

Voltammetric Determination of Metamizol Sodium in Pharmaceutical Tablets at Polypyrrole-Carbon Nanotube Modified Electrodes

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Abstract

Poly pyrrole-carbon nanotube (PPy-CNT) composite electrodes were prepared with ultrasonication assisted pulsed polymerization technique. This technique possesses both advantages of ultrasonication and electrochemical polymerization. PPy-CNT composite was modified on the bare glassy carbon electrode (GCE) surface easily with pulsed deposition technique that provide more catalytically active surface compared to the bare GCE towards metamizol oxidation. Resulted electrode was characterized by scanning electron microscopy and used for investigation of metamizaol in pH:2 Britton-Robinson buffer solution. In the differential pulse voltammetric determination, the linear range was found as 5-500 mg L⁻¹ with a detection limit of 1.6 mg L⁻¹. The overall results showed that PPy-CNT electrode has an excellent sensitivity, selectivity and anti-fouling properties for the voltammetric determination of metamizol. PPy-CNT/GCE sensor was applied succesfully to the determination of metamizol in novalgine sample.

Keywords: PPy-CNT, Metamizol Sodium, Voltammetry, Pulsed Amperometric Deposition

Poliprol-Karbon Nanotüp Modifiye Elektrotta Farmasötik Tabletlerde Metamizol Sodyumun Voltammetrik Tayini

Öz

Polipirol-karbon nanotüp (PPy-CNT) kompozit elektrot, ultrasonikasyon ile eşleştirilmiş pulslu polimerizasyon tekniği ile hazırlanmıştır. Bu teknik, hem ultrasonikasyon hem de elektrokimyasal polimerizasyonun avantajlarına sahiptir. PPy-CNT kompoziti pulslu depolama tekniği ile camımsı karbon elektrot (GCE) yüzeyine kolayca modifiye edilmiş, ve metamizol yükseltgenmesine karşı camımsı karbon elektroda göre katalitik aktivitesi yüksek bir yüzey elde edilmiştir. Hazırlanan elektrot taramalı electron mikroskopu ile karakterize edilmiş ve pH:2 Britton-Robinson tamponunda metamizol davranışı incelenmiştir. Diferansiyel pulse voltammetrisi ile lineer aralık 5-500 mg L⁻¹ olarak saptanmış ve belirtme alt sınırı 1.6 mg L⁻¹ olarak hesaplanmıştır. Yapılan tüm çalışmalar göstermiştir ki, PPy-CNT/GCE, metamizol tayini için yüksek duyarlılık, seçicilik ve kararlılığa sahiptir. PPy-CNT/GCE sensörü novalgine tablet örneğine uygulanarak gerçek örnek analizi başarı ile gerçekleştirilmiştir.

Anahtar Kelimeler: PPy-CNT, Metamizol Sodyum, voltammetry, Püslü Amperometrik Birikim

1. Introduction

Carbon nanotubes (CNT) have attracted great interest since first reported by Iijima (Esteves et al., 2018). CNTs, most commonly used carbon nanostructures, have received a remarkable attention, especially in electrochemical sensors. Their unique

electrical, mechanical, thermal properties and large specific surface area make them good electrode material (Jiang and Lee, 2018). CNTs can be functionalized both through with covalent and noncovalent interactions without any damage to their electrical and chemical properties (Rohani and Taher, 2018). They

have been used in a various fields including, batteries (Li et al., 2017; Fang et al., 2017), solar cells (Arici and Karazhanov, 2016) actuators (Bensghaïer et al., 2018), fuel cells (Huang et al., 2017) and sensing (Cittan et al., 2016; Koçak and Aslışen, 2014). Polymer films improve the electrocatalytic properties of substrates, stability and reproducibility of the electrode response, increase electron transfer rate, and decrease the overpotential. Electropolymerization method lead an ability to control the thickness, porosity, permeation and charge transport characteristics of the polymeric films by adjusting the electrochemical parameters (Pınar et al., 2018; Sangamithirai et al., 2018). Among all conducting polymers Polypyrrole (PPy) is one of the most studied conducting polymer. Ppy has ability to synthesis easily, good stability, and higher conductivity than many other polymers (Korba et al., 2013). The electrical conductivities of PPys are known to be strong functions of their oxidation states and doping anion used in the electro-polymerization process (Şenel and Nergis, 2012; Shahrokhian

and Asadian, 2009). Conducting polymer-CNT composite modified electrodes have attracted great interest due to the incorporation of this two special component can bring together a new composite materials which providing the properties of each component, with a synergistic effect that can increase the catalytic activity of the surface towards many analytes in sensor applications (Ghica et al., 2014). Carbon nanotubes can increase the conductivity of conducting polymer matrices and form a three-dimensional network which can facilitate access to the analyte and increase the rate of electron transfer (Kong et al., 2017). Composite electrodes modified with conducting polymers are reproducible and possess more active sites than conventional electrodes (Mekassa et al., 2017). Metamizol (dipyrone, analgin) (Fig. 1) the sodium salt of 1-phenyl-2,3-dimethyl-4-methylaminomethanesulphonate-5-pyrazolone, is one of the most most popular and powerful substances in analgesics class (Medeiros et al., 2004).

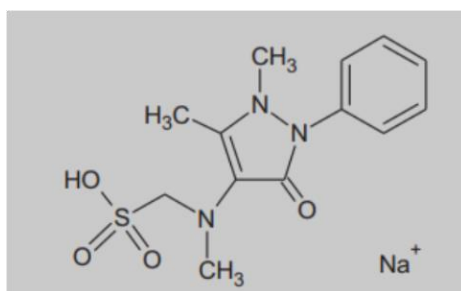


Fig. 1 Chemical structure of metamizol

After intake, metamizol is hydrolyzed by non-enzymatic pathway to 4-methylaminoantipyrine (MAA), which is absorbed from the gastrointestinal tract and further biotransformation occurred in liver by enzymatic demethylation to 4-aminoantipyrine (AA) (Assumpção et al., 2013). However, metamizol has many advantages, its use in some countries such as USA is restricted because of the risk of adverse reactions (Freitas et al., 2012). Many

methods were used for determination of metamizol such as; chromatography (Zhang et al., 2016), fluorescence (Perez-Ruiz et al., 1993) and voltammetry (Teixeira and Dadamos, 2009). Although many studies have been dedicated to metamizole research, it is still required to develop more sensitive, robust, and rapidly detecting sensors. In the present study, by exploiting the advantages offered by electropolymer/CNTs composites,

we report on the fabrication of composite electrode

by ultrasonication coupled with pulse deposition technique. CNT and pyrrole simultaneously polymerized on the glassy carbon surface. The modified composite electrode was characterized by scanning electron microscopy (SEM). After characterization, this composite electrode was used for investigation of metamizol. The resulted electrode exhibit wide concentration range, low detection limit and good reproducibility for the metamizol determination in pharmaceutical tablets.

2. Material and Method

Pyrrole was purchased from Sigma and triple distilled under Ar atmosphere until a colorless liquid was obtained. NaClO₄, Metamizol were of analytical-reagent grade and supplied from Sigma. Multi-walled carbon nanotubes (MWCNTs, purity > 95% diameter 110–170 nm, length 9 μm) were purchased from Aldrich. N,N-Dimethyl Formamide (DMF) was purchased from Merck. All of the solutions were prepared using ultrapure water provided from an 18 MΩ cm Milli-Q system. All experiments were carried out at ambient temperature and highly pure nitrogen was kept flowing over the solution during electrochemical experiments.

Bandelin sonorex ultrasonic bath was used for ultrasonic coupled measurements. The pH measurements were made with Thermo 4 pH-meter. Voltammetric experimentss were carried out using a Autolab PGST 101 Electrochemical Analyser equipped with a three electrode system consisting of a working electrode (GCE, PPy-CNT/GCE), a counter platinum electrode and an Ag/AgCl (sat. KCl) were used as a reference electrode

2.1. Pretreatment of CNT and preparation of modified electrodes

MW-CNT was treated with concentrated HNO₃ prior to usage. According to the procedure given in literature (Koçak et. Al. 2014) CNT was heated in con. HNO₃ for 15 min. and further washed with ultrapure water until the filtrate pH become neutral. Black suspension of CNT was obtained after acid treated CNT and DMF agitated in ultrasonic bath. Before modification, GCE was cleaned by polishing with a Al₂O₃ slurry (3 μm) on a synthetic cloth, then sonicated in water for 5 min.

The PPy-CNT/GCE was prepared on freshly polished GC electrode that was immersed into the cell containing 0.1 M pyrrole, 1mg CNT/10 mL DMF and 0.1 M NaClO₄. The cell was placed in to the ultrasonic bath and pulsed deposition program was applied where the potential was set at -0.25V for 5 s and then 2.2V for 5 s, sequentially. This process was repeated for 50 times and the resulting electrode abbreviated as PPy-CNT/GCE.

3. Findings

3.1. Characterizations of PPy-CNT modified electrode

SEM images were characterize the typical morphologies of the PPy/GCE (Fig. 2a), PPy-CNT prepared without ultrasonication (Fig. 2b), PPy-CNT prepared by ultrasonication coupled with polymerization with 1000x magnitude (Fig. 2c) and PPy-CNT prepared by ultrasonication coupled with polymerization with 25000x magnitude (Fig. 2d). At the PPy/GCE porous surface appeared. a three-dimensional film with high roughness,

indicating that PPy was successfully electropolymerized on the electrode surface with increase of the effective area. Fig 2b and 2c depicts the effect of ultrasonication process that more homogeneous surface was obtained for PPy-CNT/GCE in case of ultra sonication

applied with polymerization. In Fig. 2d, a wrinkled structure could be observed and indicated that the CNTs were successfully incorporated into the GCE. And spherical polymer structures were observed on both GCE and carbon nanotube surface.

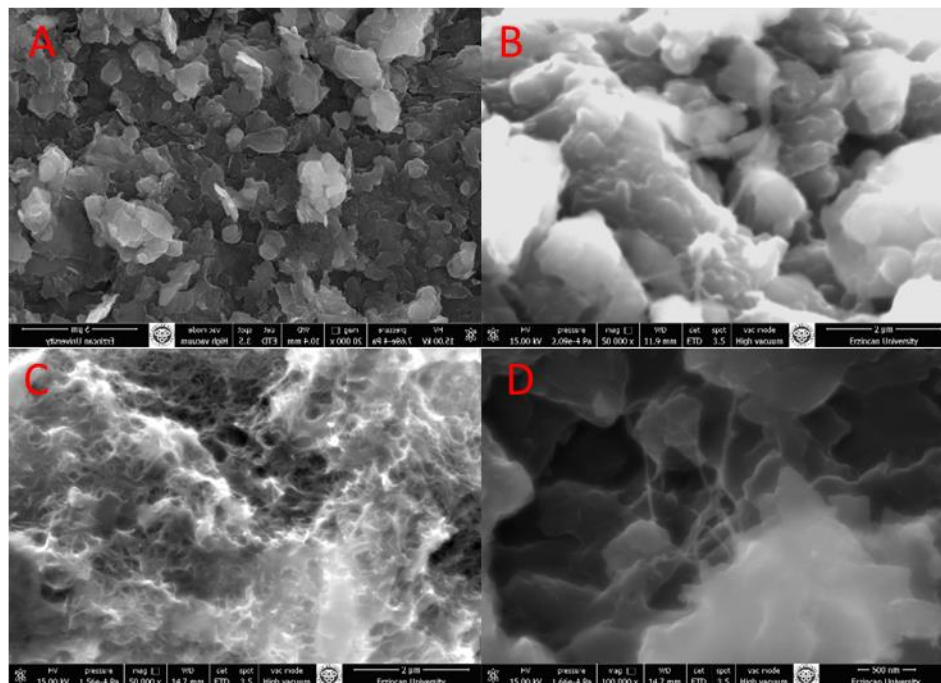


Fig. 2 SEM images of A) PPy, B) PPy-CNT (without ultrasonication), C) PPy-CNT (1000x magnitude), D) PPy-CNT(25000x magnitude).

3.2. Voltammetric measurements

The influence of pH on the electrochemical response of PPy-CNT/GC electrode toward 40 mg L⁻¹metamizol was investigated by CV in Britton Robinson buffer of different pHs ranged from 2.0 to 12.0. The obtained results are presented in current- pH graphic in Fig.

3b. As can be seen from Fig. 3, there is only one oxidation peak of metamizol observed at lower pH values, while two or more peaks observed with the increase of pH. It was found that at pH 2.0 the well-shaped, the most symmetrical and intense peak of metamizol was obtained, hence this value was chosen as the optimal for the future studies.

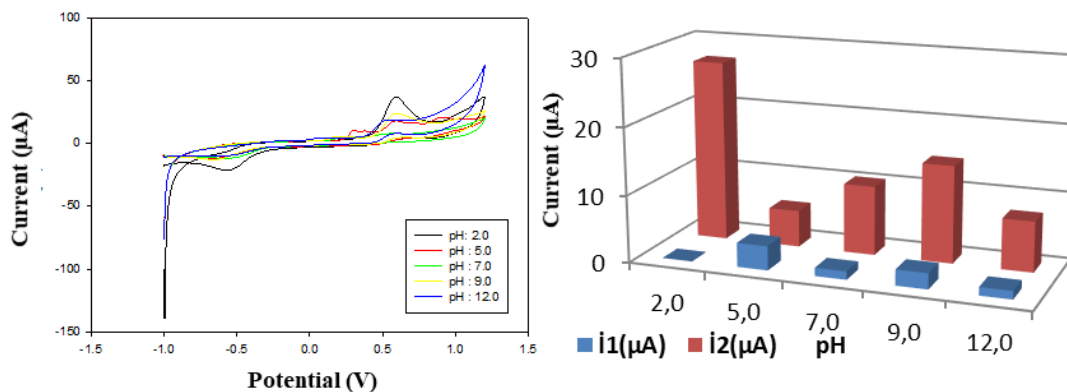


Fig. 3 a) CV behavior of PPy-CNT/GCE with different pHs of B-R buffer solutions, b) The Influence of pH on PPy-CNT/GCE responses in the presence of 40 mg L⁻¹metamizol.

Pulsed deposition technique offers the formation of nucleation sites and thus contributes to a high dispersion of the deposits compared with other deposition procedures (Yavuz et al., 2015). Surface coverage was significantly affecting the catalytic performance of the electrode that changes

with the applied pulse number. Therefore, pulse number varies 20 to 100 in order to investigate the oxidation current of metamizol. As can be seen from the Fig. 4 that 50 pulse number was provide the best catalytic activity towards metamizol oxidation.

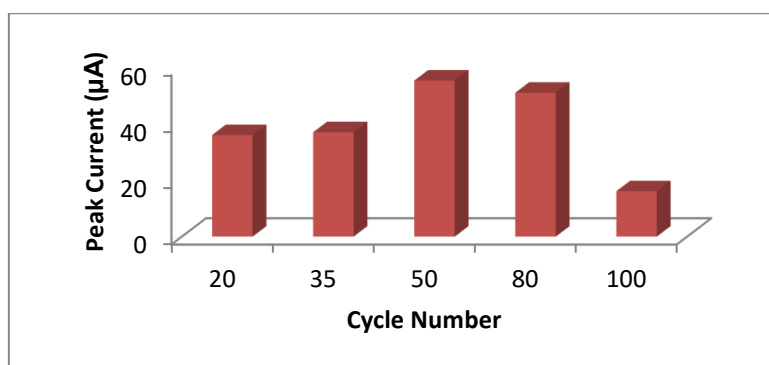


Fig. 4 The effect of applied pulse number on a deposition potential of -0.25 to 2.2V on the metamizaol signal for PPy-CNT/GCE.

Cyclic voltammograms for different concentrations of metamizol in BR buffer solution of pH 2.0 were recorded under the optimum experimental conditions. DP voltammograms were recorded for metamizol oxidation with concentration range from 5 to 500 mg L⁻¹ in pH:2 B-R buffer solution with a scan rate of 100 mV s⁻¹ (Fig. 5). The anodic peak currents (I_{pa}) of metamizaol were found

to be proportional with its concentration with linear regression equations of I_{pa} (µA)=0.0519 C metamizol (mg L⁻¹) -0.1414 ($R^2=0.9995$) (Fig. 5B). The limit of detection (LOD) of metamizaol electrooxidation on PPy-CNT/GCE was calculated as 1.6 mg L⁻¹. The LOD values were calculated using the equation $LOD=3.3\sigma/m$, where is the σ is the standard deviation of the response for blank

solution, m is the slope of the calibration graph.

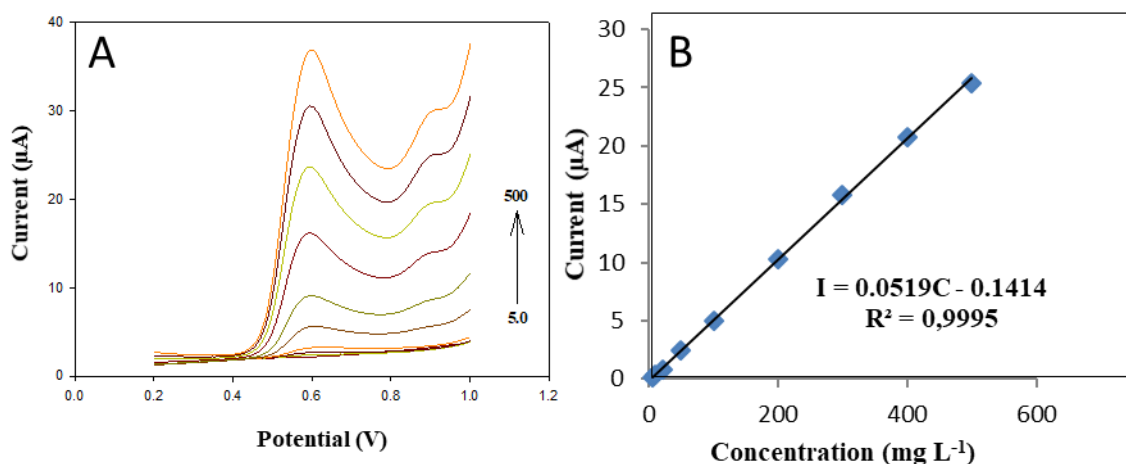


Fig. 5 DP voltammograms of metamizol at PPy-CNT/GCE. Metamizaol concentrations ; 5 to 500 mg L⁻¹ in pH:2 B-R buffer solution with a scan rate of 100 mV s⁻¹. Inset: the calibration curve.

3.3. Interference studies

The selectivity of the developed electrode towards metamizol oxidation was established in the presence of potential interferences under optimized conditions. The study of interference effects instigated by lactose and magnesium stearate that can be found in the tablets of 250 mg L⁻¹ was carried out in a standard 50 mg L⁻¹ metamizol solution. The results show that even 50 fold concentrations of the compounds did not interfere with the determination of metamizol using PPy-CNT/GCE. In all cases, the deviation in peak current response of metamizol is less than 5%. These results demonstrated that the modified electrode had a good anti-interference ability toward the determination of metamizol.

3.4. Stability, repeatability and reproducibility of modified electrode

In order to verify the repeatability of the response of the modified electrode, CVs for a solution of 50 mg L⁻¹ metamizol were obtained repeatedly for successive 5 times. The relative standard deviations (RSD) for

peak current were obtained as 6.06 % for metamizol. The reproducibility of the modification procedure was studied by preparing 5 modified electrodes at different days with a same fabrication procedure. The RSD values for current of peak in a solution of 50 mg L⁻¹ metamizol was determined as 8.62 %. In addition, the long-term stability of PPy-CNT/GCE was studied over a period of one week. The oxidation peak current after this time was retained 88.54% of its initial response.

3.5. Real sample analysis

In order to investigate the applicability of PPy-CNT/GCE on to the real samples, the method was applied to Novalgine tablet sample by standard addition method. Three standards were added into the samples with different concentration levels. Triplicate analyses were performed for all samples. Novalgine 500 mg (Sanofi-Aventis) was dissolved in pH: 2.0 buffer by ultrasonication. Filtered with a 0.45 µ filter paper and added to the voltammetric cell. 50 mg L⁻¹ of metamizol was added to the cell each time for

three standard additions. 99% recovery value was calculated from the related curve.

4. Result and Discussion

In this paper, composite PPy-CNT/GC electrode was prepared by ultrasonication coupled with pulse electropolymerization technique. The catalytic activity of bare GCE towards metamizol oxidation was improved by the poly-pyrrole and CNT modification on the electrode surface which lead an increase in electronic conductivity and effective surface area. In the differential pulse voltammetric determination, the linear range was found as 5-500 mg L⁻¹ with a detection limit of 1.6 mg L⁻¹. The overall results showed that polypyrrole-CNT electrode has an excellent sensitivity, selectivity and anti-fouling properties for the voltammetric determination of metamizol. The proposed method was successfully applied to real samples with satisfactory results.

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