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## Research Paper

# Electrocatalytic Determination of Captopril on Gold Nanoparticle-Modified Carbon Paste Electrode

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**Keywords:**
**Determination, Captopril, Gold Nanoparticle, CPE, Amperometry.**

**Abstract:**
The electrochemical behavior of captopril at the surface of a carbon-paste electrode (CPE) modified with gold nanoparticles (GNPs) is described. The prepared electrode shows an excellent electrocatalytic activity toward the oxidation of captopril, which is leading to marked considerable improvement of sensitivity. Whereas at the surface of unmodified electrode an electrochemical activity for captopril cannot be observed, a very sharp anodic wave with an anodic peak potential about 1.0 V (versus Ag/AgCl) is obtained using the prepared modified electrode. Captopril oxidation on CPE/GNPs proceeds at pH between 4.0 and 10.0. Under the optimized conditions, the electrocatalytic oxidation peak current of captopril showed two linear dynamic ranges with a detection limit of $8.28\times10^{-2}$ µM captopril. The linear calibration range was 1.14-16.98 and 21.49-62.1 µM using amperometric. Finally, the sensor was examined as a selective, simple, and precise new electrochemical sensor for the determination of captopril in pharmaceutical samples including tablets and satisfactory results were obtained.

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## 1. INTRODUCTION

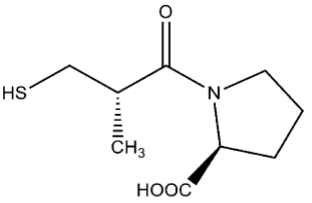
Captopril, (S)-1-(3-mercapto-2-methyl-1-oxopropyl)-1-prolin, is widely used in the treatment of hypertension, congestive heart failure and heart attack [1,2]. Captopril (CAP) contains a sulfhydryl group and it is reported to has the stimulatory effect on vascular prostacyclin synthesis [3]. Captopril is a unique antihypertensive drug as it is the only one with a thiol-group in its structure. This gives it the ability to act as a scavenger of free radicals in living systems. A further advantage of the pharmaceutical is its antioxidant properties [4–6]. It undergoes rapid oxidation to disulfide metabolites both in vitro and in vivo. Disulfide metabolites are reduced intracellularly to the free thiol, thus acting as storage of free captopril. Captopril is pharmacologically active only its free form. However, since the formation of the inactive disulfides is reversible, the blood concentration of free captopril gives an underestimation of its duration of action [4]. Thus, determination of CAP is very significant.

Titrimetry [7], an electro-analytical approach [8–10], liquid chromatograph [11,12], gas liquid chromatography (GLC) [13,14], spectrophotometry [15], and fluorimetry [16] are just a few of the methods published for the quantitative detection of CAP. Utilizing oxidizing agents including hydrogen peroxide [17], N,N dimethyl p phenylenediamine in the presence of $Fe^{+3}$ ions [18], Ag(II) [19], and thiol [20], the CAP was calculated. The previously published approaches frequently have a variety of drawbacks, such as procedures that are occasionally complex, time-consuming, expensive to implement, or that may not be appropriate for determining CAP at lower levels. However, among the various methods reported for CAP detection, electrochemical techniques are often preferred because of their low cost, high selectivity, rapid detection, and lack of a substantial sample preparation setup [21–24].

Indeed, various studies have shown that metal nanoparticles provide key properties for the electroanalysis of biological, environmental and other important electroactive compounds. These properties include roughening of the conductive sensing interface, the catalytic behavior of this class of nanomaterials, which allows them to be enlarged with metals, the amplified electrochemical detection of metal deposits, and the redox response of nanoparticles, which allows the electrocatalytic determination of compounds with high over-potentials [25,26].

Herein we report the synthesis of a novel GNPs amperometric sensor supported on a CPE framework and its use for the electrocatalytic determination of CAP in

pharmaceuticals samples.




**Scheme 1.** Captopril (1-((2S)-3-Mercapto-2-Methyl-Propionyl)-S (L)- Proline) chemical structure.

## 2. EXPERIMENTAL

### *A. Apparatus and Reagents*

All voltammetric and chronocoulometric measurements have been performed on Electrochemical Work Station, model Autolab PGSTAT 302N using NOVA software, version 1.8. A three-electrode system employing modified CPE was used as the working electrode, and platinum wire and Ag/AgCl (sat. KCl) were used as counter and reference electrodes, respectively. The pH measurements were performed using WTW 720 pH meter. The scanning electron microscope employed for surface characterization of the electrodes was a TESCAN model MIRA3.

All chemicals were of Analytical Reagent grade and were used as received without any further purification. Captopril, graphite powders (2-12µm, 99.5%) were procured from Sigma-Aldrich and were used as received without further purification. Aqueous 1.0% (w/v) $HAuCl_4 \cdot 3H_2O$ (Merck >95.0% as Au) was used for the electrodeposition of gold nanocrystals. Phosphoric acid, acetic acid and sodium hydroxide were procured from Merck. All solutions were prepared using double distilled water. Tablets of captopril were prepared from Exir pharmaceutical Company (Tehran, Iran).

Stock solutions of captopril were freshly prepared as required in 0.50M phosphate or acetate buffer at the desired pH (4.0–10.0) and purged with pure nitrogen gas (99.99%) for 5 min before the voltammetric measurements. Voltammetric experiments were carried out in the buffered solutions of Captopril, deoxygenated by purging the pure nitrogen. During the experiments, nitrogen gas was passed over the surface of test solutions in order to avoid entrance of oxygen into the solution.

### *B. General Procedure*

CPE was prepared by the hand-mixing of the Paraffin and graphite powder with a ratio of 30/70 (w/w). The paste was then filled in a Teflon micropipette tip. A copper wire was dissected through the paste, to provide an electrical contact. Smooth and fresh electrode surfaces were obtained by squeezing out 0.5 mm of paste from the syringe, scraping on the excess and polishing it against butter paper until the surface had a shiny appearance. For constructing GNPs/CPE, CPE was cycled (15 cycles) in the potential range from -0.6 to 0.9 V vs. Ag/AgCl at a scan rate of 0.1 $Vs^{-1}$ in solution containing 0.1 M $Na_2CO_3$, 0.1 M $KClO_3$ and $1.25\times10^{-3}$ M $HAuCl_4$ to electrodeposite GNPs on the electrode surface under the optimized conditions.

Ten tablets of captopril labeled with amount of 50 mg per tablet were completely grounded and 50 mg of powders was accurately weighted and dissolved via 30 min ultrasonication in 250 mL of 0.5 M buffer solution (pH 7.0) before determination.

## 3. RESULTS, AND DISCUSSION

### *A. Characterization of CPE Modified Electrode*

#### *1)* Scan Electron Microscopy (SEM)

Scanning electron micrograph (SEM) of GNPs/CPE modified electrode (Fig. 1) shows that GNPs have uniformly been deposited on CPE.

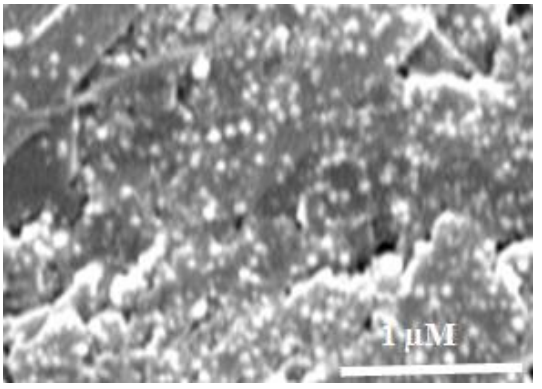



**Fig. 1.** SEM image of GNPs/CPE.

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### *2)* GNPS/CPE Modified Electrode

GNPs were electrodeposited on CPE by cyclic Voltammetric (CV) technique. CPE was cycled (15 cycles) in potential range from -0.6 to 0.9 V vs. Ag/AgCl (KCl 3.0 M) at a scan rate of 0.1 V $s^{-1}$ in a solution containing 0.1 M $Na_2CO_3$, 0.1 M $LiClO_4$ and $5.0\times10^{-4}$ M $AuCl_4^-$. A couple of peaks at about 60 and 600 mV characterized the reduction of Au complex and the oxidation of the deposited Au on CPE surface at the first potential sweep from -0.6 to 0.9 V vs. Ag/AgCl (see in Fig. 2). During the second cycle, the peak at the potential of 130 mV in reverse cycle is attributed to the reduction of $AuCl_4^-$ on the surface of previously deposited Au on CPE.

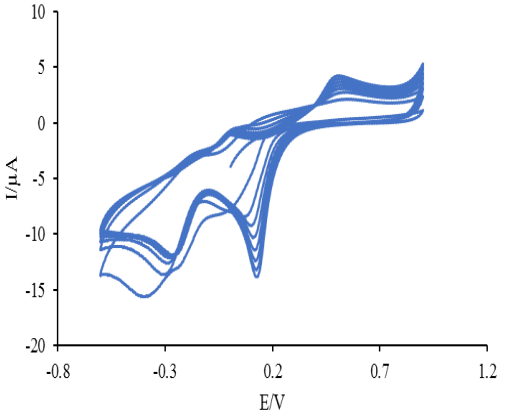


**Fig. 2.** Electrodeposition of Au on CPE by CV between -0.6 V/ref to 0.9 V/ref at a scan rate of 0.1$Vs^{-1}$ in a solution containing 0.1 M $Na_2CO_3$, 0.1 M $LiClO_4$ and $5.0\times10^{-4}$ M $AuCl_4^-$.

### *3)* Electrochemical behavior of captopril on CPE and GNPs/CPE

Voltammetric responses of 4.6 mM CAP on the surface of the CPE and GNPs/CPE electrodes at pH=7.0 (PBS) were recorded. Fig. 3 (curves b and d) shows the voltammograms of CPE and GNPs/CPE electrodes, respectively in the presence of CAP (4.6 mM). The results confirm that the oxidation of CAP at the surface of bare CPE (Fig. 3, curve b) has a weak peak current, whereas at the surface of GNPs/CPE modified electrode (Fig. 3, curve d), an increase in the peak current could be observed. As it is clear, GNPs/CPE shows an excellent electrocatalytic activity toward the oxidation of CAP with significant increased oxidation current. This improvement of peak current together with the sharpness of anodic peak related to the electrocatalytic process at the surface of modified electrode.

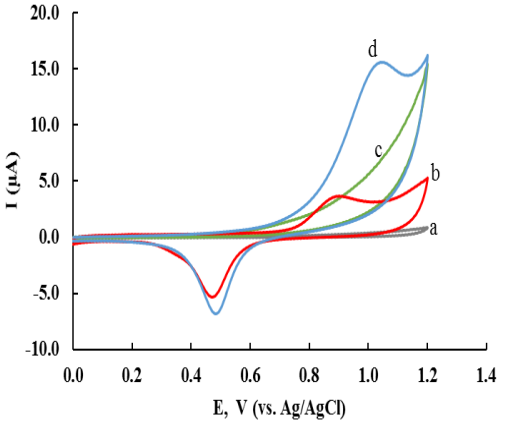


**Fig. 3**. CVes of CPI ıe absence (a,c) and in the presence (b,d) of 4.6 mM CAP, respectively, Scan rates were 0.1 V $s^{-1}$.

### *4) The Effect of pH on the Oxidation Peak Current*

The electrochemical behavior of captopril in 0.5 M phosphate or acetate buffered solutions with different pH values (4.0≤pH≥8.0) was studied with GNPs/CPE using cyclic voltammetry. Figure 3 shows the variation of $I_{pa}$ vs. pH of the solution. As can be seen, maximum current was obtained at pH= 7.0.

Therefore, pH=7.0 was selected as the optimum pH for the Current of captopril oxidation at the surface of GNPs/CPE.

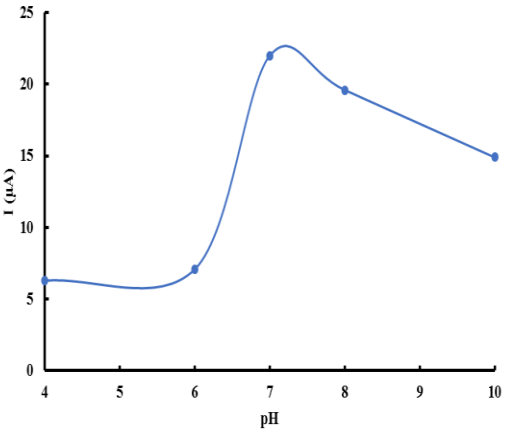


**Fig. 4**. Current vs. pH curves for electro oxidation of 4.6 mM captopril with different pH at the surface of GNPs/CPE with a scan rate 100 mV $s^{-1}$.

### *5) Study of the Scan Rate*

Cyclic voltammetry for CAP was carried out at different scan rates. Results indicated that there is a linear relationship between the peak current ($i_p$)of CAP and the scan rate (υ) in the range of 0.05 to 0.60 $Vs^{-1}$ (Fig. 5). The peak current increased linearly with the scan rate (υ) and the corresponding linear equation is I (μA)=222.35 υ +1.46 with a correlation coefficient ($R^2$) of 0.996. This means that the electrochemical process of CAP at the GNPS/CPE is an adsorption-controlled mechanism. In addition, with increase in the scan rate, $E_p$ has a slight shift toward more negative potentials, indicating slow kinetic reaction corresponding to quasi-reversible reactions.

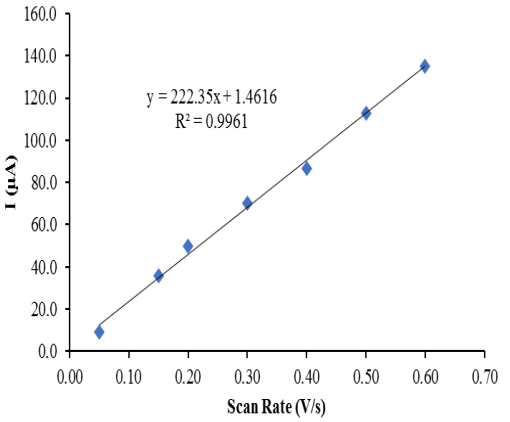


**Fig. 5**. Cyclic voltammograms of captopril 115 μM in 0.5 M PBS at pH 7.0, at different scan rates: 0.05, 0.15, 0.20, 0.30, 0.40, 0.50 and 0.60 V $s^{-1}$. The curve shows the corresponding calibration plots of cathodic current as a function of scan rate using a GNPs/CPE.

### *6) Amperometric determination of CAP at GNPs/CPE*

The current-time response of GNPs/CPE in the hydrodynamic conditions was recorded to evaluate the limit of detection and the calibration curve for captopril detection.

The sensor response at an applied potential about 1.0 V vs. Ag/AgCl (KCl 3.0 M) toward increasing concentration of captopril was recorded in 0.5 M phosphate buffer solution. Fig. 6 specifies the sensor response for successive addition of captopril from stock solution of 460 μM by 100 μL increments to electrochemical cell containing 10 mL phosphate buffer solution. Under the optimized conditions, the electrocatalytic oxidation peak current of captopril

showed two linear dynamic ranges with a detection limit of $8.28\times10^{-1}$ µM captopril. The linear calibration range was 1.14-16.98 and 21.49-62.1 µM using amperometric. Table 1 shows the parameters for captopril curves that were determined. The limit of detection (LOD) value attained here is equivalent to or better than those previously (Table 2) published. Three distinct concentrations of captopril were examined by three independent measurements in order to test the repeatability and reproducibility of the suggested amperometry approach. The results are shown in Table 2. The detection limit, linear dynamic range, and sensitivity for captopril measurement at this modified electrode are equivalent, if not superior, to those obtained using other modified electrodes (see Table 2).

**TABLE 1**

The parameters for captopril calibration curves, as well as accuracy and precision (n = 3) in PBS, were calculated.

| | |
|---|---|
| Potential Step (mV) | 1000 |
| Linear range (µM) | 1.14-16.98 |
| Slope (mAM−1 cm−1) | $3.7\times10^{-3}$ |
| Intercept (µA) | $9.0\times10^{-4}$ |
| LOD (µM) | $8.28\times10^{-1}$ |

**TABLE 2**

Efficiency comparison of some modified electrodes used in CAP electrocatalysis.

| Electrode | Modifier | Method | pH | Dynamic range (µM) | LOD (µM) | Refs. |
|---|---|---|---|---|---|---|
| Carbon paste | Benzoylferrocene | Voltammetry | 7.0 | 0.1-350 | 0.03 | [27] |
| Glassy carbon | Hexacyanoferrate (II) | Voltammetry | 2.0 | 0.5-600 | 0.02 | [28] |
| Carbon paste | Vinylferrocene | Voltammetry | 8.0 | 0.2–400 | 0.08 | [29] |
| Glassy carbon | Chlorpromazine | Voltammetry | 4.0 | 10-300 | 3.6 | [30] |
| Carbon paste | ferrocenedicarboxylicacid | Voltammetry | 7.0 | 0.3–140 | 0.091 | [31] |
| Carbon paste | zinc oxide nanoparticles | Square wave voltommetry | 8.0 | 0.09-450 | 0.05 | [32] |
| Carbon paste | amino acid oxidase | Chronoamperometric | 7.0 | 0.4-1.6 | 0.2 | [33] |
| Carbon paste | Gold nanoparticles | amperometric | 7.0 | 1.14-16.98 | 0.82 | This study |

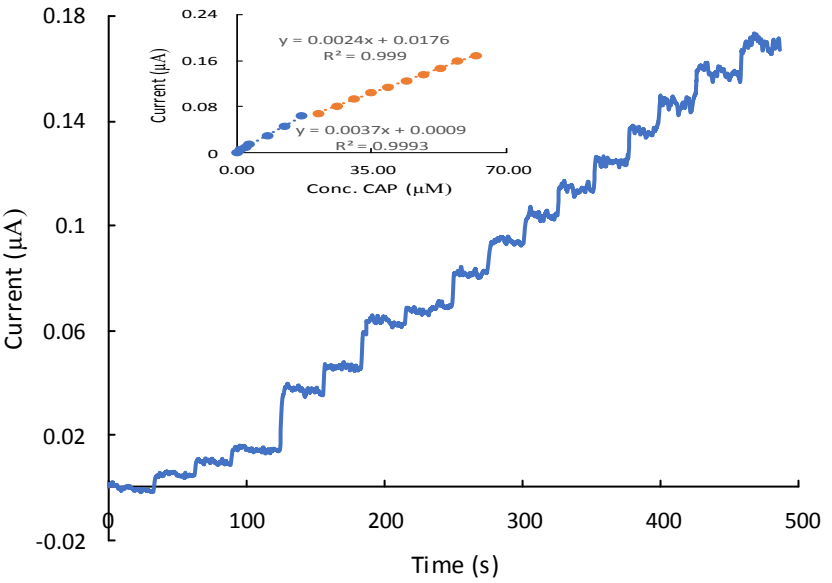


**Fig. 6**. Typical amperometric signals obtained during successive increments of CAP to PBS using GNPS/CPE at 1000 mV. Inset: the corresponding calibration curve.

The presence of active electrochemical species which can be found in biological sample containing captopril may be influence on the oxidation peak of captopril. The interference effect of these foreign compounds was investigated by using solution containing 10 µM of CAP and adding various concentration of the interfering compound under the optimum conditions. The results are reported in the Table 3, which shows the peak current of CAP is not affected by all studied interfering species. These results prove that the GNPs/CPE electrode can operate as a sensor for determination of captopril in the biological sample.

**TABLE 3**

The influence of foreign compound in the determination of captopril

| Interferences substance | Tolerance limits (WSubstance/WCAP) |
|---|---|
| L-Cysteine | 1 |
| Ascorbic Acid | 2 |
| Uric Acid | 50 |
| Sucrose | 300 |
| Glucose, Fructose | 500 |
| $Na^+$, $CO_3^{2-}$ | 800 |
| $NH_4^+$, $Cl^-$, $K^+$, $I^-$ | 300 |

## 4. CONCLUSION

The electrochemical behavior of GNPs/CPE as a new electrochemical sensor for captopril determination has been studied using cyclic voltammetry, amperometry. A carbon paste electrode modified with GNPs has been fabricated and used for electrocatalytic determination of CAP.

It has been found that, with cyclic voltammetry, the oxidation of captopril occurred at a potential about 1.02 V on the surface of the modified carbon paste electrode, while the oxidation captopril does not take place at the surface of a bare carbon paste electrode up to 1.20 V. The proposed method was also used as a selective, simple, and precise new sensor for voltammetric determination of captopril in real samples such as drug.

## ACKNOWLEDGMENT

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