

## The Dependence of Boron Concentration in Diamond Electrode for Ciprofloxacin Electrochemical Sensor Application

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**Abstract:** This study investigates the effects of boron concentration on boron-doped diamond (BDD) electrodes for electrochemical sensors of ciprofloxacin. The effects of boron concentration, scan rate, and pH of BDD electrodes with boron concentrations of 0.1, 0.5, and 1% were examined to determine the optimal conditions. Furthermore, square wave voltammetry (SWV) in phosphate buffer pH 7 was used to analyze the electrochemical behavior of ciprofloxacin. The results revealed a linear calibration curve in the concentration range of 30–100  $\mu\text{M}$  with a recovery of 85–110%. Meanwhile, BDD electrode with the highest boron concentration in this experiment (1%) showed a very low limit of detection of 0.17  $\mu\text{M}$ , meaning that 1% BDD gave a highly sensitive and significant measurement result for the electrochemical sensor of ciprofloxacin. With the results given, this study provides new insights for controlling boron concentrations in diamond electrodes for the electrochemical sensors of quinolone antibiotics.

**Keywords:** boron-doped diamond; ciprofloxacin; human and health; voltammetry

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### ■ INTRODUCTION

Ciprofloxacin (1-cyclopropyl-6-fluoro-4-oxo-7-piperazin-1-yl-quinolone-3-carboxylic acid) or CIP is a second-generation fluoroquinolone, the most active quinolone antibiotic derivative in medical treatment which has effective antibacterial activity [1-4]. CIP is commonly used in farm and animal husbandry, as well as in the prevention and etiology of microbial diseases.

However, CIP is poorly metabolized in the human body; in which 70% of this antibiotic will be excreted in feces and urine, and large amounts of the residues can be found in surface water and wastewater [2,5-6]. In addition, the residue of CIP is one of the major chemical contaminants in milk and dairy products, making them unfit for consumption and can pose several risks to public health [5-6]. Due to the presence of these antibiotic compounds in the environment for a long time,

pathogenic microorganisms can become persistent and survive in the environment as they are difficult to decompose on their own. Therefore, European countries, through the European Union law (Eur-Lex), state that CIP in the aquatic environment (threshold  $EC_{50} \leq 1$  ppm) is highly toxic to aquatic and soil organisms [7], and set the maximum residue limit for this antibiotic in the milk of  $0.1 \text{ mg L}^{-1}$  [8].

To produce CIP detection results with high sensitivity and accuracy, several methods can be employed, such as high-performance liquid chromatography (HPLC) [9], UV-VIS spectrophotometry [10], electrochemical analysis [11], and capillary electrophoresis [12]. However, these methods are expensive. They require a lot of chemicals and take a long time. As an alternative, the application of electrodes as electrochemical sensors was analyzed in this study using the electroanalytical voltammetry method. This is possible because CIP has electroactive molecules; the piperazine ring in the structure of CIP can be oxidized electrochemically. This method has numerous advantages, including being effective and efficient and having high sensitivity, low cost, fast analysis speed, and simple instrumentation [13].

Studies to determine the electrochemical properties of CIP by electrochemical methods have been carried out with various electrodes, such as glassy carbon electrode modified with graphene oxide and nickel nanoparticles (NiONPs-GO-CTS: EPH/GCE) [14], reduced-GO/GCE [5], gold nanoparticles (AuNPs), and a chitosan (CHI) nanocomposite film coated on a screen-printed electrode (SPE) [4], GCE modified with activated carbon and AuNPs (AuNPs/AC/GCE) [3], and glassy carbon paste electrode [15] for laboratory analyses of sensing in biological samples and wastewater. In the last 10 years, the uses of boron-doped diamond (BDD) electrodes have grown rapidly and attracted the attention of researchers around the world, especially for their application as electrochemical sensors. For example, the voltammetric behavior of irreversibly oxidized CIP has been investigated using the cyclic voltammetry (CV) technique with BDD electrodes [16]. The effect of doping level on the electrochemical reduction of  $\text{CO}_2$  at BDD electrodes has also been studied [17].

Different from conventional metal and carbon  $\text{sp}^2$  electrodes, BDD electrodes have good electrochemical properties, i.e., wide potential window (up to 3.5 V), good sensitivity and stability, low background current, high thermal conductivity, and electrochemical corrosion resistance, thus having been widely used for electroanalysis, electrocatalyst, and electrosynthesis applications [18-22]. These properties may depend on several factors, such as boron doping level, surface termination, and impurities of non-diamond  $\text{sp}^2$ -bonded carbon [23]. BDD electrode consists of a carbon structure with mostly  $\text{sp}^3$  C-C bonds; lattice defects generated by boron atoms can produce electrodes with adjustable conductivity [24]. In other words, the boron concentration of the BDD electrode determines the electrical conductivity of the diamond, which affects its electrochemical properties. The level of doping can control conductivity, and a diamond can be changed from an insulator to a conductor-like metal diamond if doped with boron in a relatively high doping concentration (103–104 ppm) so that it can be used as an electrode material.

This study aims to examine the effects of boron concentration in BDD electrodes on the performance of electrochemical sensors of ciprofloxacin. For experimental purposes, three BDD electrodes with different boron concentrations were prepared by controlling the ratio of boron and carbon sources to be used to study the relationship between boron concentration in BDD electrode and its ability to detect quinolone antibiotics.

## ■ EXPERIMENTAL SECTION

### Materials

CIP ( $\geq 98\%$ ), sulfuric acid ( $\text{H}_2\text{SO}_4$ , 95–98%), Levofloxacin (LEV, 98–102%), Ofloxacin (OFL,  $\geq 98\%$ ), and D-glucose (D-GLU,  $\geq 99\%$ ) were purchased from Sigma Aldrich. Two samples of pharmaceutical tablets containing 500 mg CIP were purchased at a local pharmacy. In addition, this study used sodium dihydrogen phosphate ( $\text{NaH}_2\text{PO}_4$ ,  $\geq 99\%$ ) and sodium hydrogen phosphate ( $\text{Na}_2\text{HPO}_4$ ,  $\geq 99\%$ ) from Merck, sterilized animal milk, and wastewater from a river in

East Java, Indonesia. Milk and wastewater were filtered before use, whereas all chemicals were used without further purification.

### Instrumentation

The preparation of 0.1, 0.5, and 1% (B/C) BDD electrodes refers to a previous report, namely by depositing BDD on the surface of the silicon wafer (111) using a microwave plasma-assisted chemical vapor deposition (MPCVD) machine (Model AX6500X, CORNES Technology Corp) [23]. The deposition time was 6 h. Raman spectra were recorded with Acton SP2500 (Prince Instruments) in ambient air at room temperature. All electrochemical measurements were performed with an Emstat3+ Blue PalmSens potentiostat.

### Procedure

BDD electrodes were characterized by Raman spectroscopy with an excited wavelength of 532 nm and CV. Prior to electrochemical measurements, the BDD electrodes with a diameter of 0.5 cm were always rinsed with an aqueous solution by sonication. To remove contaminants from the surface electrodes, electrochemical pretreatment was carried out by CV prepared with a potential range of  $-2.5$  to  $2.5$  V for 40 cycles in an aqueous solution of  $0.1$  M  $\text{H}_2\text{SO}_4$ . The CV measurements also checked the potential window for each BDD electrode.

CIP stock solution of  $1$  mM was prepared by dissolving CIP in  $0.1$  M  $\text{H}_2\text{SO}_4$ , while the phosphate-buffered saline (PBS) was made by mixing  $0.1$  M  $\text{NaH}_2\text{PO}_4$  and  $0.1$  M  $\text{Na}_2\text{HPO}_4$  and then adjusting it to the required pH ( $5$ – $8$ ). Meanwhile, the standard stock solution of the pharmaceutical tablet sample was produced by crushing a tablet in a mortar and dissolving the powder in  $0.1$  M  $\text{H}_2\text{SO}_4$ . A single-compartment three-electrode cell was used for electrochemical measurements with BDD as the working electrode, Ag/AgCl (saturated KCl) as the reference electrode, and Pt mesh as the counter electrode. The measurements of electrochemical sensors for CIP were performed using the square wave voltammetry (SWV) method by dissolving  $1$  mM CIP in  $0.1$  M PBS pH  $7$  and placing it into an electrochemical cell with a total volume of  $5$  mL. The optimization of parameters in these measurements includes signal per

background, potential scan rate, linearity, selectivity, and optimal pH. Linearity determines the limit of detection (LOD), limit of quantification (LOQ), and the sensitivity of the BDD electrode. LOD was defined as three times the standard deviation of the intercept, while LOQ was defined as ten times the standard deviation of the intercept, both divided by the slope of the calibration curve. In this study, the voltammetry method was applied to detect CIP in pharmaceutical tablets, milk, and wastewater samples. The parameters of the validity of this method are characterizations of %RSD, %reproducibility, and %recovery.

## ■ RESULTS AND DISCUSSION

### Characteristics of the BDD Electrode

Raman spectroscopy provides information to determine the presence of  $\text{sp}^2$ -bonded carbon on the surface electrode [23]. In addition, the structure of the diamond can be identified by the Raman peaks corresponding to the  $\text{sp}^3$ -bonded carbon [17]. Fig. S1 shows that the peaks of  $0.1$ ,  $0.5$ , and  $1\%$  BDD electrodes were at around  $1331$ ,  $1329$ ,  $1215$   $\text{cm}^{-1}$ ; none of them was around  $1500$   $\text{cm}^{-1}$ , meaning that all BDD electrodes have no  $\text{sp}^2$  carbon impurities. In the BDD electrode, boron atoms whose radius is larger than carbon displace diamond carbon atoms, which can cause expansion of the diamond lattice and tensile stresses. With an increase in the boron concentration of the BDD electrode, the wavenumber gradually becomes lower due to the tensile stress. Meanwhile, the potential window of the BDD electrodes with various boron concentrations of  $0.1$ ,  $0.5$ , and  $1\%$  was measured by CV with a potential window of  $-2.5$  to  $2.5$  V in an aqueous solution of  $0.1$  M  $\text{H}_2\text{SO}_4$  at a scan rate of  $100$   $\text{mV s}^{-1}$ . As seen in Fig. S2, the width of the potential window decreases with increasing boron concentration [25]. This may be due to the lower fraction of the exposed grain boundaries. Furthermore, the low boron concentration in the BDD structure causes the electronic state at a negative potential to decrease [17].

The signals per background (S/B) of the three BDD electrodes with various boron concentrations were measured by SWV in  $50$   $\mu\text{M}$  CIP and  $0.1$  M PBS at

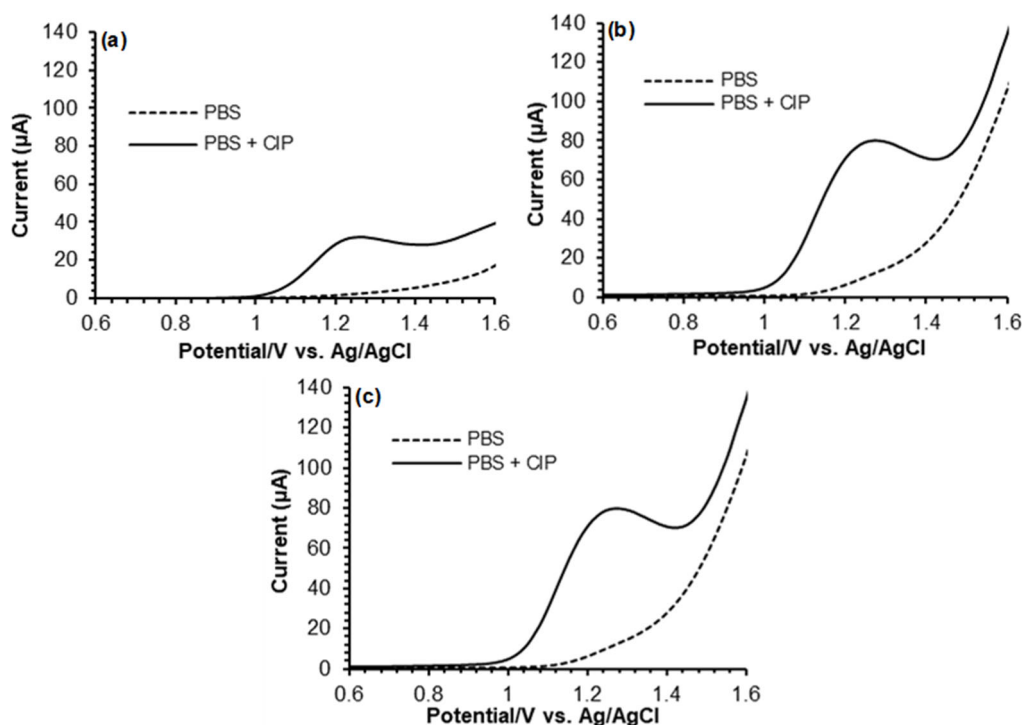
potentials ranging from 0 to 1.8 V (vs. Ag/AgCl), with and without CIP. The ratio between the background current and the CIP signal was identified from these measurements. The S/B values of 0.1, 0.5, and 1% BDD electrodes were 11.85, 14.97, and 16.90, respectively. These results show that 1% BDD electrode, which has the highest boron concentration, has a greater current response per background than the other two BDD electrodes with lower boron concentrations of 0.1 and 0.5% (Fig. 1). The higher the anodic peak current, the higher the electrochemical reactivity due to the increased density of electronic states formed between the band gaps of the diamond structure [17]. Meanwhile, the background currents of all BDD electrodes in this study are relatively low.

### Effects of Scan Rate Variations

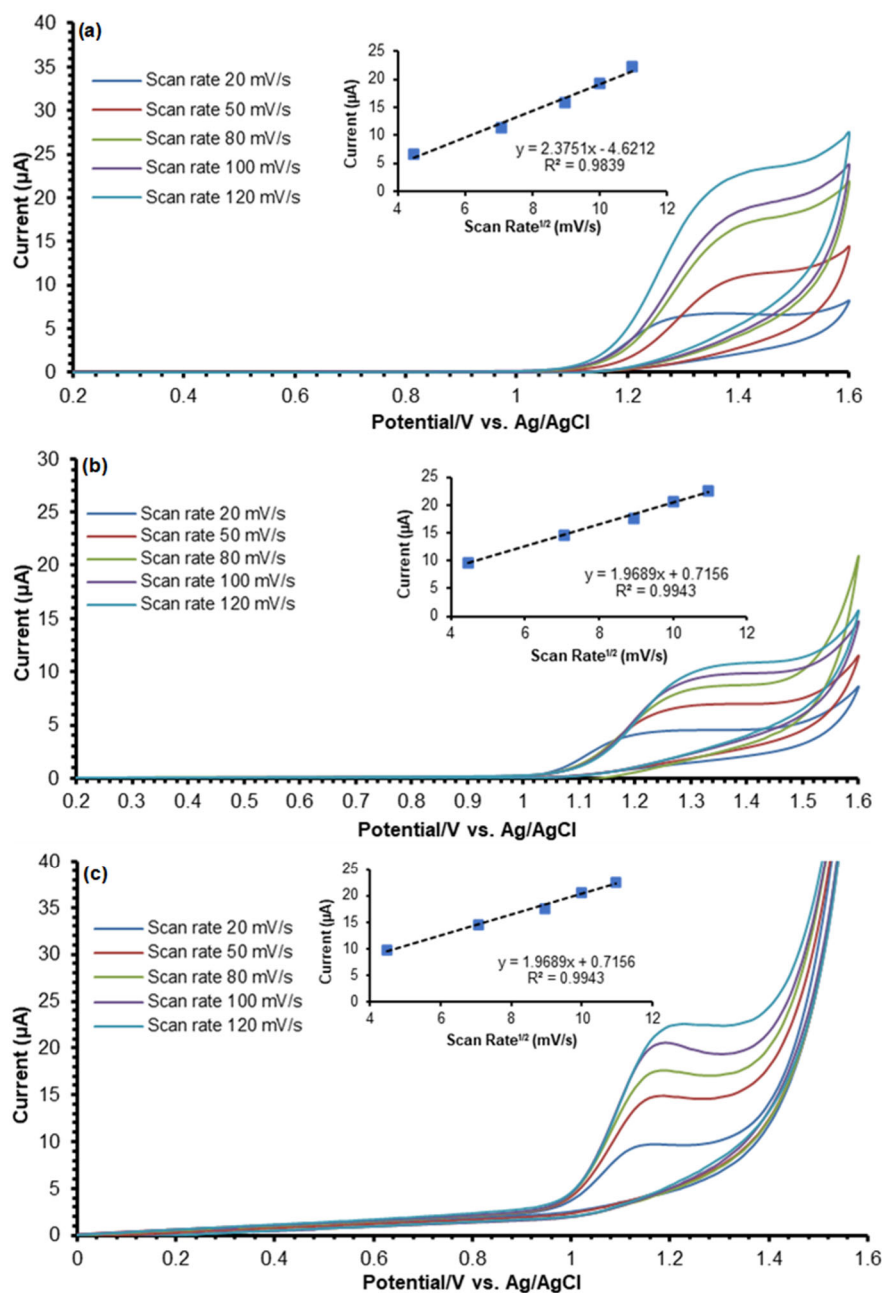
Determination of variations in the scan rate of BDD electrodes with various boron concentrations was measured by CV in 0.1 M PBS pH 7 containing 50  $\mu\text{M}$  CIP at scan rates ranging from 20 to 120 mV/s; the peak increases with increasing scan rate (Fig. 2). This proves

that the difference of scan rate affects the anodic peak current response. These results also reveal that the higher the scan rate, the faster the electron transfer occurs to the surface electrode and the higher the peak of each BDD electrode. In addition, the peak potential is shifted to the positive potential only and not to the negative potential, indicating that the electrode process is electrochemically irreversible (Fig. 2) [16].

The scan rate also corresponds to an increase in the rate of diffusion of species to the electrode; the higher the scan rate, the thinner the resulting diffusion layer. This leads to easier electron transfer on the surface of the electrode, resulting in a higher peak current. Conversely, the smaller the scan rate, the larger the diffusion layer. Thus, the electron transfer process on the surface of the electrode can be inhibited, and the peak current is also smaller. Diffusion control can be seen from the linearity between the square root of the scan rate and the peak current. The linearity between the increased square root of the scan rate and the anodic peak at the BDD electrodes with various boron concentrations of 0.1, 0.5, and 1% is shown by the correlation coefficient ( $R^2$ ) value



**Fig 1.** Background current curves by SWV technique of BDD electrodes with a boron concentration of (a) 0.1%, (b) 0.5%, and (c) 1% in 0.1 M PBS pH 7 containing 50  $\mu\text{M}$  CIP



**Fig 2.** CV with variations in scan rate and the linearity with the square root of the scan rate of BDD electrodes with boron concentration of (a) 0.1%, (b) 0.5%, and (c) 1% in 0.1 M PBS pH 7 containing 50  $\mu\text{M}$ . Inset data is the correlation between square root of scan rate and the current

of 0.99. This suggests that the electrochemical reaction is a diffusion-controlled process [26].

### Effects of pH

The investigation of the effects of pH on BDD electrode was carried out to determine the optimal pH conditions indicated by the highest current response. This

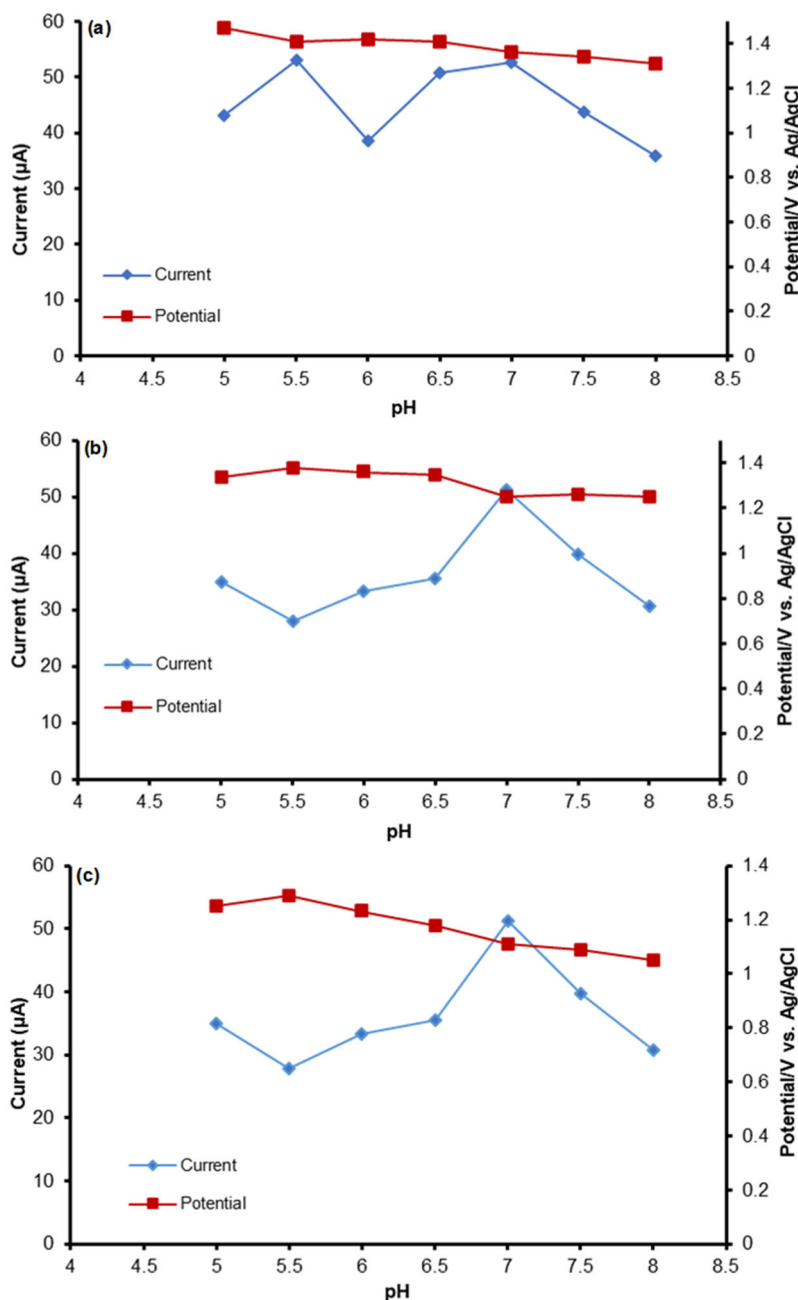
is extremely important as the redox reactions of organic compounds mainly depend on the pH of the supporting electrolyte [4]. Measurements were made using SWV, as the method is known to promote high sensitivity measurements and have a high scanning speed, thus allowing for a short analysis time. These measurements were performed in the potential range from 0 to 1.8 V in



0.1 M PBS (with a pH variation of 5 to 8) containing 50  $\mu\text{M}$  CIP. From these measurements, PBS pH 7 was determined for use in further experiments in this study. Phosphate buffer is used to maintain the pH of the solution and reduce the rate of migration. In addition, the use of phosphate buffer also produces better peak intensity, peak resolution, and voltammogram curves [4].

As shown in Fig. 3, the CIP oxidation potential and current are influenced by pH. The different peak current responses can be caused by the large number of measurable molecules of CIP on the surface electrode; the higher the peak current, the more analyte molecules are measured on the surface electrode.

An increase in pH shifts the potential to a negative



**Fig 3.** SWV of BDD electrodes with a boron concentration of (a) 0.1%, (b) 0.5%, and (c) 1% in PBS pH 5–8 containing 50  $\mu\text{M}$  CIP; the effects of pH on the anodic peak current and peak potential at the three BDD electrodes are shown in the inset

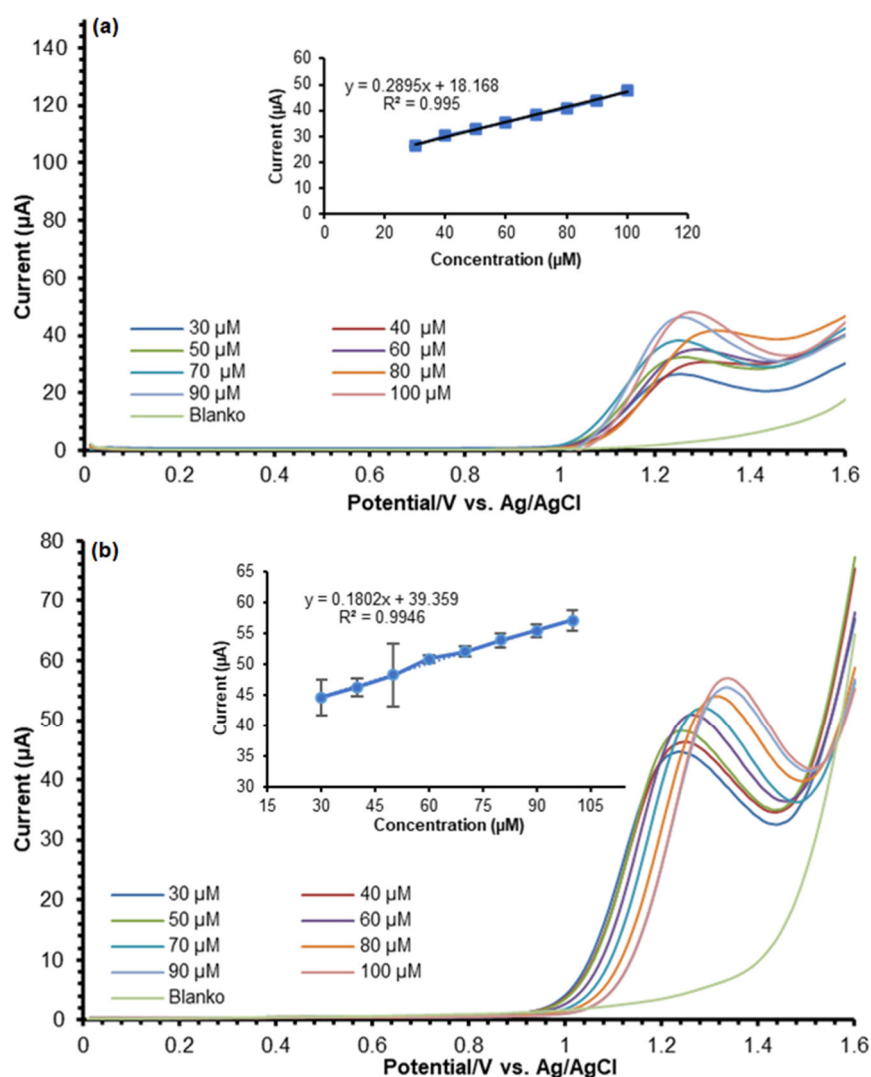
value, suggesting the involvement of protons in the electrooxidation of CIP. Furthermore, the pKa values of CIP, which were reported to be 6.16 and 8.23, can also be negatively and positively charged under various pH values (Fig. 3). CIP is present in the cationic form at  $\text{pH} < 6.16$ , in zwitterionic form at  $\text{pH} 6.16\text{--}8.23$ , and in the anionic form at  $\text{pH} > 8.23$  [27].

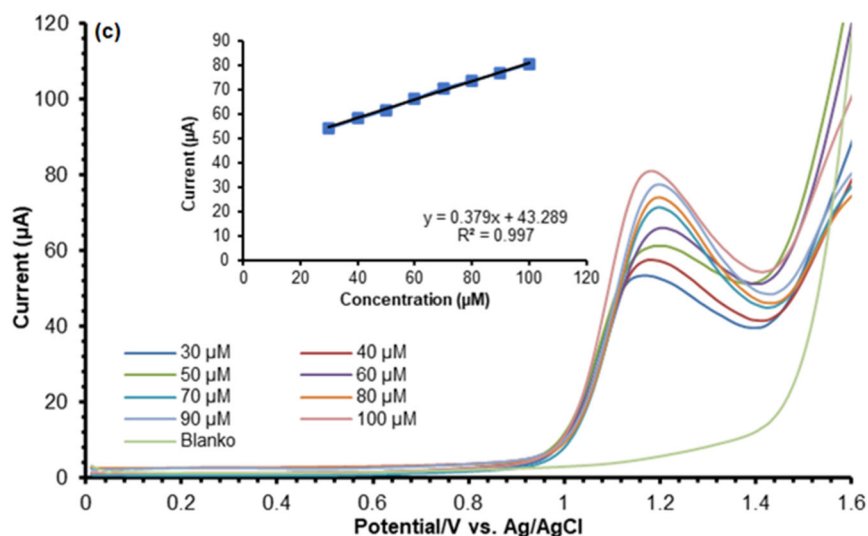
### Effects of CIP Concentration

The electrochemical behavior of CIP in the three BDD electrodes was examined using SWV in 0.1 M PBS at potentials ranging from 0 to 1.8 V (vs. Ag/AgCl) and compared. In this analysis, linearity is the ability of the method to provide a balanced response to the analysis of concentrations in a sample. The calibration curves for the

detection of CIP in the BDD electrodes were plotted linearly from the range of 30 to 100  $\mu\text{M}$ . Meanwhile, the correlation coefficient ( $R^2$ ) values of 0.1, 0.5, and 1% BDD electrodes were 0.995, 0.9946, and 0.997, respectively (Fig. 4).

Limit of detection (LOD) is the smallest quantity of detectable analyte contained in a sample that gives a significant response compared to the blank [28]. The LOD of the three BDD electrodes was measured by the SWV method at various concentrations of CIP from 0 to 1.8 V, with an amplitude of 0.05 V, a frequency of 50 Hz, and a step potential of 0.012 V (Table 1). Measurements were repeated three times for each concentration to obtain the average peak current. To find the LOD, the standard deviation is multiplied by three and divided by





**Fig 4.** SWV of the BDD electrode with the boron content of (a) 0.1%, (b) 0.5%, (c) 1% in different CIP concentrations range 30–100  $\mu\text{M}$ . The insets show the linear correlation between CIP concentration and CIP oxidation current response

**Table 1.** Comparison of the performance of CIP electrochemical sensors in the present work with the results of other published studies

Working electrode	Linear range ( $\mu\text{M}$ )	LOD ( $\mu\text{M}$ )	Ref.
NiONPs-GO-CTS: EPH/GCE	0.04–0.97	6.00	[14]
rGO/GCE	6.00–40.00	0.21	[5]
AuNPs/AC/GCE	0.50–25.00	0.20	[3]
BDDP-printed	1.00–30.00	0.58	[30]
0.1% BDD	30.00–100.00	0.53	This work
0.5% BDD	30.00–100.00	0.43	This work
1% BDD	30.00–100.00	0.17	This work

the slope of the calibration curve. The limits of detection for the measurement of CIP in 0.1, 0.5, and 1% BDD electrodes were 0.53, 0.43, and 0.17  $\mu\text{M}$ , respectively. Meanwhile, the limits of quantitation (LOQ) for CIP of the three BDD electrodes were 1.78, 1.44, and 0.59  $\mu\text{M}$ , respectively. These results show that 1% BDD electrode has the smallest LOD and LOQ among the three BDD electrodes. This can be explained by the relatively higher electrical conductivity of 1% BDD electrode compared to the other BDD electrodes with boron concentrations of 0.5 and 0.1% [17,29], which then can drive higher current response for CIP analysis. On the other hand, as displayed in Fig. 3 and 6, the background current is relatively the same for all BDD electrodes. In addition, from the inset data presented in Fig. 4, it can be seen that the 1% BDD electrode shows the highest sensitivity (0.379  $\mu\text{M}/\mu\text{A}$ ).

The LOD of 1% BDD electrode is 0.17  $\mu\text{M}$ , while the maximum residue limit for CIP in milk, according to Eur-Lex is 0.1  $\text{mg L}^{-1}$  ( $= 0.30 \mu\text{M}$ ). Thus, the developed method can be considered successful in detecting CIP after simple dilution of real samples, which does not require laborious extraction procedures or other materials to maintain the electroactivity of the sensor. Overall, the wide linear concentration range and good sensitivity of the developed method make it a suitable electrochemical application for sensing CIP in pharmaceuticals and real samples.

### Reproducibility and Selectivity

In this study, the %RSD shows the stability and good precision of the BDD electrodes. The lower the concentration of the analyte tested, the greater the %RSD



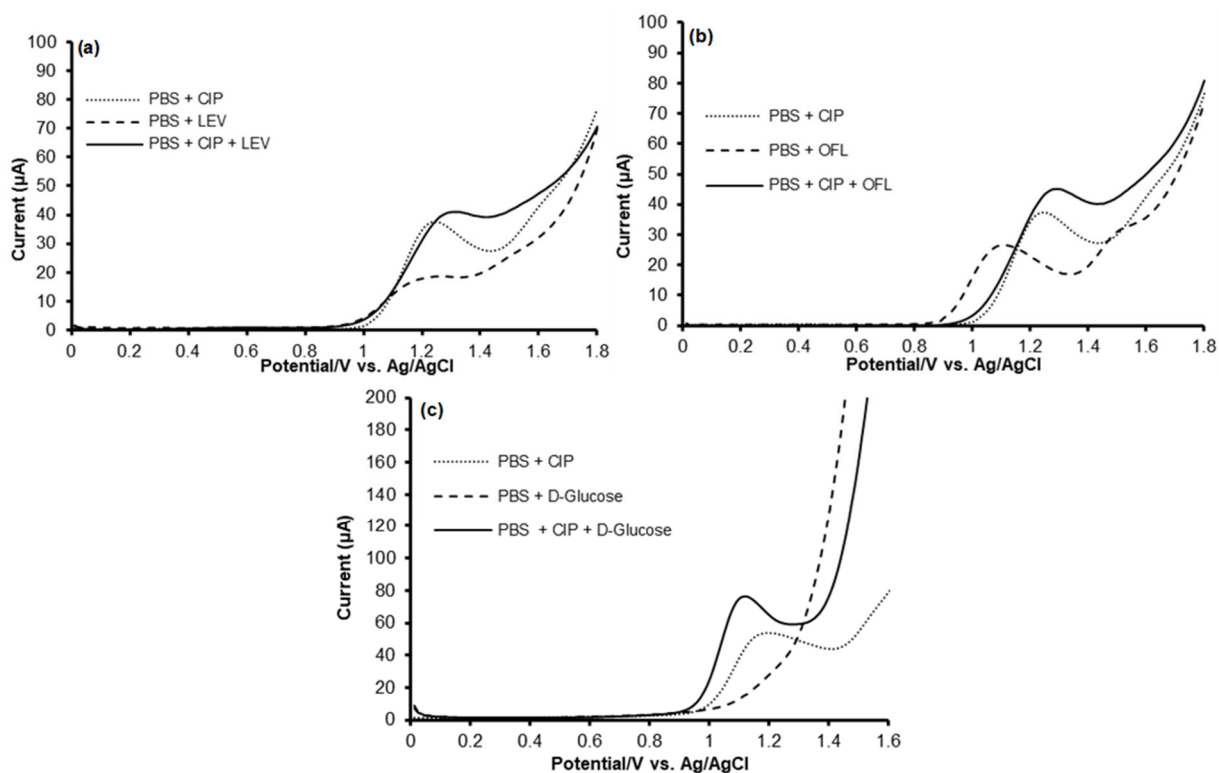
value and the higher the difficulty of the test to achieve good precision. The developed method was employed with 10 replications on different measurement days using 50  $\mu\text{M}$  CIP to test its reproducibility. The %RSD values of the BDD electrodes with boron concentrations of 0.1, 0.5, and 1% were 1.46, 3.23, and 1.77%, respectively. The acceptable %RSD value can be determined by the Horwitz ratio (HorRat) based on the concentration of the analyte used, where the %RSD of the three BDD electrodes is acceptable as the value is  $< 7$  at 50  $\mu\text{M}$  analyte concentration, meaning that all BDD electrodes have good precision. This also indicates good reproducibility of the developed method. The validation parameters for the determination of CIP electrochemical sensors are shown

in Table 2. Among the three electrodes, 1% BDD electrode shows better sensitivity, lower LOD, and higher S/B compare to 0.1 and 0.5% BDD electrodes.

In the analysis, selectivity is the ability of the method to measure a particular substance, such as an analyte, for an accurate and specific determination of the presence of other compounds in an aquatic environment or other environments that may be present in complex matrices. Apart from CIP, two other antibiotics, namely LEV and OFL are considered as potential interfering agents. These antibiotics, as well as D-GLU which may be contained in milk, are known to oxidize at potentials close to that of CIP. Therefore, these compounds can affect the voltammetry response of CIP.

**Table 2.** Validation parameters for the determination of CIP electrochemical sensors

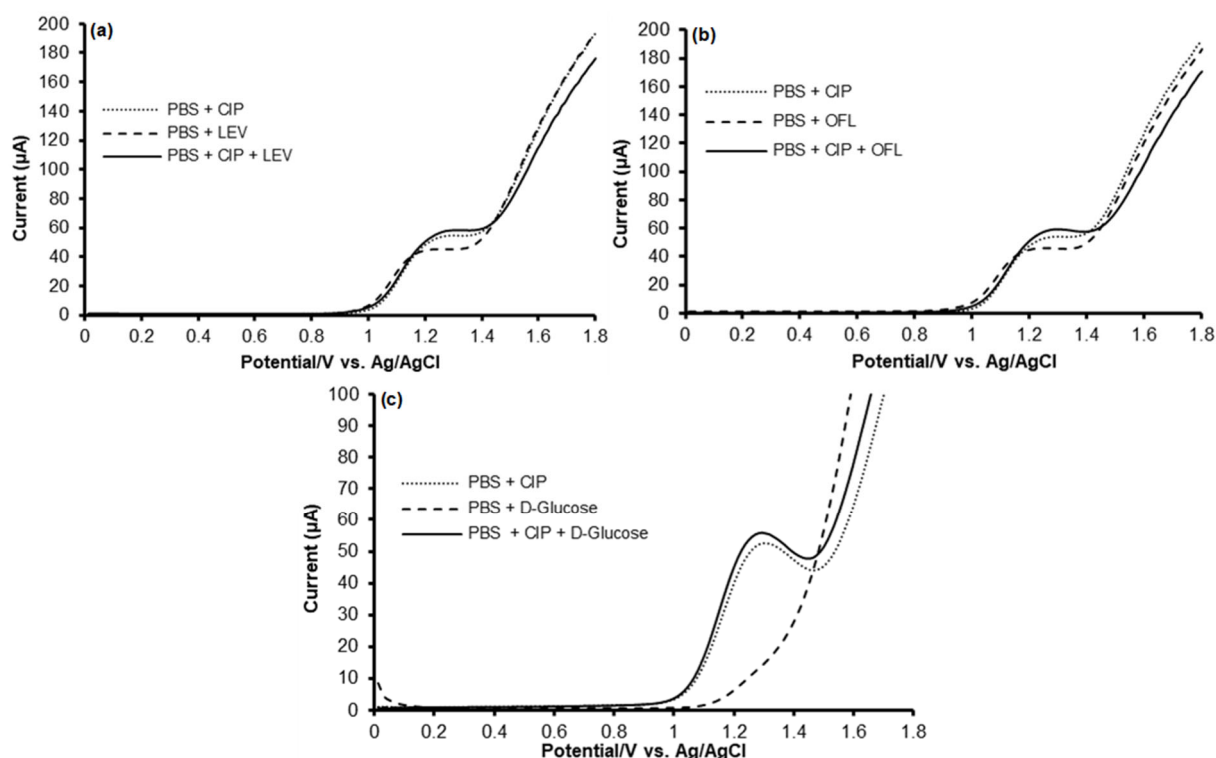
Electrode	Parameter				
	S/B	Sensitivity	R <sup>2</sup>	LOD ( $\mu\text{M}$ )	%RSD
0.1% BDD	11.850	0.280	0.995	0.530	1.460
0.5% BDD	14.970	0.180	0.994	0.430	3.230
1% BDD	16.900	0.370	0.997	0.370	1.770



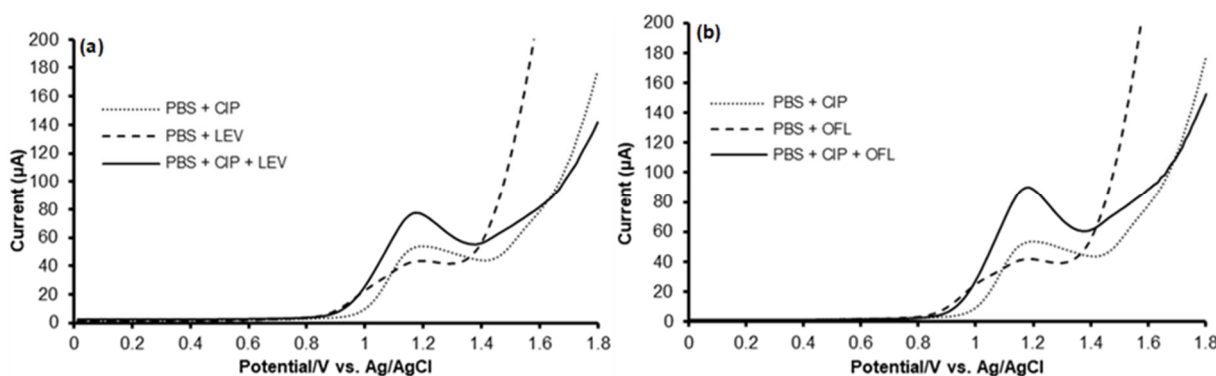
**Fig 5.** SWV of BDD electrodes with boron concentration of (a) 0.1%, (b) 0.5%, and (c) 1% in 0.1 M PBS pH 7 containing 50  $\mu\text{M}$  CIP and LEV

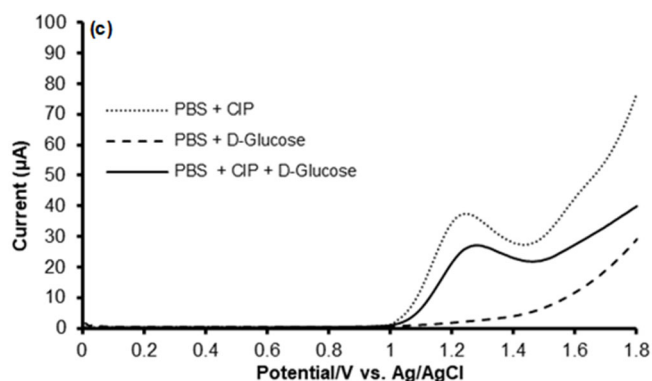
The ratio of the concentrations of CIP to interfering substances is 1:1. In this study, the oxidation peaks of CIP at 0.1, 0.5, and 1% BDD electrodes were found to increase after the addition of LEV and OFL, with LEV and OFL peaks having different currents and potentials from CIP peak. This suggests that the presence of LEV and OFL in an aqueous solution together with CIP is unobtrusive as they have different current peaks (Fig. 5-7). Furthermore, in the presence of D-GLU, only the peak of CIP gives a

signal response, meaning that the presence of D-GLU does not interfere with the detection of CIP. Overall, LEV and OFL have the greatest impact on CIP as they are quinolone antibiotics, and the structural similarity of the coexisting antibiotics and interfering ions affects the detection of CIP within an acceptable level. The differences between the peak current and peak potential of CIP with the addition of interferences are shown in Table 3.



**Fig 6.** SWV of BDD electrodes with boron concentration of (a) 0.1%, (b) 0.5%, and (c) 1% in 0.1 M PBS pH 7 containing 50  $\mu\text{M}$  CIP and OFL





**Fig 7.** SWV of BDD electrodes with boron concentration of (a) 0.1%, (b) 0.5%, and (c) 1% in 0.1 M PBS pH 7 containing 50  $\mu$ M CIP and D-GLU

**Table 3.** The differences between the peak current and peak potential in the selectivity test with the addition of interferences to the BDD electrodes

Electrode	Current			Potential				
	CIP	Interference	Difference	CIP	Interference	Difference		
0.1% BDD	37.48	OFL	45.15	7.66	1.24	OFL	1.30	0.06
	37.48	LEV	41.05	3.56	1.24	LEV	1.30	0.06
	37.48	D-GLU	27.04	10.43	1.24	D-GLU	1.28	0.03
0.5% BDD	54.33	OFL	45.87	8.45	1.29	OFL	1.29	0.00
	54.33	LEV	45.63	8.70	1.29	LEV	1.30	0.01
	54.33	D-GLU	55.92	1.59	1.29	D-GLU	1.29	0.00
1% BDD	53.63	OFL	89.96	36.33	1.18	OFL	1.17	0.01
	53.63	LEV	77.26	23.63	1.18	LEV	1.17	0.01
	53.63	D-GLU	76.48	22.85	1.18	D-GLU	1.11	0.07

**Table 4.** Results obtained by analysis of CIP in pharmaceutical tablets

Electrode	Pharmaceutical tablets	Concentration ( $\mu$ M)		%Recovery	%RSD
		Expected	Found		
0.1% BDD	Sample 1	50	48.16	96.33	2.13
	Sample 2	50	42.78	85.56	3.39
0.5% BDD	Sample 1	50	51.61	103.23	2.24
	Sample 1	50	48.58	97.17	3.08
1% BDD	Sample 1	50	53.11	106.22	2.93
	Sample 2	50	43.81	87.63	0.22

**Table 5.** Results obtained by analysis of CIP in wastewater and milk

Electrode	Samples	Concentration ( $\mu$ M)		%Recovery	%RSD
		Expected	Found		
0.1% BDD	Wastewater	50	45.96	91.92	2.36
	Milk	50	46.18	92.37	3.93
0.5% BDD	Wastewater	50	50.32	100.64	3.45
	Milk	50	48.58	97.17	3.08
1% BDD	Wastewater	50	53.40	106.80	1.44
	Milk	50	53.45	106.91	1.93

### Detection of CIP in Real Samples

The analyses of two pharmaceutical tablets containing 500 mg of CIP and the sensors used in real samples were carried out in environmental water matrices. To verify the developed method, CIP simultaneously detected in synthetic samples was measured by the standard addition method. Furthermore, all samples were spiked with 50  $\mu\text{M}$  CIP in an electrochemical cell to evaluate the accuracy of the developed method. The wastewater and milk samples were only diluted in phosphate-buffered saline as the supporting electrolyte prior to analysis. Tables 4 and 5 present the %recovery of each BDD electrode with a boron concentration of 0.1, 0.5, and 1%.

These results indicate that the %recovery in all measurement analyses is in the range of 85–110%, signifying good accuracy and good results of the method developed in this study. In addition, the developed sensor is proven to allow the simultaneous determination of analytes with high accuracy. Sensors with BDD electrodes of various boron concentrations are capable of detecting CIP in pharmaceutical, wastewater, and milk samples with simple dilution which does not require laborious extraction procedures or chemical additives to maintain the electroactivity of the sensor.

### CONCLUSION

In this study, three BDD electrodes with a boron concentration of 0.1, 0.5, and 1% prepared through the microwave plasma-assisted CVD method were used as sensors for CIP antibiotics. From the Raman spectroscopy, three BDD electrodes do not contain  $\text{sp}^2$  carbon impurities. In addition, the CV characterization shows that the potential window of BDD electrode becomes narrower with increasing boron concentration. Although 0.1 and 0.5% BDD electrodes have a wider potential window, they have a slower response to redox systems compared to 1% BDD electrodes. Furthermore, evaluation of the effects of possible interfering compounds such as D-GLU, LEV, and OFL shows significant results on the current response of the observed analyte. Based on the results, the method developed in this study is proven to have higher accuracy and precision

than other methods employed to real samples. Among the three BDD electrodes, 1% BDD electrode is highly recommended for application as electrochemical sensor of CIP in pharmaceutical samples, wastewater, and milk due to its good response and fast redox reaction. This study reveals that boron concentration in BDD electrode affects the determination of its application as the electrochemical sensor of ciprofloxacin; it is successfully applied in the analysis of sensors of antibiotics in complex samples and can be potentially used in future development of real detection devices.

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### AUTHOR CONTRIBUTIONS

Prastika Krisma Jiwanti conceptualized, writing—review and editing, resources, funding acquisition, supervision. Ilmi Nur Indriani Savitri written original draft preparation, formal analysis, and data curation. Ilmanda Zalzabhila Danistya Putri did the formal analysis, and data curation. Irkham and Yasuaki Einaga provided resources and supervision. Ganden Supriyanto, Yew Hoong Wong, Sachin Kumar Srivastava, Che Azurahaman Che Abdullah supervised the research.

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