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Research Article

Investigation of Some Crown Ether Compounds for Electrochemical Determination of Dopamine

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ABSTRACT

In this study, the use of three different crown ether-modified electrodes prepared by electropolymerization of different crown ether compounds (CE1, CE2 and CE3) on multi-walled carbon nanotube (MWCNT) modified glassy carbon electrode (GCE) surfaces was investigated for electrochemical dopamine determination. The number of cycles during the electropolymerization of crown ethers and the pH of the buffer solution were optimized. Under optimum conditions, the sensitivities of MWCNT-modified GCE and crown ether-MWCNT-modified electrodes were determined in the range of $4.0\times10^{-6} – 5.7\times10^{-4}$ M dopamine. The sensitivity of MWCNT/GCE was found to be 6.71 µA mM^{-1}, while the sensitivities of CE1/MWCNT/GCE, CE2/MWCNT/GCE and CE3/MWCNT/GCE were 19.53, 16.32 and 20.80 µA mM^{-1}, respectively. The performance characteristics of the crown ether-MWCNT-modified electrodes such as detection limit, quantification limit, reusability and reproducibility were also investigated. The study showed that crown ether compounds significantly enhanced the electrochemical response in dopamine determination.

Keywords: *Crown ether, electrochemical sensor, dopamine, modified electrode, multi-walled carbon nanotube*

Dopaminin Elektrokimyasal Tayini için Bazı Taç Eter Bileşiklerinin Kullanımının Araştırılması

ÖZ

Bu çalışmada çok duvarlı karbon nanotüp (MWCNT) modifiye edilmiş camsı karbon elektrot (GCE) yüzeylerine farklı taç eter bileşiklerinin (CE1, CE2 ve CE3) elektropolimerizasyonu ile hazırlanan üç farklı taç eter-modifiye elektrodun elektrokimyasal dopamin tayininde kullanımı araştırıldı. Taç eterlerin elektropolimerizasyonu sırasındaki döngü sayısı ve çalışılan tampon çözelti pH'sı optimize edildi. Optimum koşullarda, MWCNT modifiye edilmiş GCE ile taç eter-MWCNT-modifiye elektrotların $4,0\times10^{-6} – 5,7\times10^{-4}$ M dopamin derişimi aralığında duyarlılıkları belirlendi. MWCNT/GCE'nin duyarlılığı 6,71 µA mM^{-1} olarak bulunurken, CE1/MWCNT/GCE, CE2/MWCNT/GCE ve CE3/MWCNT/GCE'nin duyarlılıkları sırasıyla 19,53; 16,32 ve 20,80 µA mM^{-1} olarak belirlendi. Taç eter-modifiye elektrotların gözlenebilme sınırı, tayin sınırı, tekrar kullanılabilirlik ve tekrar üretilebilirlik gibi performans özellikleri de incelendi. Çalışma, taç eter bileşiklerinin dopamin tayininde elektrokimyasal cevabı önemli ölçüde arttırdığını ve dopamin tayinine olumlu yönde etki ettiğini gösterdi.

Anahtar Kelimeler: *Taç eter, elektrokimyasal sensör, dopamin, modifiye elektrot, çok duvarlı karbon nanotüp*

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I. INTRODUCTION

Supramolecular chemistry is a field of interdisciplinary science that encompasses the chemical, physical and biological characteristics of highly complex species that are bound and ordered through non-covalent bonding interactions between molecules. Interactions such as enzyme binding to substrate or signal transduction between cells are related to supramolecular chemistry [1]. It has progressed with the discovery of several synthetic receptor molecules for the strongly and selectively binding of substrates of organic, inorganic or biological structure through a variety of interactions [1]. In supramolecular systems, intermolecular bonds are non-covalent interactions that consist of hydrogen bonds, π-π interactions, electrostatic interactions and host-guest interactions which give them unique properties that differ from molecular chemistry based on covalent bonds [2].

Supramolecular chemistry begins with the discovery of crown ethers by Pedersen [1, 3-5]. Crown ethers are cyclic compounds consisting of a ring with several ether groups [4, 6]. Crown ethers are among the most widely used host compounds in supramolecular systems based on host-guest interactions [2, 7]. Having binding sites for guest molecules allows them to attract attention as hosts [8]. The ability of crown ethers to form selective hydrogen bonds with a large number of molecules in their cavities results in the formation of stable supramolecular complexes [9]. These features of crown ethers allow them to form stable complexes with many biological components. Therefore, they act as selective hosts for various biological species [10]. Crown ethers can form host-guest complexes with small organic molecules that contain RNH_3^+ groups, such as catecholamines, by hydrogen bonding [11, 12].

Dopamine (3,4-dihydroxyphenylethylamine), which plays an important role in the human nervous, hormonal and renal systems, is one of the most important catecholamine neurotransmitters produced in various regions of the brain [13-15]. It is involved in the regulation of cognitive functions such as attention, memory and learning as well as emotions including pleasure, enthusiasm and motivation [16-18]. High levels of dopamine in the human body lead to cardiological problems such as heart rhythm irregularities, hypertension and heart failure. Dopamine deficiency causes Parkinson's disease, Alzheimer's disease, depression and schizophrenia. [19, 20]. Therefore, rapid, reliable and sensitive determination of dopamine is of critical concern. Dopamine has been determined by various methods such as high-performance liquid chromatography [21], spectrophotometry [22], capillary electrophoresis [23], fluorimetry [24] and chemiluminescence [25]. Although traditional methods are reliable, they are time-consuming, difficult and expensive [20, 26]. Electrochemical sensors have gained attention for the determination of dopamine, due to their advantages of high sensitivity, selectivity, low cost and fast response [14, 27, 28]. Electrochemical determination of dopamine is based on a redox reaction involving two electrons/two protons [15, 29, 30]. However, dopamine is difficult to determine with bare electrodes, especially since it coexists at very low concentrations in physiological fluids with other small electroactive species such as ascorbic acid and uric acid, which are oxidized at similar potentials. [16, 19, 28, 30]. To overcome these limitations, the determination of dopamine with modified electrodes has gained importance [15, 28]. Carbon nanomaterials [14, 31], conductive polymers [32], metal nanoparticles [33, 34], metal oxide nanoparticles [35, 36] have been utilized in electrode modification for the determination of dopamine.

Carbon nanotubes (CNT) are used as modification materials in electrochemical sensors due to their unique properties including high electrical and thermal conductivity, large surface area, chemical and mechanical stability, biocompatibility and functionality [37-39]. CNT exert electrocatalytic effects on the redox reactions of various electroactive biomolecules [38-40]. Multi-walled carbon nanotubes (MWCNT) improve the performance of electrochemical sensors, including detection limit and sensitivity, owing to their unique characteristics [41].

The utilization of crown ethers as electrode modification materials in electrochemical sensors for the determination of various species has attracted much attention in recent years [42, 43]. For instance, Rounaghi and co-workers modified a carbon paste electrode with a newly synthesized crown ether and silver nanoparticles and used this modified electrode for the quantitative determination of 4-nitrophenol by cyclic voltammetry [44]. 4-carboxybenzo-18-crown-6 and 4-carboxybenzo-15-crown-5 modified graphite-epoxy composite electrodes were developed by Serrano et al. These crown ether-modified electrodes were used for the simultaneous determination of Cd(II), Pb(II) and Cu(II) by differential pulse anodic stripping voltammetry [45]. Atta and coworkers developed an electrochemical sensor for the determination of neurotransmitters by modifying the GCE surface with CNT, ionic liquid crystal and 18-crown-6. In the study, serotonin in blood serum was determined by differential pulse method [9]. Modifying the electrode surface with crown ethers in electrochemical sensors results in a decrease in the detection limit of target analytes and an increase in selectivity [6]. The use of crown ethers as electrode modification materials for the determination of dopamine is based on the formation of complexes with hydrogen bonds between oxygen atoms in the crown ether ring and the amino group of dopamine [46].

In this study, the surface of GCE was modified with MWCNT to increase the electrode surface area and enhance the electron transfer property (MWCNT/GCE). In order to investigate the ability of crown ether compounds to form a host-guest complex with dopamine as a recognition component, crown ethers were electropolymerized on the surface of MWCNT/GCEs and three different crown ether-modified electrodes, CE1/MWCNT/GCE, CE2/MWCNT/GCE and CE3/MWCNT/GCE, were prepared. The electrochemical responses of each crown ether-MWCNT-modified electrode to dopamine were investigated and compared with the response of MWCNT/GCE. The performance characteristics of the crown ether-modified electrodes such as sensitivity, limit of observability and reproducibility were determined.

II. EXPERIMENTAL

A. CHEMICALS AND ELECTRODES

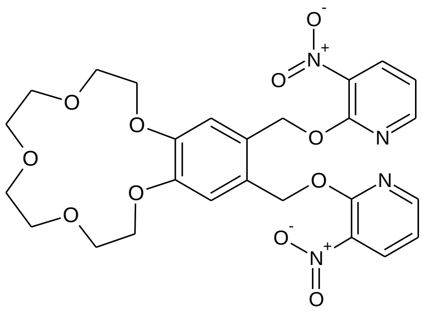
The nitropyridine-substituted benzo-15-crown-5 crown ether compounds used in the study were synthesized and purified by Koçoğlu et al. [47, 48]. Dopamine hydrochloride, chitosan, disodium monohydrogenphosphate, sodium dihydrogenphosphate, potassium chloride, potassium hexacyanoferrate(III), potassium hexacyanoferrate(II) were obtained from Sigma-Aldrich and MWCNT (outer diameter 10-20 nm and length 10-30 μm) from Cheap Tubes Inc. For electrochemical studies, a three-electrode system consisting of a glassy carbon electrode (GCE) (3.0 mm diameter, ItalSens) as working electrode, Ag/AgCl (IS-AG/AGCL.AQ.RE, ItalSens) as reference electrode and Pt wire (IS-PT.W.CE, ItalSens) as counter electrode was used.

B. INSTRUMENTS AND MEASUREMENTS

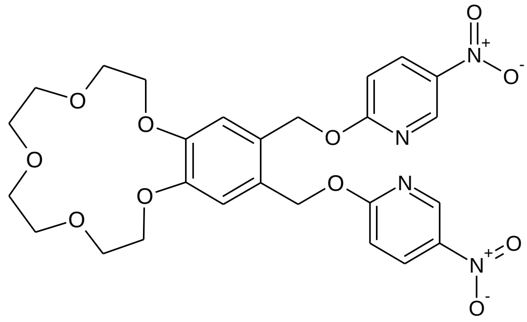
Electrochemical measurements were performed using a PalmSens EmStat^3 (PalmSens BV, Netherlands) electrochemical analyzer. Cyclic voltammetry (CV) studies were carried out in 5 mM $[Fe(CN)_6]^{3-/4-}$ solution containing 0.1 M KCl at a scan rate of 50 mV s^{-1} between the potential of −0.40 and +0.80 V. Differential pulse voltammetry (DPV) measurements were recorded between −0.20 and +0.80 V in 0.05 M phosphate buffer solution (PBS) at a scan rate of 50 mV s^{-1} (instrument parameters: pulse potential 0.2 V and pulse duration 0.02 s). Amperometric measurements were conducted in 0.05 M PBS (pH 6.0) at a potential of +0.25 V.

C. PREPARATION OF MODIFIED ELECTRODES

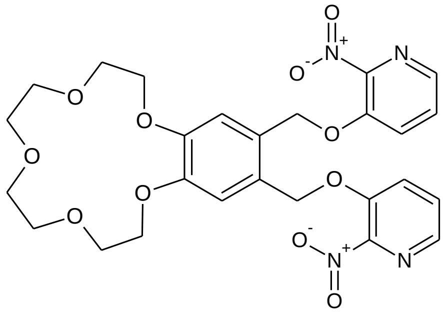
The structures of nitropyridine-substituted benzo-15-crown-5 crown ether compounds (CE1, CE2 and CE3) used as modification materials for the preparation of electrochemical sensors in this study are given in Figure 1. Glassy carbon electrode (GCE) surfaces were first modified with MWCNT to increase the surface area and electron transfer, and then three different crown ether-modified electrodes were prepared by electropolymerization of crown ether compounds on the surface of these MWCNT-modified electrodes.



CE1



CE2



CE3

Figure 1. *Structures of crown ether compounds used in electrode modification*

The preparation steps of the modified electrodes were described as follows:

i. GCEs were polished with alumina solution and washed with distilled water before each use. They were then ultrasonicated in ethyl alcohol and distilled water, respectively.

ii. 0.5 g of chitosan was dissolved in 50 mL of pH 4.0 acetate buffer to prepare chitosan solution. 10 mg MWCNT was added into 1 mL chitosan solution and ultrasonicated for four hours. 3 µL of the chitosan-MWCNT mixture was dropped onto the GCE surface and dried at room temperature to obtain MWCNT/GCE.

iii. Solutions of 0.1 mM of the crown ether compounds were prepared in pH 6.0 0.05 M PBS. The electropolymerization of crown ethers on MWCNT/GCE surfaces was carried out in crown ether solutions by cyclic voltammetry at a potential range of −2.0 to +2.5 V with 5 cycles at 50 mV s^{-1} scan rate. The cyclic voltammograms recorded for the electropolymerization of crown ethers on MWCNT/GCE surfaces are given in Figure 2. The resulting crown ether-MWCNT-modified electrodes were designated as CE1/MWCNT/GCE, CE2/MWCNT/GCE and CE3/MWCNT/GCE.

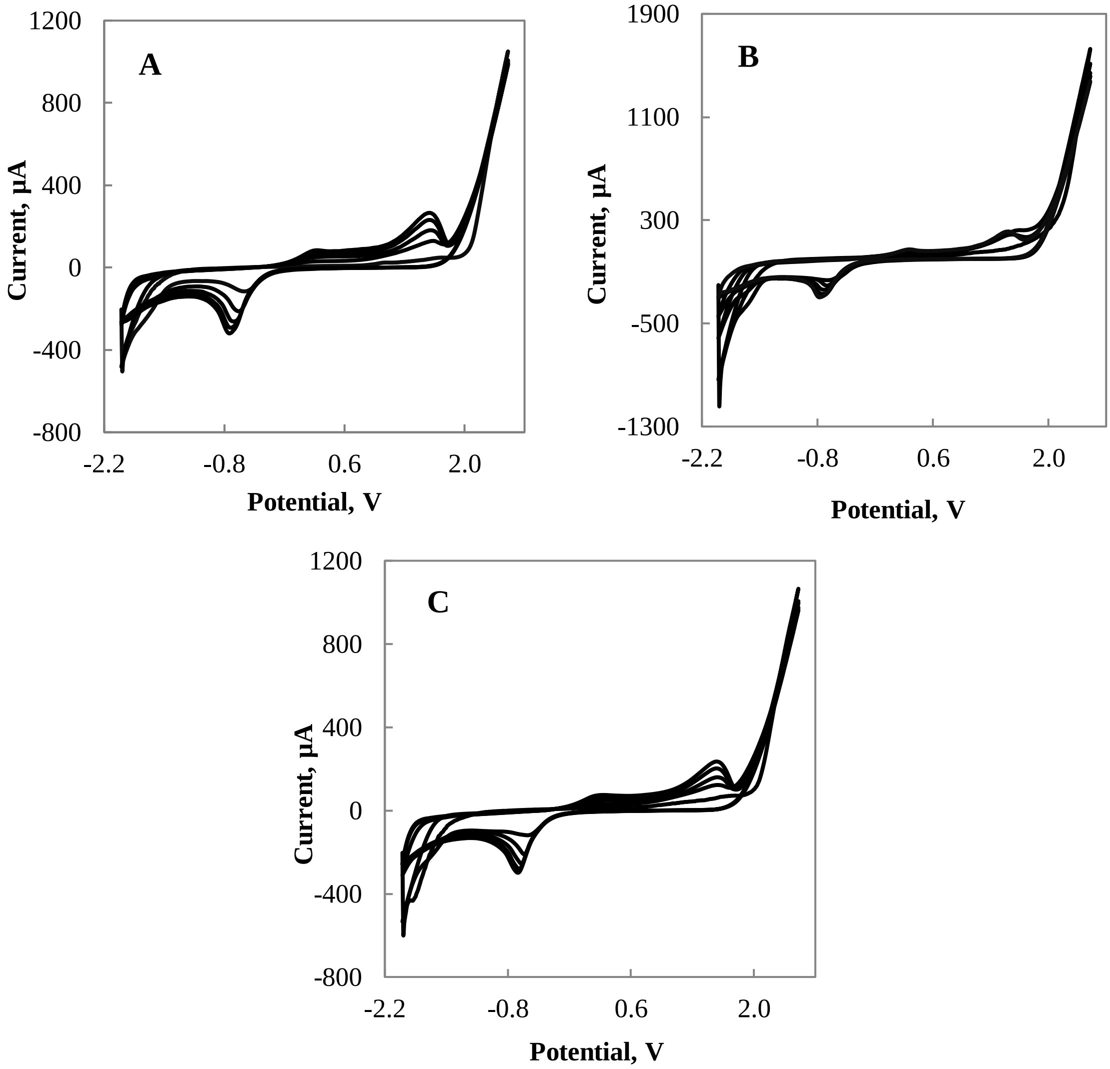


Figure 2. *Cyclic voltammograms for electropolymerization of (A) CE1, (B) CE2 and (C) CE3 on MWCNT/GCE surface (in 0.05 M pH 6.0 PBS containing 0.1 mM crown ether)*

III. RESULTS AND DISCUSSION

A. OPTIMIZATION PARAMETERS

The number of cycles during electropolymerization affects the thickness of the polymer film [49, 50]. Thus, the effect of the number of cycles in electropolymerization of crown ethers on the electrochemical response of the modified electrodes to dopamine was investigated. For this purpose, CE3 was electropolymerized on the MWCNT/GCE by cyclic voltammetry using 3, 5 and 7 cycles. The response of different CE3/MWCNT/GCEs fabricated at 3, 5 and 7 cycles to 3.0×10^{-5} M dopamine was recorded by DPV (Figure 3). The highest peak current was obtained with the modified electrode prepared by electropolymerization with 5 cycles. Since the thickness of the polymer film increased with the increase in the number of cycles, it was considered that the electrical resistance of the electrode surface increased and the transfer of electrons required for the oxidation of dopamine was blocked when the number of cycles increased from 5 to 7 [49, 51]. Therefore, the cycle number of 5 was selected as optimum.

To determine the effect of pH on the electrochemical response of the crown ether-MWCNT-modified electrodes to dopamine, five different PBS at a concentration of 0.05 M with pH ranging from 5.0 to 9.0 were prepared. Differential pulse voltammograms of CE1/MWCNT/GCE, CE2/MWCNT/GCE and

CE3/MWCNT/GCE in each PBS containing 3.9×10^{-5} M dopamine were recorded and shown in Figure 3B, 3C and 3D, respectively. All crown ether-MWCNT-modified electrodes gave the best response to dopamine at pH 6.0 and this value was determined as the optimum.

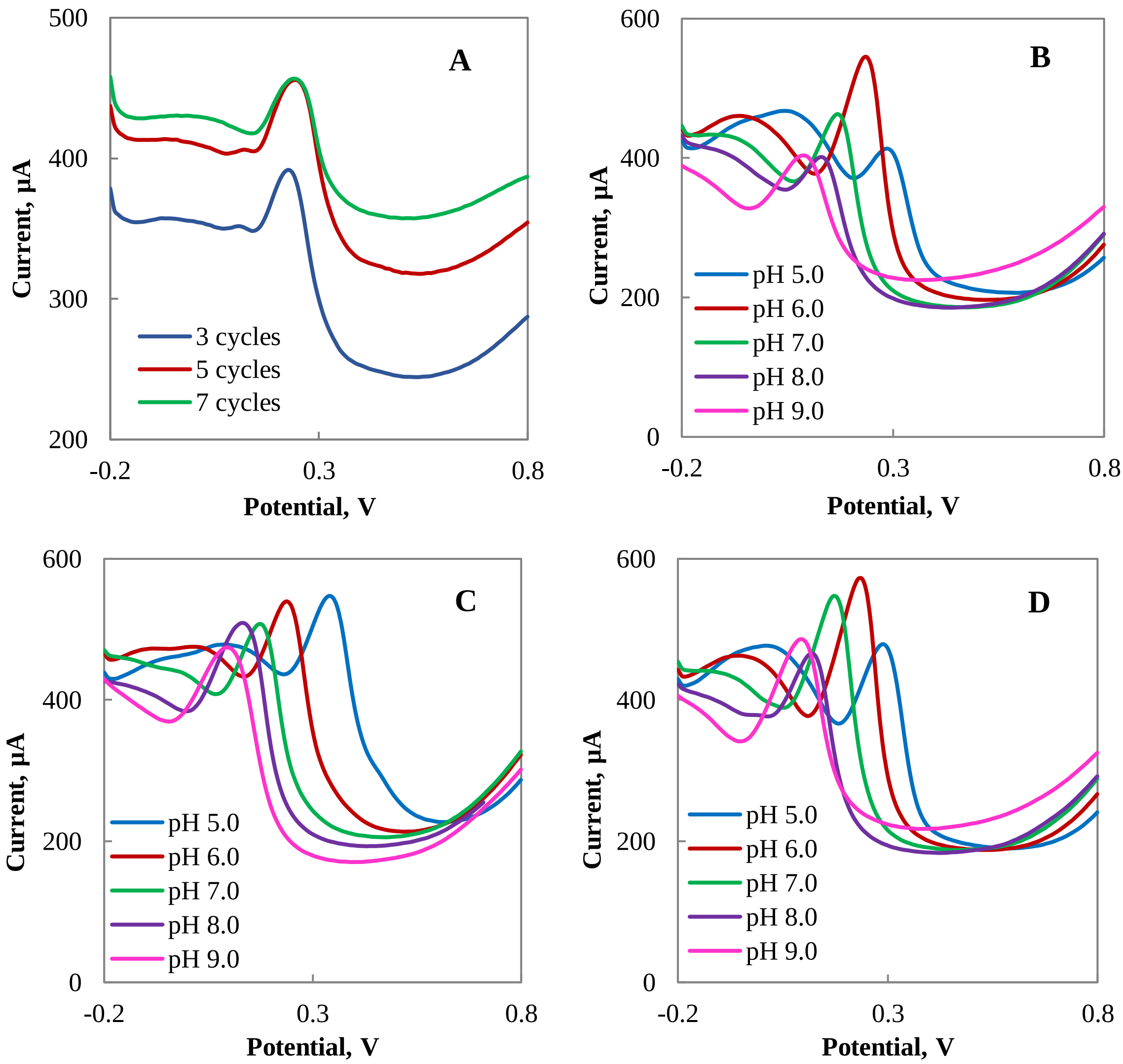


Figure 3. *Differential pulse voltammograms recorded for (A) cycle number optimization for electropolymerization of CE3 (in pH 6.0 PBS containing 3.0×10^{-5} M dopamine) and pH optimization for (B) CE1/MWCNT/GCE, (C) CE2/MWCNT/GCE and (D) CE3/MWCNT/GCE (in PBS containing 3.9×10^{-5} M dopamine)*

B. ELECTROCHEMICAL CHARACTERIZATION

For electrochemical characterization of the prepared electrodes, cyclic voltammograms of (a) GCE, (b) MWCNT/GCE, (c) CE1/MWCNT/GCE, (d) CE2/MWCNT/GCE and (e) CE3/MWCNT/GCE were recorded at a scan rate of 50 mV s^{-1} between −0.4 V and +0.8 V in 5 mM of $[Fe(CN)_6]^{3-/4-}$ solution containing 0.1 M KCl (Figure 4A). The peak currents of the bare GCE (curve a) were very low compared to the modified electrodes. The dramatic increase in the peak currents obtained with the MWCNT/GCE (curve b) was attributed to the superior properties of MWCNT such as increasing the electrode surface area and enhancing electron transfer. The decrease in peak currents recorded at all three crown ether-MWCNT-modified electrodes (curve c, d and e) was considered to be due to the formation of an insulating layer on the surface as a result of polymerization of crown ethers with large molecular structure on the electrode surface. In addition, the decrease in the peak currents of these electrodes in a similar manner was interpreted as successful electropolymerization of crown ethers.

In order to determine the effect of modification of the crown ethers on the electrochemical behavior to dopamine, differential pulse voltammograms of (a) MWCNT/GCE, (b) CE1/MWCNT/GCE, (c) CE2/MWCNT/GCE and (d) CE3/MWCNT/GCE were recorded in pH 6.0 PBS containing 3.9×10^{-5} M dopamine (Figure 4B). The electrochemical response of the crown ether-MWCNT-modified electrodes to dopamine was found to be significantly higher than the MWCNT/GCE response at the same concentration. The remarkable increase of the dopamine response may be attributed to the interaction of the crown ether rings with dopamine and as a result, sensitive determination of dopamine with crown ether-MWCNT-modified electrodes would be possible.

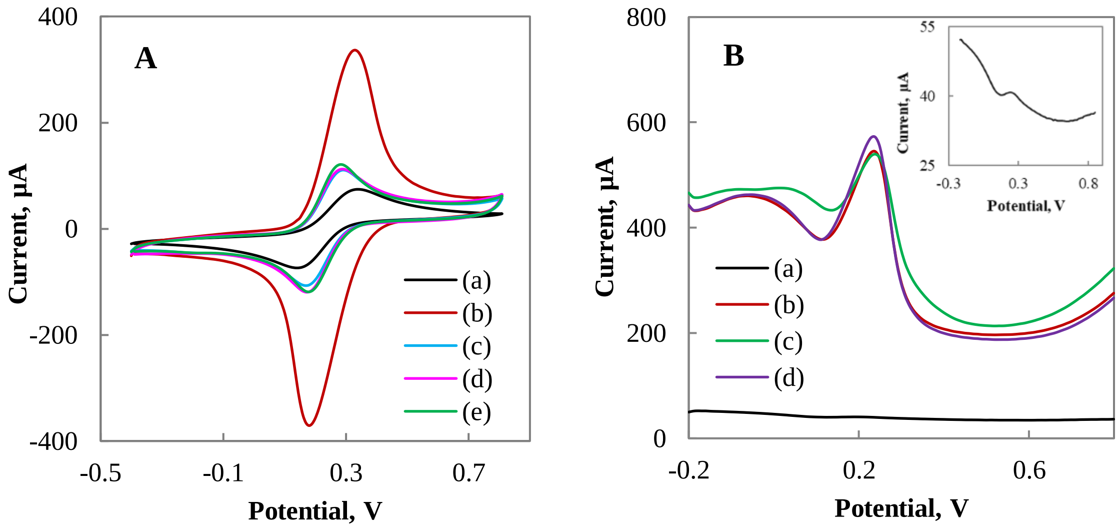


Figure 4. *(A) Cyclic voltammograms of (a) GCE, (b) MWCNT/GCE, (c) CE1/MWCNT/GCE, (d) CE2/MWCNT/GCE and (e) CE3/MWCNT/GCE in 5 mM of $[Fe(CN)_6]^{3-/4-}$ solution containing 0.1 M KCl (at a scan rate of 50 mV s^{-1}), (B) Differential pulse voltammograms of (a) MWCNT/GCE, (b) CE1/MWCNT/GCE, (c) CE2/MWCNT/GCE and (d) CE3/MWCNT/GCE in pH 6.0 PBS containing 3.9×10^{-5} M dopamine (Inset: differential pulse voltammogram for MWCNT/GCE)*

In order to determine the effect of scan rate on the electrochemical response of each crown ether-MWCNT-modified electrode to dopamine, cyclic voltammograms of CE1/MWCNT/GCE, CE2/MWCNT/GCE and CE3/MWCNT/GCE were recorded in pH 6.0 PBS containing 1.2×10^{-4} M dopamine by increasing the scan rate from 5 mV s^{-1} to 250 mV s^{-1} and the results are presented in Figure 5A, B and C, respectively. It was observed that the peak currents increased with increasing scan rate.

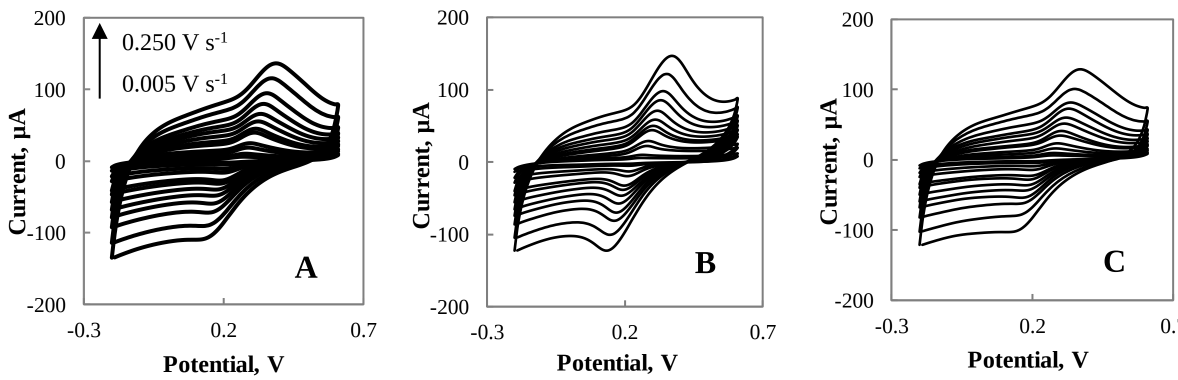


Figure 5. *Cyclic voltammograms for (A) CE1/MWCNT/GCE, (B) CE2/MWCNT/GCE and (C) CE3/MWCNT/GCE at various scan rates (from 5 mV s^{-1} to 250 mV s^{-1}) in pH 6.0 PBS containing 1.2×10^{-4} M dopamine*

The variation of peak currents with scan rate for CE1/MWCNT/GCE (a), CE2/MWCNT/GCE (b) and CE3/MWCNT/GCE (c) are given in Figure 6A. For all three crown ether-MWCNT-modified electrodes, the peak currents increased linearly with scan rate. This indicated that electron transfer occurs at the electrode surface and the electron transfer mechanism is adsorption controlled. It was also found that the logarithm of the peak currents versus the logarithm of the scan rates was linear (Figure 6B-a, b and c). The slopes of log I_p - log v plots for CE1/MWCNT/GCE, CE2/MWCNT/GCE and CE3/MWCNT/GCE were 0.81, 0.82 and 0.78, respectively. The slopes close to 1.0 also contributed to the conclusion that the systems were adsorption controlled [52, 53].

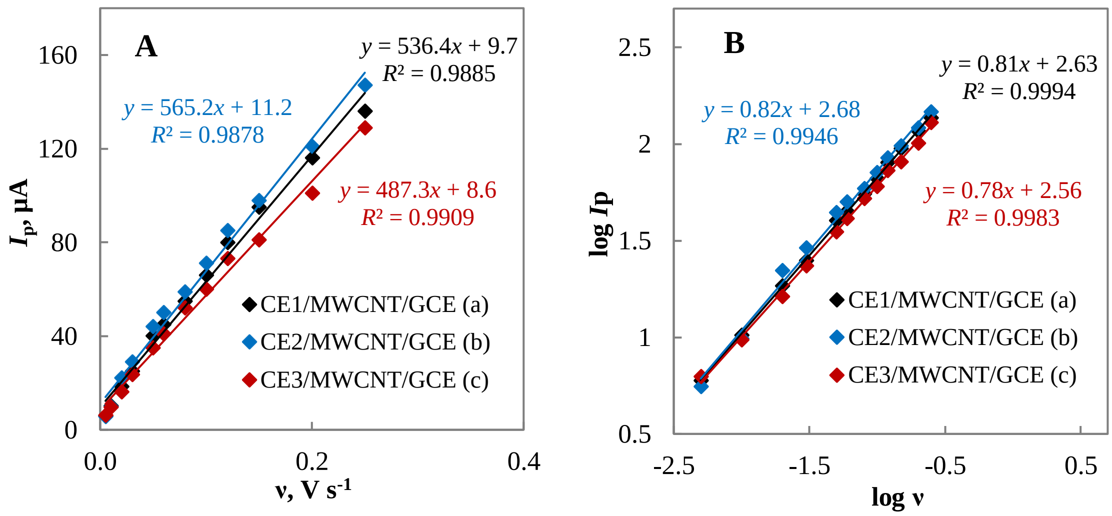


Figure 6. *(A) $I_p - v$ plots and (B) log I_p − log v plots for (a) CE1/MWCNT/GCE, (b) CE2/MWCNT/GCE and (c) CE3/MWCNT/GCE*

C. PERFORMANCE PARAMETERS OF THE MODIFIED ELECTRODES

In order to determine the performance characteristics of the modified electrodes towards dopamine, amperometric current responses of (a) MWCNT/GCE, (b) CE1/MWCNT/GCE, (c) CE2/MWCNT/GCE and (d) CE3/MWCNT/GCE were recorded for successive dopamine additions between 4.0×10^{-6} and 5.7×10^{-4} M at a potential of +0.25 V in 0.05 M pH 6.0 PBS (Figure 7). Since the oxidation peak of dopamine was observed around +0.25 V with each crown ether-MWCNT-modified electrode at pH 6.0 (Figure 4B), the working potential for amperometric studies was chosen to be +0.25 V. The amperometric current responses of each modified electrode versus dopamine concentration are plotted and given in Figure 8 for (A) MWCNT/GCE, (B) CE1/MWCNT/GCE, (C) CE2/MWCNT/GCE and (D) CE3/MWCNT/GCE. In the same dopamine concentration range, the sensitivities of MWCNT/GCE, CE1/MWCNT/GCE, CE2/MWCNT/GCE and CE3/MWCNT/GCE were determined as 6.71, 19.53, 16.32 and 20.80 µA mM^{-1}, respectively. The sensitivities of the crown ether-MWCNT-modified electrodes were found to be about three times higher than the sensitivity of MWCNT/GCE. This was attributed to the positive effect of crown ethers on dopamine determination due to the unique cavity size of crown ethers. This cavity structure acts as a host, the amino groups of dopamine molecules bind well to the oxygen molecules in these cavities as guests with hydrogen bonds and stable host-guest complexes are formed [9, 46]. It was also found that different crown ether compounds have different responses to dopamine. It was considered that the difference of the side groups attached to the crown ether compounds may have positive or negative effects on the determination of dopamine for various factors such as electrostatic effect or steric effect in the interaction of crown ethers with dopamine. Therefore, it was concluded that this is a subject that could shed light on further studies and is worthy of further investigation.

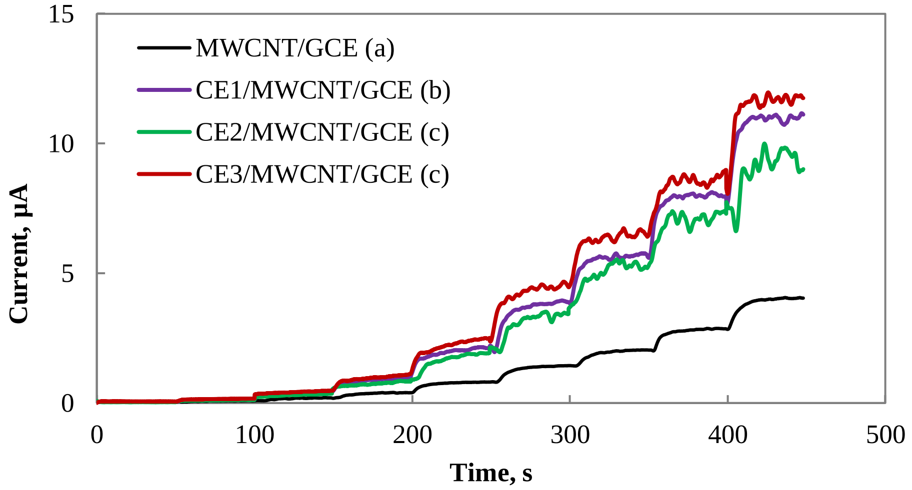


Figure 7. *i-t plots for (a) MWCNT/GCE, (b) CE1/MWCNT/GCE, (c) CE2/MWCNT/GCE and (d) CE3/MWCNT/GCE (in 0.05 M PBS, pH 6.0, +0.25 V)*

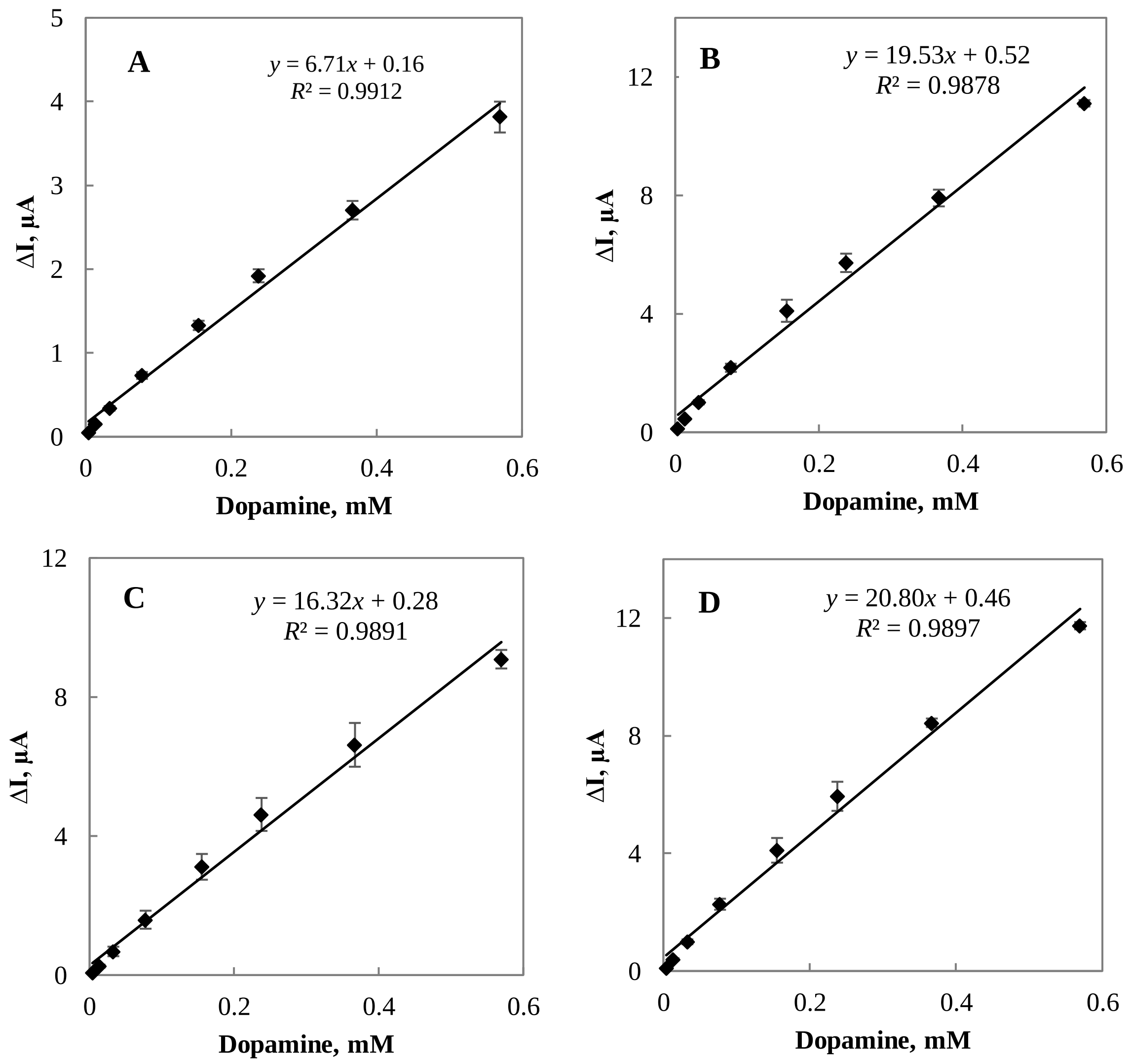


Figure 8. *Calibration plots for (A) MWCNT/GCE, (B) CE1/MWCNT/GCE, (C) CE2/MWCNT/GCE and (D) CE3/MWCNT/GCE (in 0.05 M PBS, pH 6.0, +0.25 V, N=3)*

The limit of detection (LOD) and limit of quantification (LOQ) of the crown ether-MWCNT-modified electrodes were determined using the standard deviation (s) of the intercept and the slope (m) of the calibration plot. Using the equations LOD=$3s/m$ and LOQ=$10s/m$, these values were calculated for each crown ether-MWCNT-modified electrode and given in Table 1. To determine the reusability (RU) of the crown ether-MWCNT-modified electrodes, three consecutive calibration plots were generated with the same modified electrode and the relative standard deviation (RSD) of the sensitivities was calculated. In addition, the reproducibility (RP) of the electrodes was determined by preparing three electrodes under the same conditions and calculating the RSD of the sensitivities obtained from the calibration graphs. The RU and RP of each crown ether-MWCNT-modified electrode are presented in Table 1. The reusability and reproducibility of the crown ether-MWCNT-modified electrodes were found to be quite good.

Table 1. *Performance characteristics of crown ether-MWCNT-modified electrodes*

Electrode	Linear Range *(M)*	Sensitivity *(μA mM^{-1})*	LOD *(M)*	LOQ *(M)*	RU *(RSD%)*	RP *(RSD%)*
CE1/MWCNT/GCE	$4.0\times10^{-6} – 5.7\times10^{-4}$	19.53	2.1×10^{-6}	7.1×10^{-6}	5.7	0.6
CE2/MWCNT/GCE	$4.0\times10^{-6} – 5.7\times10^{-4}$	16.32	2.4×10^{-6}	8.1×10^{-6}	1.1	4.3
CE3/MWCNT/GCE	$4.0\times10^{-6} – 5.7\times10^{-4}$	20.80	1.7×10^{-6}	5.8×10^{-6}	3.1	0.9

IV. CONCLUSION

In this study, the GCE surface was modified with MWCNT and the electropolymerization of three different crown ether compounds (CE1, CE2 and CE3) on MWCNT/GCE surface was carried out to investigate the usability of CE1/MWCNT/GCE, CE2/MWCNT/GCE and CE3/MWCNT/GCE for dopamine determination. The use of MWCNT as a modification material aims to increase the surface area and improve the electrical conductivity of bare GCE. The purpose of using crown ethers in electrode modification is based on their ability to form stable host-guest complexes by selective hydrogen bonding with small molecules such as catecholamines in the cavities in their structure. The electrochemical responses of the crown ether-MWCNT-modified electrodes to dopamine, which is a catecholamine with an amino group, were investigated and compared with the response of MWCNT/GCE to determine the advantage of the crown ethers as discussed. Crown ethers were found to enhance the electrochemical response to dopamine quite significantly. The performance characteristics of each crown ether-MWCNT-modified electrode including sensitivity, detection limit, reusability and reproducibility were investigated and the best results for sensitivity and LOD were obtained with CE3/MWCNT/GCE. The effects of different crown ether compounds and side groups attached to the crown ether ring on the electrochemical response are considered to be investigated in further studies.

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V. REFERENCES

[1] J. M. Lehn, "Supramolecular Chemistry," *Science*, vol. 260, no. 5115, pp. 1762–1763, Jun. 1993, doi: 10.1126/science.8511582.

[2] H. Che and J. Yuan, "Recent advances in electrospinning supramolecular systems," *Journal of Materials Chemistry B*, vol. 10, no. 1, pp. 8–19, 2022, doi: 10.1039/D1TB02304G.

[3] A. Müller, H. Reuter, and S. Dillinger, “Supramolecular Inorganic Chemistry: Small Guests in Small and Large Hosts,” *Angewandte Chemie International Edition in English*, vol. 34, no. 21, pp. 2328–2361, 1995, doi: 10.1002/anie.199523281.

[4] C. J. Pedersen, “Cyclic polyethers and their complexes with metal salts,” *Journal of the American Chemical Society*, vol. 89, no. 10, pp. 2495–2496, May 1967, doi: 10.1021/ja00986a052.

[5] C. J. Pedersen and H. K. Frensdorff, “Macrocyclic Polyethers and Their Complexes,” *Angewandte Chemie International Edition in English*, vol. 11, no. 1, pp. 16–25, 1972, doi: 10.1002/anie.197200161.

[6] N. F. Atta, A. Galal, and Y. M. Ahmed, “Highly Conductive Crown Ether/Ionic Liquid Crystal-Carbon Nanotubes Composite Based Electrochemical Sensor for Chiral Recognition of Tyrosine Enantiomers,” *Journal of The Electrochemical Society*, vol. 166, no. 8, p. B623, May 2019, doi: 10.1149/2.0771908jes.

[7] S. Koçoğlu, Z. Hayvalı, and H. Ogutcu, “A polydentate ligand based on 2,2’-dipyridylamine unit linked benzo-15-crown-5; alkali and transition metal complexes; photoresponsive ligand; antimicrobial evaluation against pathogenic microorganisms,” *Transition Metal Chemistry*, vol. 46, no. 7, pp. 509–522, Oct. 2021, doi: 10.1007/s11243-021-00469-1.

[8] L. Chen *et al.*, “High-throughput and selective solid-phase extraction of urinary catecholamines by crown ether-modified resin composite fiber,” *Journal of Chromatography A*, vol. 1561, pp. 48–55, Aug. 2018, doi: 10.1016/j.chroma.2018.05.041.

[9] N. F. Atta, Y. M. Ahmed, and A. Galal, “Electrochemical Determination of Neurotransmitters at Crown Ether Modified Carbon Nanotube Composite: Application for Sub-nano-sensing of Serotonin in Human Serum,” *Electroanalysis*, vol. 31, no. 7, pp. 1204–1214, 2019, doi: 10.1002/elan.201800065.

[10] N. F. Atta, A. Galal, and A. R. El-Gohary, “Crown ether modified poly(hydroquinone)/carbon nanotubes based electrochemical sensor for simultaneous determination of levodopa, uric acid, tyrosine and ascorbic acid in biological fluids,” *Journal of Electroanalytical Chemistry*, vol. 863, p. 114032, Apr. 2020, doi: 10.1016/j.jelechem.2020.114032.

[11] L. Chen, X. Zhu, D. Huang, Z. Xu, J. Shen, and W. Zhang, “Polystyrene/poly(dibenzo-18-crown-6) composite nanofibers for the selective adsorption of plasma catecholamines,” *RSC Advances*, vol. 7, no. 22, pp. 13263–13271, 2017, doi: 10.1039/C7RA00430C.

[12] L. Chen, X. Zhu, J. Shen, and W. Zhang, “Selective solid-phase extraction of catecholamines from plasma using nanofibers doped with crown ether and their quantitation by HPLC with electrochemical detection,” *Analytical and Bioanalytical Chemistry*, vol. 408, no. 18, pp. 4987–4994, Jul. 2016, doi: 10.1007/s00216-016-9596-7.

[13] H. Beitollahi, M. Safaei, and S. Tajik, “Different Electrochemical Sensors for Determination of Dopamine as Neurotransmitter in Mixed and Clinical Samples: A Review,” *Analytical and Bioanalytical Chemistry Research*, vol. 6, no. 1, pp. 81–96, Jun. 2019, doi: 10.22036/abcr.2018.142219.1229.

[14] Q. Huang, X. Lin, L. Tong, and Q.-X. Tong, “Graphene Quantum Dots/Multiwalled Carbon Nanotubes Composite-Based Electrochemical Sensor for Detecting Dopamine Release from Living Cells,” *ACS Sustainable Chemistry & Engineering*, vol. 8, no. 3, pp. 1644–1650, Jan. 2020, doi: 10.1021/acssuschemeng.9b06623.

[15] K. Jackowska and P. Krysinski, “New trends in the electrochemical sensing of dopamine,” *Analytical and Bioanalytical Chemistry*, vol. 405, no. 11, pp. 3753–3771, Apr. 2013, doi: 10.1007/s00216-012-6578-2.

[16] S. M. Siddeeg, “Electrochemical detection of neurotransmitter dopamine: a review,” *International Journal of Electrochemical Science*, vol. 15, no. 1, pp. 599–612, Jan. 2020, doi: 10.20964/2020.01.61.

[17] I. R. Suhito, N. Angeline, and T.-H. Kim, “Nanomaterial-modified Hybrid Platforms for Precise Electrochemical Detection of Dopamine,” *BioChip Journal*, vol. 13, no. 1, pp. 20–29, Mar. 2019, doi: 10.1007/s13206-019-3106-x.

[18] N. Yusoff, A. Pandikumar, R. Ramaraj, H. N. Lim, and N. M. Huang, “Gold nanoparticle based optical and electrochemical sensing of dopamine,” *Microchimica Acta*, vol. 182, no. 13, pp. 2091–2114, Oct. 2015, doi: 10.1007/s00604-015-1609-2.

[19] F. B. Kamal Eddin and Y. Wing Fen, “Recent Advances in Electrochemical and Optical Sensing of Dopamine,” *Sensors*, vol. 20, no. 4, Art. no. 4, Jan. 2020, doi: 10.3390/s20041039.

[20] S. K. Revanappa, I. Soni, M. Siddalinganahalli, G. K. Jayaprakash, R. Flores-Moreno, and C. Bananakere Nanjegowda, “A Fukui Analysis of an Arginine-Modified Carbon Surface for the Electrochemical Sensing of Dopamine,” *Materials*, vol. 15, no. 18, Art. no. 18, Jan. 2022, doi: 10.3390/ma15186337.

[21] J. Chen, Y.-P. Shi, and J.-Y. Liu, “Determination of noradrenaline and dopamine in Chinese herbal extracts from *Portulaca oleracea* L. by high-performance liquid chromatography,” *Journal of Chromatography A*, vol. 1003, no. 1, pp. 127–132, Jun. 2003, doi: 10.1016/S0021-9673(03)00786-6.

[22] N. O. A. Al-Salahi, E. Y. Hashem, and D. A. Abdel-Kader, “Spectrophotometric Methods for Determination of Dopamine Hydrochloride in Bulk and in Injectable Forms,” *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, vol. 278, p. 121278, Oct. 2022, doi: 10.1016/j.saa.2022.121278.

[23] Y. H. Park, X. Zhang, S. S. Rubakhin, and J. V. Sweedler, “Independent Optimization of Capillary Electrophoresis Separation and Native Fluorescence Detection Conditions for Indolamine and Catecholamine Measurements,” *Analytical Chemistry*, vol. 71, no. 21, pp. 4997–5002, Nov. 1999, doi: 10.1021/ac990659r.

[24] H. Y. Wang, Y. Sun, and B. Tang, “Study on fluorescence property of dopamine and determination of dopamine by fluorimetry,” *Talanta*, vol. 57, no. 5, pp. 899–907, Jul. 2002, doi: 10.1016/S0039-9140(02)00123-6.

[25] H. Duan, L. Li, X. Wang, Y. Wang, J. Li, and C. Luo, “A sensitive and selective chemiluminescence sensor for the determination of dopamine based on silanized magnetic graphene oxide-molecularly imprinted polymer,” *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, vol. 139, pp. 374–379, Mar. 2015, doi: 10.1016/j.saa.2014.12.051.

[26] H. A. M. S. A. Yashıl and İ. Okman Koçoğlu, “Amperometric dopamine sensor based on carbon nanofiber, Fe3O4 nanoparticles, and silver nanoparticles modified glassy carbon electrode,” *Monatshefte für Chemie-Chemical Monthly*, vol. 155, no. 7, pp. 663–672, Jul. 2024, doi: 10.1007/s00706-024-03219-y.

[27] S. Lakard, I.-A. Pavel, and B. Lakard, "Electrochemical Biosensing of Dopamine Neurotransmitter: A Review," *Biosensors*, vol. 11, no. 6, Art. no. 6, Jun. 2021, doi: 10.3390/bios11060179.

[28] M. Sajid, M. K. Nazal, M. Mansha, A. Alsharaa, S. M. S. Jillani, and C. Basheer, "Chemically modified electrodes for electrochemical detection of dopamine in the presence of uric acid and ascorbic acid: A review," *TrAC Trends in Analytical Chemistry*, vol. 76, pp. 15–29, Feb. 2016, doi: 10.1016/j.trac.2015.09.006.

[29] Q. Gong, H. Han, Y. Wang, C. Yao, H. Yang, and J. Qiao, "An electrochemical sensor for dopamine detection based on the electrode of a poly-tryptophan-functionalized graphene composite," *New Carbon Materials*, vol. 35, no. 1, pp. 34–41, Feb. 2020, doi: 10.1016/S1872-5805(20)60473-5.

[30] S. Umapathi, J. Masud, H. Coleman, and M. Nath, "Electrochemical sensor based on CuSe for determination of dopamine," *Microchimica Acta*, vol. 187, no. 8, p. 440, Jul. 2020, doi: 10.1007/s00604-020-04405-5.

[31] H. Yang, C. Zhou, J. An, L. Yang, Y. Yang, and X. Liu, "Ultra-fast synthesis of iron decorated multiwalled carbon nanotube composite materials: A sensitive electrochemical sensor for determining dopamine," *Journal of Alloys and Compounds*, vol. 897, p. 163257, Mar. 2022, doi: 10.1016/j.jallcom.2021.163257.

[32] P. Paulraj *et al.*, "Solid-state synthesis of Ag-doped PANI nanocomposites for their end-use as an electrochemical sensor for hydrogen peroxide and dopamine," *Electrochimica Acta*, vol. 363, p. 137158, Dec. 2020, doi: 10.1016/j.electacta.2020.137158.

[33] L. N. Rizalputri *et al.*, "Facile and controllable synthesis of monodisperse gold nanoparticle bipyramid for electrochemical dopamine sensor," *Nanotechnology*, vol. 34, no. 5, p. 055502, Nov. 2022, doi: 10.1088/1361-6528/ac9d3f.

[34] N. Sofia Anuar, W. Jeffrey Basirun, M. Shalauddin, and S. Akhter, "A dopamine electrochemical sensor based on a platinum–silver graphene nanocomposite modified electrode," *RSC Advances*, vol. 10, no. 29, pp. 17336–17344, 2020, doi: 10.1039/C9RA11056A.

[35] S. E. Elugoke, O. E. Fayemi, A. S. Adekunle, B. B. Mamba, T. T. I. Nkambule, and E. E. Ebenso, "Electrochemical sensor for the detection of dopamine using carbon quantum dots/copper oxide nanocomposite modified electrode," *FlatChem*, vol. 33, p. 100372, May 2022, doi: 10.1016/j.flatc.2022.100372.

[36] S. Paramparambath *et al.*, "Nonenzymatic Electrochemical Sensor Based on CuO-MgO Composite for Dopamine Detection," *IEEE Sensors Journal*, vol. 21, no. 22, pp. 25597–25605, Nov. 2021, doi: 10.1109/JSEN.2021.3112009.

[37] Z. A. Alothman, N. Bukhari, S. M. Wabaidur, and S. Haider, "Simultaneous electrochemical determination of dopamine and acetaminophen using multiwall carbon nanotubes modified glassy carbon electrode," *Sensors and Actuators B: Chemical*, vol. 146, no. 1, pp. 314–320, Apr. 2010, doi: 10.1016/j.snb.2010.02.024.

[38] B. Rezaei, A. M. Shoushtari, M. Rabiee, L. Uzun, W. C. Mak, and A. P. F. Turner, "An electrochemical immunosensor for cardiac Troponin I using electrospun carboxylated multi-walled carbon nanotube-whiskered nanofibres," *Talanta*, vol. 182, pp. 178–186, May 2018, doi: 10.1016/j.talanta.2018.01.046.

[39] G. C. Zhao, L. Zhang, X.-W. Wei, and Z.-S. Yang, “Myoglobin on multi-walled carbon nanotubes modified electrode: direct electrochemistry and electrocatalysis,” *Electrochemistry Communications*, vol. 5, no. 9, pp. 825–829, Sep. 2003, doi: 10.1016/j.elecom.2003.07.006.

[40] P. Y. Chen, R. Vittal, P.-C. Nien, and K.-C. Ho, “Enhancing dopamine detection using a glassy carbon electrode modified with MWCNTs, quercetin, and Nafion®,” *Biosensors and Bioelectronics*, vol. 24, no. 12, pp. 3504–3509, Aug. 2009, doi: 10.1016/j.bios.2009.05.003.

[41] H. Wang, S. Yao, Y. Liu, S. Wei, J. Su, and G. Hu, “Molecularly imprinted electrochemical sensor based on Au nanoparticles in carboxylated multi-walled carbon nanotubes for sensitive determination of olaquindox in food and feedstuffs,” *Biosensors and Bioelectronics*, vol. 87, pp. 417–421, Jan. 2017, doi: 10.1016/j.bios.2016.08.092.

[42] P. B. Desai, R. M. Kotkar, and A. K. Srivastava, “Electrochemical behaviour of pyridoxine hydrochloride (vitamin B6) at carbon paste electrode modified with crown ethers,” *Journal of Solid State Electrochemistry*, vol. 12, no. 9, pp. 1067–1075, Sep. 2008, doi: 10.1007/s10008-007-0435-9.

[43] R. M. Kotkar, P. B. Desai, and A. K. Srivastava, “Behavior of riboflavin on plain carbon paste and aza macrocycles based chemically modified electrodes,” *Sensors and Actuators B: Chemical*, vol. 124, no. 1, pp. 90–98, Jun. 2007, doi: 10.1016/j.snb.2006.12.004.

[44] G. Rounaghi, R. M. kakhki, and H. Azizi-toupkanloo, “Voltammetric determination of 4-nitrophenol using a modified carbon paste electrode based on a new synthetic crown ether/silver nanoparticles,” *Materials Science and Engineering: C*, vol. 32, no. 2, pp. 172–177, Mar. 2012, doi: 10.1016/j.msec.2011.10.014.

[45] N. Serrano, A. González-Calabuig, and M. del Valle, “Crown ether-modified electrodes for the simultaneous stripping voltammetric determination of Cd(II), Pb(II) and Cu(II),” *Talanta*, vol. 138, pp. 130–137, Jun. 2015, doi: 10.1016/j.talanta.2015.01.044.

[46] M. L. Colombo, S. McNeil, N. Iwai, A. Chang, and M. Shen, “Electrochemical Detection of Dopamine via Assisted Ion Transfer at Nanopipet Electrode Using Cyclic Voltammetry,” *Journal of The Electrochemical Society*, vol. 163, no. 4, p. H3072, Dec. 2015, doi: 10.1149/2.0091604jes.

[47] S. Koçoğlu, Z. Hayvalı, H. Ogutcu, and O. Atakol, “Synthesis, antimicrobial and thermal studies of nitropyridine-substituted double armed benzo-15-crown-5 ligands; alkali (Na+ and K+) and transition metal (Ag+) complexes; reduction of nitro compounds,” *Journal of Inclusion Phenomena and Macrocyclic Chemistry*, vol. 102, no. 9, pp. 763–780, Oct. 2022, doi: 10.1007/s10847-022-01157-y.

[48] S. Koçoğlu, H. Ogutcu, and Z. Hayvalı, “Photophysical and antimicrobial properties of new double-armed benzo-15-crown-5 ligands and complexes,” *Research on Chemical Intermediates*, vol. 45, no. 4, pp. 2403–2427, Apr. 2019, doi: 10.1007/s11164-019-03741-3.

[49] A. E. F. Oliveira, G. B. Bettio, and A. C. Pereira, “Optimization of an Electrochemical Sensor for Determination of Imidacloprid Based on β-cyclodextrin Electropolymerization on Glassy Carbon Electrode,” *Electroanalysis*, vol. 30, no. 9, pp. 1929–1937, 2018, doi: 10.1002/elan.201800235.

[50] İ. Okman Koçoğlu, P. E. Erden, and E. Kılıç, “Disposable biosensor based on ionic liquid, carbon nanofiber and poly(glutamic acid) for tyramine determination,” *Analytical Biochemistry*, vol. 684, p. 115387, Jan. 2024, doi: 10.1016/j.ab.2023.115387.

[51] Y. H. Chang, P. M. Woi, and Y. Alias, "Optimization parameters for electropolymerization of melamine in deep eutectic solvent," *Malaysian Journal of Analytical Sciences*, vol. 26, no. 2, pp. 202–214, 2022.

[52] J. Ahmed, M. Faisal, F. A. Harraz, M. Jalalah, and S. A. Alsareii, "Development of an amperometric biosensor for dopamine using novel mesoporous silicon nanoparticles fabricated via a facile stain etching approach," *Physica E: Low-dimensional Systems and Nanostructures*, vol. 135, p. 114952, Jan. 2022, doi: 10.1016/j.physe.2021.114952.

[53] E. Wudarska, E. Chrzescijanska, E. Kusmierek, and J. Rynkowski, "Electrochemical Behavior of 2-(p-isobutylphenyl)propionic Acid at Platinum Electrode," *International Journal of Electrochemical Science*, vol. 10, no. 11, pp. 9433–9442, Nov. 2015, doi: 10.1016/S1452-3981(23)11191-6.