Cucurbit [6] Uril Modified Platinum Electrode for Electrochemical Detection of Norepinephrine

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***Abstract*—An electrochemical sensor based on cucurbit [6] uril has been developed for sensitive detection of an important neurotransmitter, norepinephrine (NEP). On a platinum wire electrode, the cucurbit [6] uril solution was drop-casted and is known as a modified electrode. The modified sensor has been characterized by scanning electron microscopy (SEM) to understand the morphological properties of the sensor surface. Electrochemical responses of norepinephrine at a CB [6] modified sensor were investigated by cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS). CV studies of NEP at the modified electrode were carried out in the potential range of 0 V to 0.8 V in phosphate buffer solution (pH 7.0) and impedance studies at potential 0.4 V in the frequency range of 0.1 Hz to 10^3 kHz. The modified electrode showed increased current response and decreased charge transfer resistance towards the oxidation of NEP compared to the bare electrode.**

***Index Terms*—Norepinephrine, Electrode modification, Electrochemical sensor, Electrochemical Techniques, Cyclic Voltammetry, Macrocyclic oligomer.**

I. INTRODUCTION

Norepinephrine (NEP), also known as the "hormone of stress," is an important monoamine neurotransmitter present in the nervous tissue and biological body fluid [1]. It influences and affects every day actions and daily routines and regulates vital physiological functions such as sleep, anxiety, blood pressure, learning, and memory [2]. It activates hormones, increases heart rate, increases blood pressure, releases glucose, and sends blood to muscles [3]. It is also helpful in the identification of cardiac conditions, congestive heart failure, hypertension, and diabetes mellitus [4, 5]. Various techniques such as spectrophotometry [6], high-performance liquid chromatography [7], capillary electrophoresis [8], and fluorescence [9] are commonly used methods to analyze norepinephrine. NEP is an electroactive compound, so researchers and microchemists concentrate their study on its electrochemical detection [10, 11]. Electrochemical techniques provide benefits such as high sensitivity, fast response, simplicity of miniaturization, a straightforward procedure, and low cost [12, 13].

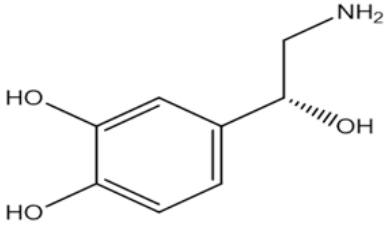

Fig 1: Structure of Norepinephrine

Numerous modification approaches and electrode materials have been developed to enhance sensitivity and selectivity of electrodes such as grapheme [14], carbon nanotube composites [15], MIP [16], conducting polymers [17], metal-organic frameworks (MOFs) [18], and macrocyclic oligomers. Macrocyclic oligomers such as calixarenes, cucurbit [n] urils (CB [n]), crown ethers, and pill arenes modified electrodes are used for neurotransmitter detection [19, 20]. Incorporation of CB [n] on the surface of the electrode increases the sensitivity of the electrode surface, as these molecules have the ability to form selective host-guest complexes [21]. Cucurbiturils (CB [n]) (Fig. 2) belong to the class of macrocyclic oligomers, which are synthesized by the acid-catalyzed condensation reaction of glycoluril and formaldehyde [22]. CB [6] has six glycoluril units and has an inner cavity, which is hydrophobic and is a potential inclusion site, whereas both portals are surrounded by carbonyl groups, allowing hydrogen bond interactions and ion-dipole interactions [23].

This property makes it a promising molecular host with a wide variety of species, such as cations, anions, and neutral molecules [24].

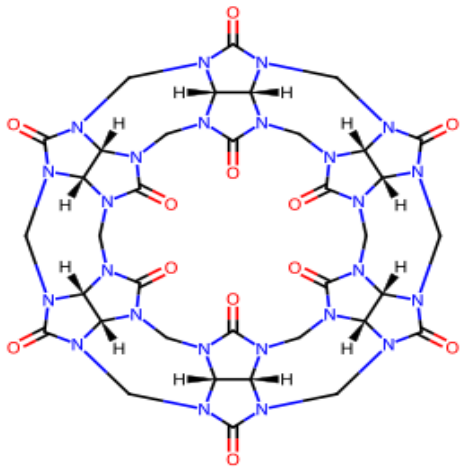

Fig 2: Structure of Cucurbit [6] uril

Cucurbit [6] uril modified electrodes are earlier used for the detection of 4,4'-oxydianiline [25], 3,4-methylenedioxymethamphetamine (MDMA) [26], ranitidine hydrochloride [27], and the drug Metformin [28]. Supramolecular self-assembly between cucurbit [6] uril and 1-(2-hydroxyphenyl) piperazine hydrochloride shows an inclusion complex with a host-guest ratio of 1:2. Formation of the complex is driven by weak non-covalent forces such as ion-dipole interaction and weak hydrogen bonding (e.g., C-H----O) between the host and guest [29]. For sensitive detection of hazardous air pollutants, a cucurbit [6] uril-enhanced electrochemical sensor was also developed [30]. NEP undergoes oxidation to give norepinephrine quinone, and in the backward direction, norepinephrine quinone undergoes reduction to give NEP, as shown in the Fig 3.

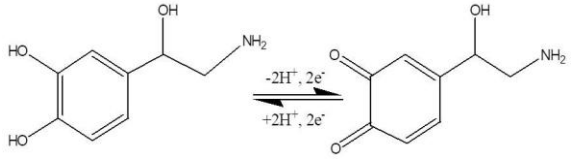

Fig 3: Oxidation mechanism of NEP

In this research, platinum electrode modified by CB [6] solution was used for the sensitive detection of NEP. The analytical performance of the developed sensor was investigated using cyclic voltammetry and electrochemical impedance spectroscopy. The experimental results showed that the modified electrode displayed a significant increase in current response in CV and decrease in charge transfer resistance towards NEP oxidation compared to the bare electrode. To the best of our knowledge, the employment of a CB [6] solution on a platinum electrode for NEP detection has not been reported yet. Surface morphology of the modified electrode was studied by scanning electron microscopy (SEM).

II. EXPERIMENTAL SECTION

2.1 Reagents and apparatus

All chemicals and solvents employed were of analytical reagent grade and used without further purification. Norepinephrine and macrocyclic oligomer cucurbit [6] uril were purchased from Sigma Aldrich. All solutions were prepared with triple distilled water (TDW). A conventional three-electrode system was used for the electrochemical measurements, which comprised a platinum wire as the auxiliary electrode, a saturated calomel electrode (SCE) as the reference electrode, and a CB [6] modified electrode as the working electrode. Phosphate buffer solution (PBS) of pH 7 was prepared by mixing 2.99 g potassium dihydrogen phosphate (NaH_2PO_4) and 4.44 g dipotassium hydrogen phosphate (Na_2HPO_4). All electrochemical measurements were performed at 25°C using a Multi Auto lab M 204 potentiostat equipped with Nova 2.1 software. Morphological images of CB [6] modified electrodes were recorded using a scanning electron microscope (SEM), ZEISS, EVO 18. Cyclic voltammetry is performed in the potential range of 0.0 to 0.8 V vs SCE, and impedance studies are carried out at potential 0.4 V in the frequency range of 0.1 Hz to 10^3 kHz.

2.2 Preparation of modified electrode

For electrochemical measurements, platinum wire (purity 99.5%) with a diameter of 0.5 mm sealed in soft glass was used as a working electrode. After being cleaned and washing it with triple-distilled water, cucurbit [6] uril solution was drop casted on platinum wire electrode and then the obtained modified electrode is used for norepinephrine sensing.

2.3 Morphological characterization

The morphology of CB [6] modified electrode was characterized by scanning electron microscope and is shown in the figure 4.

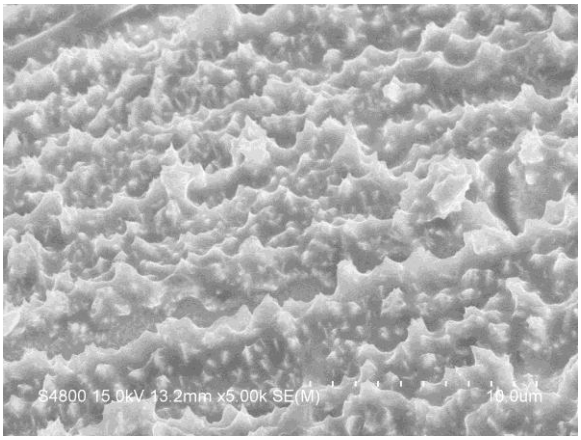

Figure 4: SEM images of CB [6] modified platinum electrode

III. RESULTS AND DISCUSSION

3.1 Cyclic voltametric studies

The electrochemical behavior of NEP at CB [6] modified electrode was investigated in 0.1 M PBS (pH 7.0) by means of cyclic voltammetry technique in aqueous buffered solution. To assess the electrochemical performance of the electrode, cyclic voltammograms of 10^{-3} M NEP at a scan rate of 100 mV s^{-1} in 0.1 M phosphate-buffered saline (PBS, pH 7.00) were recorded at CB [6] modified electrode as shown in Fig. 5. Cyclic voltammetry (CV) analysis demonstrated that the oxidation peak current response (I_p) of the redox species NEP at the CB [6] modified electrode (red line) significantly enhanced than that of the bare electrode. Green line indicates current response of electrochemical oxidation of norepinephrine on bare electrode, and red line is the current response at CB [6] modified electrode. The increased I_p of the modified electrode reflected its superior performance in the redox reaction of the species on the electrode surface. It was concluded that the current response improved after CB [6] modification (red line). Because of the sluggish electron transfer phenomenon low redox peak currents response was obtained at bare electrode. However, in the same identical condition the CB [6] modified electrode exhibited static increment of redox peak currents with the improvement in the electron transfer kinetics. The result suggests that the surface property of the modified electrode has been changed significantly. The oxidation peak current of the modified electrode increased, which indicates that the specific surface area of the electrode increased.

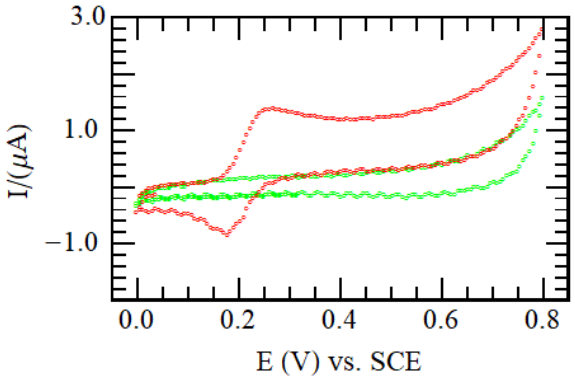

Figure 5: Cyclic voltammetric response of 10^{-3} M NEP in 0.1 M PBS at bare electrode (green line) and CB [6] modified electrode (red) pH 7 scan rate 100 mV/S

3.2 Electrochemical impedance studies

EIS is a useful technique for determining the interface properties of electrode surfaces. The electrochemical impedance spectra in the presence of NEP at bare and CB [6] modified electrode are represented by the Nyquist curves in Fig. 6. The impedance changes of the interface properties before and after surface modification was investigated via EIS. The charge transfer resistance (R_{ct}) at the electrode surface of the electrodes was calculated by analyzing the semicircle diameter of the EIS Nyquist plot. Fig. 6 presents the compared Nyquist plots of norepinephrine at bare and CB [6] modified electrode. As evident, the semicircle diameter of the Nyquist plot for the modified electrode was smaller than that of the bare electrode. This finding corresponds to the lower R_{ct} values of the modified electrode.

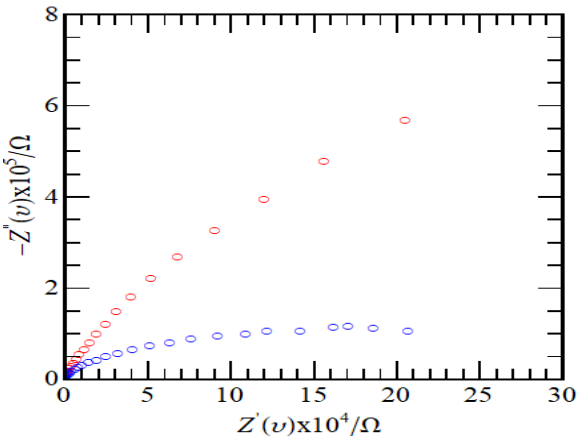

Figure 6: Electrochemical impedace response of NEP at bare electrode (red) and CB [6] modified electrode (blue) at potential 0.4 V in the frequency range of 0.1 Hz to 10^3 kHz.

IV. CONCLUSION

In this research, a sensitive electrochemical sensor as an advanced platform for detection of norepinephrine (NEP) was developed by modifying platinum electrode with CB [6]. The morphological and electrochemical characterization of the modified electrode was studied using SEM, CV and EIS. The cyclic voltametric detection of norepinephrine shows that after modification oxidation peak currents enhanced ensuring remarkable sensitivity. The impedance studies show that there is decrease in the charge transfer resistance after modification of electrode. Thus, the CB [6] modified sensor sets a new benchmark for electrochemical biosensors. In conclusion, the developed electrochemical sensor based on cucurbit [6] uril modified electrode demonstrates highly sensitive detection of norepinephrine, overcoming the limitations of conventional bare electrodes.

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