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Highly Sensitive Aspartame Electrochemical Sensor in Beverages Sample Using Glassy Carbon Electrode Modified with Boron Doped Nanodiamond/ZnO Nanoparticles Composite

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Abstract. This study reports an electrochemical sensor for detecting aspartame using square wave voltammetry (SWV) on ZnONP/BDDNP electrode. ZnONP/BDDNP was able to oxidize aspartame at a potential of 0.34 V in a phosphate buffer solution pH 2.0 with a current of 80.1 μA. The limit of detection (LOD) was found to be 0.07 μM, the limit of quantitation (LOQ) was 0.25 μM and sensitivity was 1.23 μA μM-1. The relative standard deviation (RSD) was 1.6%, less than 5% indicating that ZnONP/BDDNP has good precision. ZnONP/BDDNP showed better results compared with the BDDNP electrode. The developed method showed good linearity in the concentration range of 30-100 μM. This method was successfully applied to determine aspartame in beverage samples with a recovery range of 85-110%. This shows that ZnONP/BDDNP with the suggested method is potentially applied in practical used.

Keywords: Aspartame; Boron-doped diamond powder; Human & health; Metal oxide nanoparticles

1. Introduction

Aspartame N-(L-α-aspartil-L-phenylalanine methyl ester) is one type of artificial sweetener used by people with diabetes mellitus and obesity (Zafar, 2017; Yılmaz and Uçar, 2014). The human body will convert aspartame into aspartic acid, phenylalanine, and methanol, which will accumulate in the blood (Saeed, 2020). Organoleptically similar to sucrose but approximately 180-200 times sweeter than sucrose (Debras *et al.*, 2022; Jain Grover, and Scholar, 2015; Kirkland and Gatehouse, 2015). Excessive aspartame

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metabolism has a negative impact on the body if consumed in excess. The methanol produced by aspartame is converted to formic acid. This will cause the pH level in the blood to become acidic so our brain will experience a lack of oxygen and cause the mitochondria of nerve cells to be unable to carry out cellular respiration to produce ATP. Reduced energy supply in the brain damages neuron cells, and various toxic processes can occur (Hussein *et al.,* 2022; Rycerz and Jaworska-Adamu, 2013). Phenylalanine, considered a neurotoxin, can stimulate brain neurons in high concentrations causing seizures and other neurological defects. This is dangerous for people born with phenylketonuria (PKU), which prevents them from metabolizing phenylalanine (Newbould *et al.,* 2021; Naik, Zafar, and Shrivastava, 2018). The increasing use of aspartame in the food industry has given new impetus to developing rapid and efficient methods for its determination.

Various methods have been used to detect aspartame levels, some of which are high-performance liquid chromatography (HPLC) (Barakat *et al.,* 2022; Shoeb *et al.,* 2022; Berset and Ochsenbein, 2012), liquid polydimethylsiloxane (PDMS) plasma cavity as a substrate for surface-enhanced Raman spectroscopy (SERS) to detect aspartame added in purified water, ion chromatography (Chen *et al.,* 2020), and electrophoresis (de Carvalho *et al.,* 2014). However, most methods require more complicated procedures, more expensive analysis time, and more expensive instrumentation than electrochemical methods. Electrochemical methods have many advantages, including high sensitivity, low cost, fast analysis speed, effectiveness, efficiency, and simple instrumentation (Munteanu and Apetrei, 2022; Rahmawati *et al.,* 2022; Tajik *et al.,* 2021; Hardi and Rahman, 2020). This research uses the voltammetric analysis method with square wave voltammetry (SWV) measurement technique. The square wave voltammetry technique has the advantage of high sensitivity and fast speed.

BDDNP can be used as an electrode material with a large specific surface area (Kondo, 2019). Compared to conventional BDD electrodes (Prayikaputri *et al.,* 2021; Jiwanti *et al*., 2019; Tomisaki *et al*, 2019; Ivandini *et al*, 2017), BDDNP exhibits a low background current, and a wide potential window, which enable sensitive electrochemical detection with a large S/B ratio (Kondo, 2019; Kondo, 2014). Due to its excellent properties, BDD was an excellent substrate for oxide electrodeposition (Jiwanti, 2020). On the other hand, semiconductor nanoparticles have become a major concern for researchers because of their potential applications in chemistry (Shetti *et al.,* 2019). In particular, ZnONP's unique properties, such as small size, large surface area, higher sensitivity, and being environmentally friendly and inexpensive, make it widely used for electrochemical sensor construction (Agarwal *et al*, 2019; Chaudhary *et al*, 2018; Kumar *et al*, 2015). Moreover, no potential oxidation peak of Zn in the aspartame potential oxidation range makes it suitable for sensitively and selectively detecting aspartame. In this study, the attractive properties of ZnONP and BDDNP will be developed to prepare boron-doped diamond nanoparticle-modified ZnO nanoparticles to detect the artificial sweetener aspartame. The ZnONP/BDDNP modification provided a larger and wider surface area for detection. Thus, more aspartame molecules were detected on the electrode surface and could produce highly sensitive measurements.

2. Methods

2.1. Chemicals

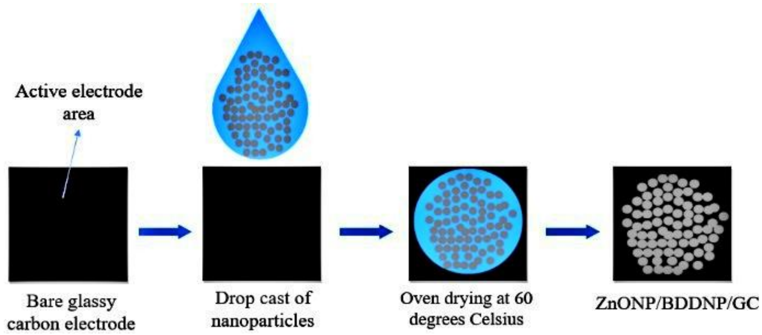
NaH_2PO_4 (99%) and Na_2HPO_4 (99.5%) from Merck (USA), ethanol (99.9%) was purchased from Millipore Corporation (USA), ZnONP 10 nm from Sigma Aldrich (USA), aspartame (98.56%), sodium cyclamate (100.45%), acesulfame potassium (100.41%), neotame (100.49%), and saccharin (101.96%) were obtained from the National Food and

Drug Agency, H_2SO_4 (98%) from SAP Chemical (Indonesia), Nafion (5%) were obtained from Sigma Aldrich (USA), beverage samples were obtained from local supermarkets, BDDNP (0 - 250 nm) from Somebetter (China) and ultrapure water.

2.2. Preparation and fabrication of electrode for electrochemical sensor aspartame

GC (glassy carbon) electrode used as a supporting electrode was first pre-treated with alumina slurry on one side of the surface (the surface to be modified) until the surface was shiny like glass. Subsequently, the electrode was sonicated in 1-propanol and ultrapure water for 10 minutes each. After that, the GC electrode was optimized in 0.1 M H_2SO_4.

The preparation of the modified BDDNP/GC electrode and the ZnONP/BDDNP/GC electrode was carried out using the drop casting method. The 0.01 g of BDDNP and ZnONP/BDDNP each were added to 0.5 mL of 30% ethanol in different beakers. The mixture is dispersed using a sonication device to ensure the ink mixture is completely dispersed. Then 20 µL of ink was drop-casted onto a GC electrode and oven dried at 60 °C for 60 minutes. Subsequently, 10 µL of 5% Nafion was drop-casted onto a modified GC electrode. A schematic showing drop-casting of BDDNP or ZnONP/BDDNP on a GC electrode is shown in Scheme 1. The GC electrodes that have been modified with ZnONP/BDDNP was characterized by SEM-EDX. The sample was attached on the sample holder using carbon tape and put into the SEM chamber. The magnification up to 25000x was applied to get the clear sample surface topography. The EDX characterization was carried out for element C, O, and Zn.



Scheme 1 Schematic drop-casting of nanoparticles onto an electrode

2.3. Electrochemical sensor of aspartame

In all electrochemical measurements, 5 mL of 0.1 M PBS (pH 2.0) was added to an electrochemical cell in which modified GC was immersed. Cells were cleaned by ultrasonication for 5 minutes by immersing them in ultrapure water to remove impurities that might be left in the cells. CV and SWV were performed with an Emstat^{3+} Blue Palmsens potentiostat using a three-compartment cell system with ZnONP/BDDNP/GC and BDDNP/GC as the working electrodes, Ag/AgCl as the reference electrode, and platinum as counter electrode. Aspartame electrochemical sensor measurements were carried out by adding 60 µM aliquot solution of aspartame analyte into an electrochemical cell containing 0.1 M PBS pH 2. The mixture solution was permitted to equilibrate for 5s and sweep from -1.0 V to 1.0 V at the amplitude of 0.05 V, a frequency of 50 Hz, and a step potential of 0.012 V in SWV mode.

3. Results and Discussion

3.1. Characterization of ZnONP/BDDNP/GC

ZnONP/BDDNP/GC was characterized using SEM-EDX to determine the electrode surface topography. Figure 1 (a) shows the result SEM image of ZnONP/BDDNP/GC, it can be seen that the deposition of ZnONP/BDDNP on the surface of the GC electrode was successful. Figure 1 (b) shows the results of EDX mapping on ZnONP/BDDNP/GC, and showing a blue color indicating the presence of ZnO nanoparticles on the electrode. The shape of the ZnO nanoparticles attached to the electrode surface is quite homogeneous. Based on SEM analysis data processing using ImageJ software**,** ZnONP/BDDNP has a nanostructure with an average particle size of 235.50 ± 2.95 nm. The EDX results show that the elements contained are carbon, oxygen, and zinc at 85.90%, 11.15%, and 2.95%, respectively.

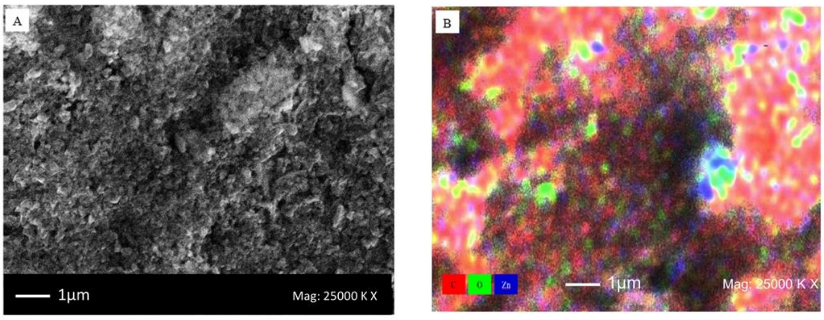


Figure 1 (a) SEM image of ZnONP/BDDNP/GC (b) EDX Mapping image of ZnONP/BDDNP/GC

3.2. Determination of signal per background (S/B)

The results of determining S/B from the two electrodes are shown in Table 1. Aspartame showed anodic peak potential and peak current at 0.32 V and 195.91 μA for BDDNP/GC electrode, while the ZnONP/BDDNP/GC electrode obtained anodic peak potential and peak current at 0.34 V and 80.01 μA. The S/B analysis revealed that the electrode modified with metal nanoparticles and ZnO nanoparticles had a higher S/B compared to the electrode without nanoparticle modification. Moreover, ZnONP/BDDNP/GC showed lower background current when compared to BDDNP/GC, attributed to the catalytic behavior and sensitivity enhancement properties of nanoparticles. As a result, the ZnONP/BDDNP/GC electrode is capable of detecting low concentrations of aspartame with higher sensitivity than the BDDNP/GC electrode.

Table 1 Signal per background of each electrode

Electrode	Background	Signal	S/B
BDDNP/GC	45.85	197.41	4.30
ZnONP/BDDNP/GC	17.22	80.10	4.65

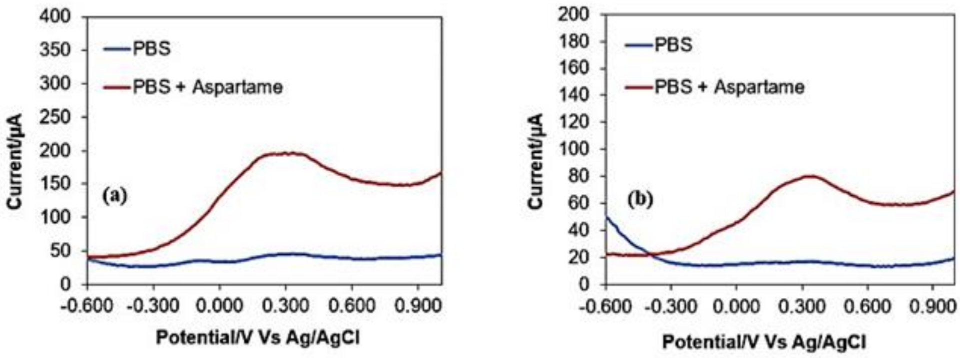


Figure 2 SWV curves for determining S/B of aspartame measurement on (a) BDDNP/GC electrode (b) ZnONP/BDDNP/GC electrode

3.3. Effect of the scan rate

Measurements of 60 µM aspartame solutions were carried out at various predetermined scan rates 30 mV/s, 50 mV/s, 80 mV/s, 100 mV/s, and 120 mV/s with a current range of -1.0 V to 1.2 V (vs Ag/AgCl). A high scan rate causes the diffusion layer to be thin thus that the transfer of electrons around the surface of the working electrode occurs properly. However, if the scan rate is too high then the diffusion layer formed around the electrode surface is too thin, making the analyte is not oxidize completely. On the other side, if the scan rate is too small, the diffusion layer will be too thick; thus, the transfer of electrons will be hampered, and the resulting current will not be perfect. The optimum scan rate used in the measurement is 120 mV/s. The linear increase as the square root of scan rate with increasing current indicates a diffusion control process (Figure 3). BDDNP/GC, electrode relation coefficient value, is 0.990 while the ZnONP/BDDNP/GC electrode relation coefficient is 0.991. A good linearity relationship can be shown by the coefficient relation (R^2), which is close to 1 (Konieczka and Namieśnik, 2016). These results indicate that the peak current of aspartame increases linearly as the root scan rate increases. Thus, it can be concluded that the aspartame oxidation process undergoes a diffusion control process.

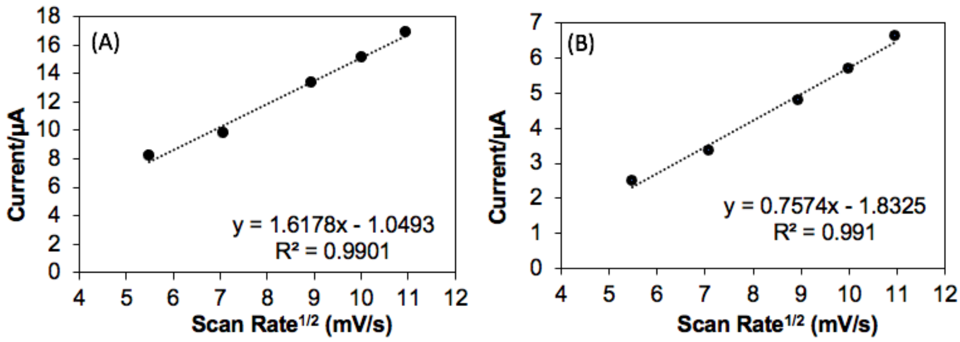


Figure 3 Current relationship curves vs root scan rate at (a) BDDNP/GC, (b) ZnONP/BDDNP/GC electrodes

3.4. Determination of optimum pH on the modified electrodes

The effect of pH on aspartame measurements was studied between pH 2.0 - 7.0 (Figure 4). The results of determining pH optimum at the BDDNP/GC and ZnONP/BDDNP/GC electrodes showed an increase in optimum peak current of aspartame linearly along with the decrease in pH. It is because aspartame has a carboxylic group in aspartic acid which has a pKa = 3.1. The lower the pKa, the stronger the acid and the greater its ability to donate protons to water. Due to the low pKa of the carboxylate group, aspartame's detection is optimum at an acidic pH. The range used for pH variations was measured at pH 2.0 – 7.0 because GC electrodes can be damaged at very low pH levels. Therefore, pH levels below 2.0 were not included. The results showed that pH had an influence on the high and low peak currents produced in the aspartame measurements. The optimal pH for aspartame measurement was determined at pH 2.0 because it gave a higher peak current response than other pH levels. The difference in the measured peak current value is caused by the number of aspartame molecules measured on the electrode surface. The higher the peak current value, the greater the number of analyte molecules measured on the electrode surface, and the faster the electron transfer process.

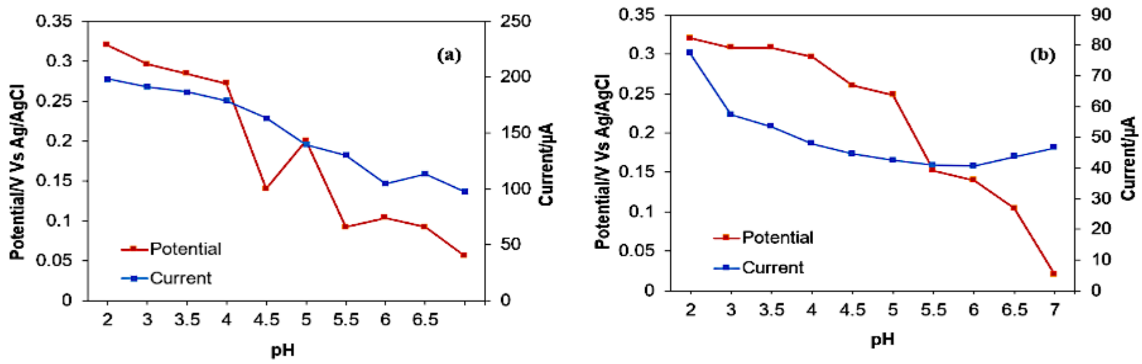


Figure 4 Effect of pH on peak current and peak potential of aspartame using (a) BDDNP/GC, (b) ZnONP/BDDNP/GC electrodes

3.5. Linear range, limit of detection and limit of quantification

The effect of aspartame concentration was evaluated by measuring aspartame solutions in 5 mL of 0.1 M PBS using the SWV method. The concentration range measured was 30 μM to 100 μM and blank. As shown in (Figure 5) the peak current of aspartame increased linearly with the concentration of aspartame. The linearity range of aspartame is shown in the equations below:

$$Ipa\ (\mu A) = 1.2316\ C\ (\mu M) + 9.279 \quad (R^2 = 0.9928) \tag{1}$$

$$Ipa\ (\mu A) = 1.1956\ C\ (\mu M) + 115.65\ (R^2 = 0.9963) \tag{2}$$

From the Equation (1) and (2) obtained linear regression y = ax + b, a is the slope of the regression equation. The slope of the regression line will provide an idea of the measurement sensitivity of the method to be validated (Konieczka and Namieśnik, 2016). The slope obtained in this study for ZnONP/BDDNP/GC electrode is 1.2316 μA μM^{-1} then for BDDNP/GC electrode is 1.1956 μA μM^{-1}. The value of the two electrodes is quite large. However, when the two electrodes are compared, ZnONP/BDDNP/GCE has better sensitivity than the BDDNP/GC electrode. The value of the relation coefficient (R^2) on aspartame measurements using ZnONP/BDDNP/GC and BDDNP/GC electrodes is close to 1. This indicates that the calibration curve produces a good response linearity in the range of 30-100 μM.

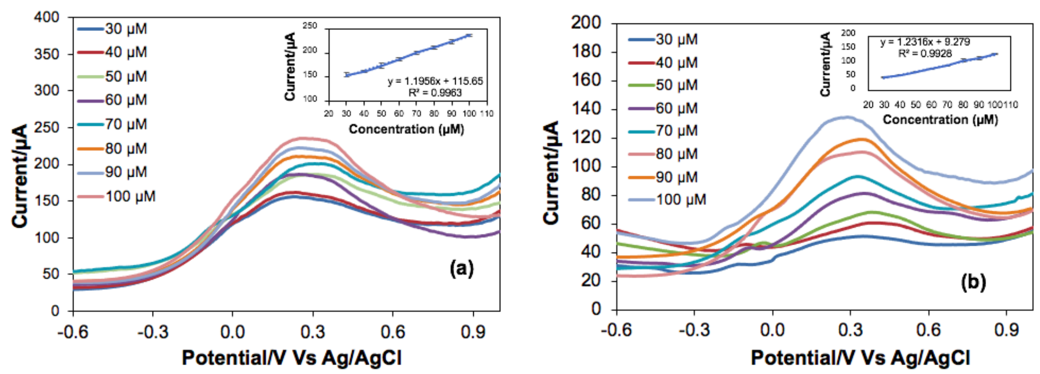


Figure 5 Voltammogram square wave voltammetry response of 30-100 μM aspartame (Conditions: amplitude: 0.05 V, frequency: 50 Hz and step potential: 0.012 V) on (a)BDDNP/GC, (b) ZnONP/BDDNP/GC

The limit of detection (LOD) and limit of quantitation (LOQ) for ZnONP/BDDNP/GC electrodes were calculated to be 0.07 μM and 0.25 μM, respectively, while for BDDNP/GC electrodes, they were found to be 1.86 μM and 6.16 μM. Several prior studies have used various methods for analyzing aspartame using modified working electrodes and other detection methods based on the obtained limit of detection data. As shown in Table 2, the analysis of aspartame using ZnONP/BDDNP/GC electrodes has a lower detection limit (LOD) compared to the other methods, indicating that ZnONP/BDDNP/GC electrodes have higher sensitivity.

Table 2 Comparison of electrochemical sensors with other reported methods for determining aspartame in beverage samples

Method	Electrode	Linear Range (μM)	LOD (μM)	Ref.
DPV	ZnONPs/MWCNTs/GC	12.0-24.0	3.68	(Balgobind *et al.*, 2016)
SWV	BDD	5.0- 50	0.47	(Medeiros *et al.*, 2008)
FIA	SPCE/Bienzyme/CoPc	5-600	0.2	(Radulescu *et al.*, 2014)
DPV	APT-BDD	4.4-110	1.6	(Deroco *et al.*, 2015)
SWV	BDDNP/GC	30-100	1.86	This work
SWV	ZnONP/BDDNP/GC	30-100	0.07	This Work

Note: DPV (Differential Pulse Voltammetry), SWV (Square Wave Voltammetry), and FIA (Flow Injection Analysis)

3.6. Selectivity and reproducibility

Determination of selectivity in aspartame measurements using ZnONP/BDDNP/GC and BDDNP/GC electrodes was carried out using several interfering solutions that could potentially interfere with aspartame measurements in actual samples, including sodium cyclamate, saccharin, acesulfame-K, and neotame. Measurements were made by measuring 60 μM of aspartame sample in 5 mL of 0.1 M PBS, then adding 60 μM of the interference solution using the SWV method. The peak current of aspartame is known to increase after the addition of an interfering solution. The four interfering solutions were known to be oxidized at a potential close to the aspartame oxidation potential. Table 3 showed that the difference in current and potential produced by aspartame solution with interfering solution had a higher current than the current by aspartame itself. However, the potential of the interference solution above is close to the aspartame.

Table 3 The difference in current and potentials of aspartame under interferences

Electrode	Current				Potential			
	Aspartame	Interference		Difference	Aspartame	Interference		Difference
ZnONP/ BDDNP/GC	80.09	Saccharin	60.56	19.44	0.34	Saccharin	0.36	0.02
	80.09	Acesulfame-K	72.45	7.55	0.34	Acesulfame-K	0.33	0.01
	80.09	Sodium cyclamate	67.28	12.81	0.34	Sodium cyclamate	0.33	0.01
	80.09	Neotame	61.73	18.36	0.34	Neotame	0.33	0.01
BDDNP/GC	197.4	Sakarin	217.78	20.37	0.32	Sakarin	0.28	0.04
	197.4	Asesulfam K	221.35	23.94	0.32	Asesulfam K	0.28	0.04
	197.4	Natrium siklamat	159.97	37.44	0.32	Natrium siklamat	0.37	0.05
	197.4	Neotam	183.97	13	0.32	Neotam	0.34	0.02

The reproducibility of ZnONP/BDDNP/GC and BDDNP/GC electrodes was determined by measuring 60 μM of aspartame sample in 5 ml of 0.1 M PBS using the SWV method. To test the reproducibility of the proposed method, 10 replicates were performed on different days. The relative standard deviation (RSD) values obtained were 1.60% for ZnONP/BDDNP/GC electrode and 1.96% for BDDNP/GC electrode When compared, ZnONP/BDDNP/GC has a smaller %RSD than BDDNP/GC. It shows that ZnONP/BDDNP/GC is an electrode that has a better level of precision and stability than BDDNP/GC. The %RSD obtained is less than 5%, this indicates that the two electrodes have a fairly good level of precision and stability. The summary of validation parameters is described in Table 4.

Table 4 The summary of validation parameter

Parameter Validation	Electrode modification	
	ZnONP/BDDNP/GC	BDDNP/GC
S/B	4.65	4.30
pH Optimum	2.0	2.0
Sensitivity	1.23	1.19
LOD (μM)	0.07	1.86
LOQ (μM)	0.25	6.16
% RSD	1.60	1.96

3.7. Aspartame determination in real sample

The determination of aspartame in the actual sample was determined using the SWV method. The sample used is a sample of a drink purchased from a local supermarket that already contains aspartame in it. The signal obtained from the sample was recorded, and aspartame concentration was calculated using a calibration graph. The analysis of each sample was carried out three times, and the results of the analysis using ZnONP/BDDNP/GC and BDDNP/GC electrodes are presented in Table 5. These results indicate that ZnONP/BDDNP/GC and BDDNP/GC electrodes using the SWV method in aspartame analysis can be applied to actual samples with high accuracy. In addition, the relative standard deviation (RSD) value of the performed measurements is lower than 5%. This indicates that the proposed method and modification can meet the requirements for a better aspartame sample sensor in real samples.

Table 5 Aspartame detection in beverage samples

Electrode	Sample	Added (μM)	Founded (μM)	% Recovery	% RSD
ZnONP/BDDNP/GC	Sweetener type-1	60	54.90	91.14	0.48
	Sweetener type-2	60	65.60	109.33	0.83
	Carbonated drink	60	55.90	93.16	4.83
BDDNP/GC	Sweetener type-1	60	51.94	86.60	2.27
	Sweetener type-2	60	53.67	89.46	1.65
	Carbonated drink	60	54.48	90.79	1.4

4. Conclusions

ZnONP/BDDNP has been successfully prepared. It was utilized for the electrochemical sensors of aspartame in beverage samples. SEM-EDX characterization successfully showed the distribution of ZnONP/BDDNP homogeneously on the surface of the GC electrode. Aspartame detection using the SWV method was carried out with a linear calibration curve with R^2 = 0.9928. The modified electrode was used for aspartame detection in the presence of interfering compounds such as sodium cyclamate, saccharin, acesulfame-K, and neotame. They produced different current peaks with aspartame, thus that the possibility of interfering with the measurements was quite small. From the results of the method carried out, the ZnONP/BDDNP electrode has a good level of sensitivity, good precision, good stability, and is able to detect aspartame at a good level of μM concentration. Thus, the ZnONP/BDDNP electrode can be further developed for real application in detecting aspartame, and potentially miniaturized as facile use screen printed sensor.

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