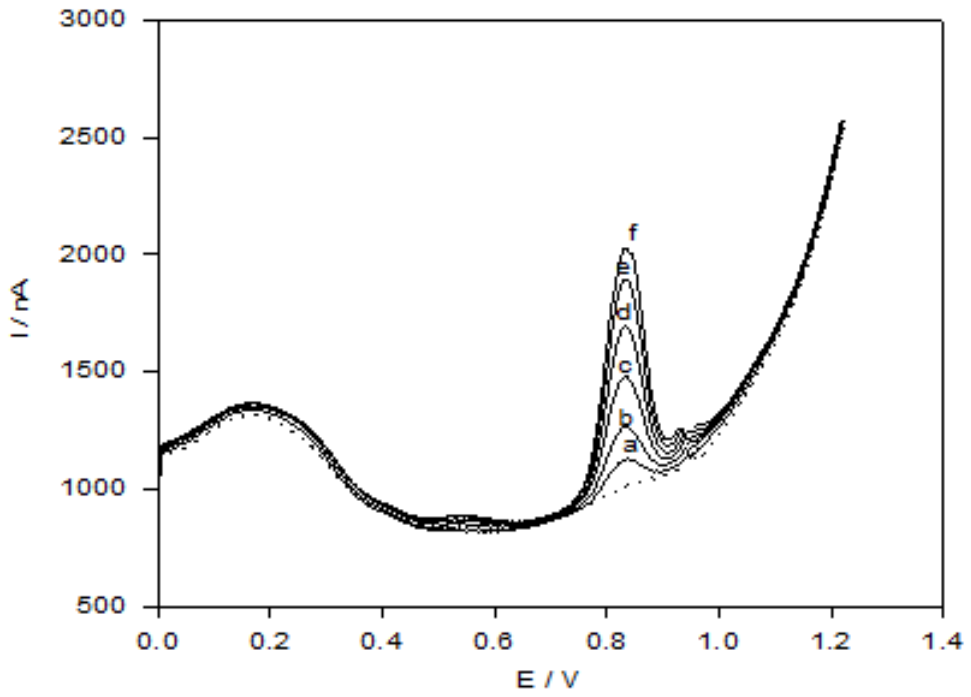


Figure 8a DP voltammograms for various ABZ concentrations, using the optimum conditions mentioned before.

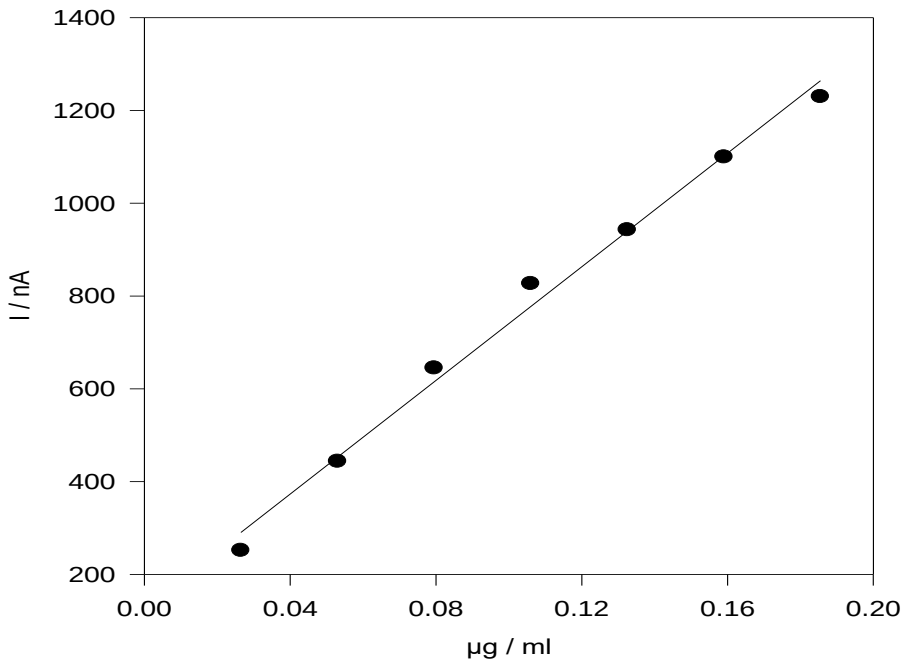


Figure 8b. Calibration plot for ABZ using the optimum conditions mentioned before.

Table 2. Summary of reported method for detection of ABZ

LOD	Technique	Reference
$1.5x10^{-5}$ M	DPV	Present work
$3.0x10^{-5}$ M	LSV	35
$6.2x\ 10^{-5}$ M	SWV	35
$4.0x10^{-5}$ M	DPV	35
$0.3x10^{-6}$ M	DPV	36
$6.08x10^{-8}$ M	DPV	37

3.7. Repeatability and robustness

The intraday and inter-day accuracy presented as RSD are 1.036% and 1.630%, respectively. The robustness of the suggested solution has been measured by investigation of the influence of minor variations in some relevant methods, such as pH of the BR buffer (3.97-4.07), pulse amplitude (57-63), and accumulation time (87-93). None of the improvements greatly impact the recovery of the drug as mentioned in Table 3.

Table 3. Reliability results of the proposed method.

Variable	Recovery, %	SD
pH		
3.97	99.20	0.825
4.01	100.99	0.655
4.07	99.84	2.13
Pulse amplitude (mV)		
57	96.98	2.181
60	100.99	0.655
63	100.015	1.838
Accumulation time (s)		
87	98.95	0.855
90	100.99	0.655
93	98.50	2.480

(Average of four determinations).

3.8. Interferences

The effect of excipient interferences commonly observed in pharmaceuticals has been studied. No interference (< 3% shift in current height) was found by adding 100 times excess magnesium stearate, talc, maize starch, lactose or microcrystalline cellulose. The results have clearly shown that the developed method has a good selectivity.

3.9. Analytical applications

For the ABZ assay in Bendax tablets (200 mg ABZ/tablet), the proposed DPAV approach was successfully applied. Fig. 9 represents the obtained DPV for ABZ using standard addition method.

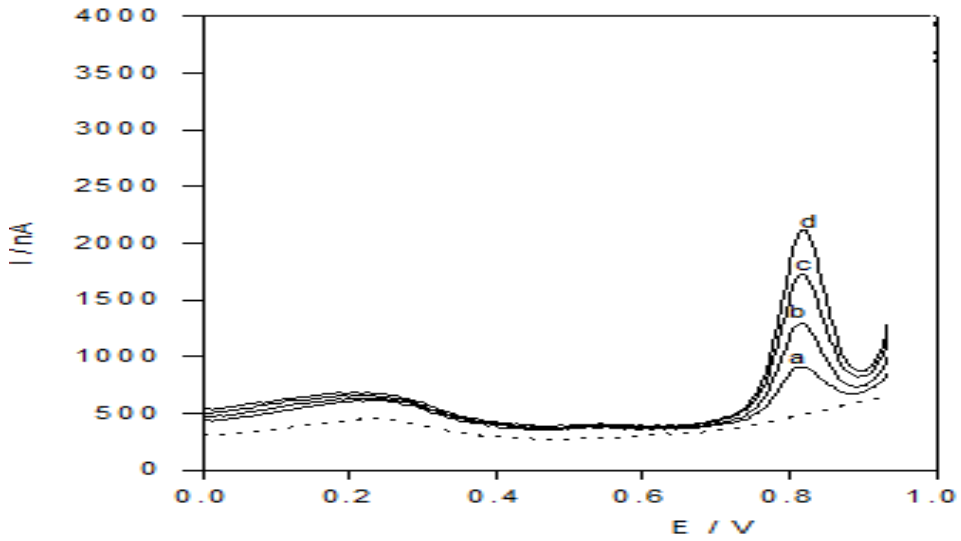


Figure 9 DPV obtained for the determination of ABZ in the Bendax tablets using the optimum conditions mentioned before (a) 1.50×10^{-7} M ABZ in tablets; (b) 1.49×10^{-7}; (c) 2.97×10^{-7}; (d) 4.45×10^{-7} M ABZ.

Table 4. Determination of ABZ in Bendax tablets using the proposed voltammetric method.

Taken (M)	Found (M)	Recovery, %	SD	RSD, %
7.49×10^{-8}	7.25×10^{-8}	96.80	1.542	1.593
1.50×10^{-7}	1.48×10^{-7}	98.80	1.610	1.630

(Average of four determinations)

Table 5. Statistical analysis between the analysis of the Bendax tablets using the proposed DPV approach and the other approaches listed in the literature.

Parameter	Proposed DPV method	Reference method [34]
Mean recovery, %	97.80	97.85
SD, %	1.576	1.448
RSD, %	1.612	1.480
F-ratio (9.28)*	1.185	
T-test (2.447)**	0.047	

(Average of 4 determinations for DPV method and the reference methods).
* Tabbulated F-value at 95% confidence level.
** Tabbulated t- value at 95% confidence level and six degrees of freedom.

Average recovery percentage based on the four-determination average of the SD and RSD values shown in Table 4. The results show that there is no effect from the excipients used in the preparation of the tablets. The obtained results were compared with other data obtained from the reference HPLC method [28] (Table 5). Student's t-and F-tests (95% trust level) were used [38]. The findings showed that the measured t-and F-values did not surpass the theoretical values from which it can be inferred that the precision and accuracy of the suggested voltammetric method did not vary substantially from the reference HPLC method.

3.10. Detection of ABZ *in human urine*

The higher selectivity of this method allowed ABZ to be determined in human urine using standard addition method at $8x10^{-8}$ and $1.5x10^{-7}$ M ABZ. Mean recoveries were 99.10% and 98.87% for the two concentrations, with SD of 1.770 and 0.998 (Table 6). Typical differential pulse voltammograms for the determination of ABZ in spiked human urine are shown in (Fig. 10).

Table 6. Detection of ABZ in urine samples by the suggested procedure.

Taken (M)	Found (M)	Recovery, %	SD
8.00×10^{-8}	7.928×10^{-8}	99.10	1.770
1.50×10^{-7}	1.48×10^{-7}	98.87	0.998

(Average of five determinations)

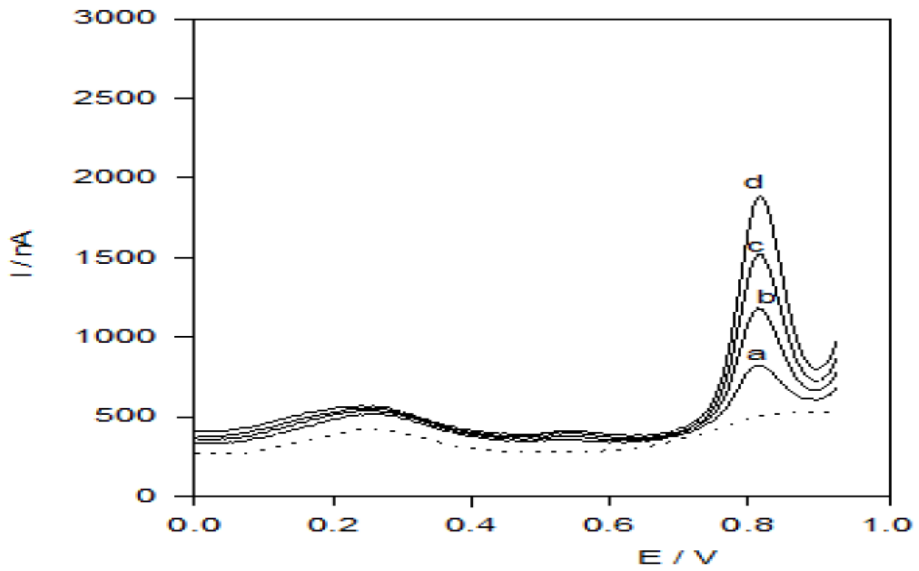


Figure 10. DPV obtained for the determination of ABZ spiked into human urine using the optimum conditions mentioned before. (a) spiked urine sample containing $1.50x10^{-7}$ M ABZ; (b) $1.49x10^{-7}$; (c), $2.97x10^{-7}$ and (d), $4.45x10^{-7}$ M ABZ. The dotted line represents the blank solution.

4. CONCLUSION

ABZ can be determined with high efficiency by using DPAV technique based on its oxidation over CPE. DPAV technique provides a useful tool for its detection of ABZ at lower concentration levels. The suggested methodology showed different benefits, such as detection without pre-treatment for samples or low time consuming, No extraction steps were needed, simple preparation and easy surface renovation of CPE. This approach is sensitive and there is no intervention in the study of other elements (excipients) found in urine. The positive results obtained in the study indicate that the suggested methods are sufficient for the detection of ABZ in pharmaceutical formulations and urine. The suggested approach is cheaper than alternative methods such as HPLC and can also be extended to the routine detection of drugs in quality control labs.

ACKNOWLEDGEMENTS
The authors thank Taif University for generous financial support by Taif university Researchers Supporting Project number (TURSP-2020/14).

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