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Development of biomimetic sensor for selective identification of cyanide

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A biomimetic sensor is proposed as a promising new analytical method for determination of cyanide in different samples. The sensor was prepared by modifying a carbon paste electrode with Cobalt II 1,2,3,4,8,9,10,11,15,16,17,18,22,23,24,25-hexadecafluoro-29H,31H-phthalocyanine complex [CoPc]. The measurements were carried out using cyclic voltammetry (CV) and square wave voltammetry (SWV) for electrochemical characterization and quantification purposes, respectively. SWV measures were carried out vs. Ag/AgCl (KCl_{sat}), using a 0.5 mol L⁻¹ NaOH solution at pH 12.0 as the support electrolyte, provided the best responses, with a linear range of 2.4 × 10⁻⁵ to 1.7 × 10⁻⁴ mol L⁻¹ and limits of detection and quantification 3.6 × 10⁻⁶ and 1.2 × 10⁻⁵ mol L⁻¹, respectively. A detailed investigation of the sensor selectivity, employing eleven different ions, was also performed. Recovery studies were carried out using rivers and drinking waters and the results obtained demonstrated that it is a reliable alternative method for the detection of this analyte.

Keywords: Biomimetic sensor, electrochemical detection cyanide.

1. Introduction

Cyanide is an extremely toxic ion readily absorbed by living organisms by inhalation, oral and dermal routes of exposure. The acute toxic effects of an ingestion or inhalation of cyanide from suicide or homicide attempts [1–5] are generated by the process whereby cyanides transferred through the blood and then bound to ferric iron of cytochrome oxidase inhibit electron transport and disrupt cells in their use of oxygen [6,7], then leading to vomiting, convulsion, loss of consciousness, and eventual death [8–13]. Fatal

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ARTICLE

Journal Name

oral doses for adults are 0.2 g for cyanide potassium and 0.3 g for cyanide sodium, and 1.2–5 mg kg⁻¹ for children [1, 14]. In addition, the World Health Organization (WHO) recommends for cyanide in drinking water, the limit of 0.07 mg L⁻¹ [15] which is also followed by the Brazilian Health Department [16]. On the other hand, a particular troubling posed by WHO regards the daily consumption of cyanide from the cassava, by populations in developing Countries in the tropics and subtropics areas, being between 300 and 500 million people. In this cases was found than people of these regions can ingest daily very high levels of cyanide, as high as 0.61 mg kg⁻¹ of their body weight [17]. Finally, being a problem that directly affects the world population with fewer resources, analytical methods to quantify this ion, in a simple, cheap, selectively and in situ way, are still needed.

Several analytical methods have been reported for the determination of cyanide such as titration [18–21], colorimetry and fluorescent method [13, 22–25], voltammetry [26–29] chromatography [30–32] and atomic absorption spectrometry [33, 34]. But most of them require complex preprocessing, expensive equipment, special operators, and consume a large amount of time. Therefore, there is need to develop quick and portable analytical methods that contribute to solving cases and especially to determine the cyanide concentration levels in samples of forensic interest.

Fast, sensitive and selective techniques for in situ monitoring of various classes of substances include electrochemical sensors, amongst which are biomimetic sensors. Biomimetic sensors are a result of attempts to produce chemical sensors that are more stable and durable than conventional biosensors based on the use of biological materials such as redox enzymes. These devices aim to overcome limitations of conventional enzymatic biosensors, such as availability, cost and enzyme instability, as well as to improve electronic transfer between electrode/active site (biomimetic catalyst/substrate), since in biomimetic sensors the “active site” is free, in contrast to enzymes, where the active site is surrounded by a dense layer of residual amino-acids [35,36].

Metalophthalocyanines and metaloporphyrins have been widely employed in sensor construction with different transducer systems, mainly electrochemical [37–45] using these macrocycle as biomimetic active sites of

redox enzymes P450 [46,47] as it has been described. They contain a common active site, protoporphyrin IX, which is an iron porphyrin (protohemin IX) complex, and the selectivity of each P450 is a consequence of the chemical environment surrounding the hemin group in the enzyme.

This paper describes the development and application of a simple, cheap and environmentally friendly method for the rapid determination of cyanide in drinking water and river water samples. A voltammetric sensor based on a carbon paste electrode modified with the Cobalt II 1,2,3,4,8,9,10,11,15,16,17,18,22,23,24,25 – hexadecafluoro – 29 H, 31 H – phthalocyanine complex, a potential biomimetic catalyst of the P450 enzyme for the sensitive and selective quantification of cyanide.

2. Materials and methods

2.1. Reagents and solutions

All the chemicals used were analytical or HPLC grade. Cobalt II 1,2,3,4,8,9,10,11,15,16,17,18,22,23,24,25 – hexadecafluoro – 29 H, 31 H – phthalocyanine complex, cyanide, mineral oil and graphite powder were purchased from Sigma–Aldrich. NaH₂PO₄, H₃BO₃ and NaOH were purchased from Synth-Brazil®. The cyanide and buffer solutions were prepared with purified water using a Milli-Q (Direct-0.3) system.

2.2. Instruments

The electrochemical measurements were conducted at room temperature in a conventional three-electrode cell, with the modified carbon paste electrode used as the working electrode. An Ag/AgCl(KCl_{sat}) electrode and a platinum wire were used as the reference and counter electrodes, respectively. The measurements were performed using a potentiostat model μ-Autolab type III of Autolab/Eco Chemie®, which was interfaced with a microcomputer running GPES software for control of potential and acquisition of data.

The electroanalytical techniques used in this work were cyclic voltammetry and square wave voltammetry. Cyclic voltammetry was first used to investigate the electrochemical behavior of cyanide on the sensor

surface. The square wave voltammetry technique was used in the optimization studies and for quantification of cyanide.

2.3. Sensor construction

The modified paste was prepared by mixing 15 mg of [CoPc] with 85 mg of graphite powder and 1.0 mL of 0.1 mol L⁻¹ phosphate buffer solution (pH 7.0), in order to obtain a homogeneous material. After drying at room temperature, mineral oil was added, mixing it to obtain a homogeneous paste. The paste was then placed into the cavity of a glass tube, with a platinum slide inserted for electrical contact with the paste. Additionally, for comparative purposes, an unmodified paste was prepared by mixing 100 mg of graphite powder with 1.0 mL of 0.1 mol L⁻¹ phosphate buffer solution (pH 7.0).

2.4 Study of selectivity and interferences

The selectivity/interference of the sensor was investigated by means of square wave voltammetry response to 9 different ions. For this, 1.0 × 10⁻³ mol L⁻¹ work solutions of all the ions were dissolved in the water.

2.5. Preparation of real samples

The water samples were collected in two rivers in Araraquara at 298 Km of São Paulo city (Brazil). A concentration of 1.0 × 10⁻³ mol L⁻¹ of KCN was added to the samples. To this, there was prepared a solution of 1.0 × 10⁻² mol L⁻¹ of KCN, 2.5 mL of the same which was diluted in a flask using a 25.0 mL of river water.

After dilution, the simple filtration was performed to remove the solid particles and the supernatant analyses were performed by the proposed sensor in the batch system, for further calculating the recovery percentage. The mineral water sample was spiked with cyanide in a concentration of 1.0 × 10⁻³ mol L⁻¹ and added without any prior treatment.

3. Results

3.1. Electrochemical Characterization of the Sensor Response

The electrochemical behaviours of the cyanide on the carbon paste electrode unmodified or modified with [Co(II)Pc] are showed in Figure 1.

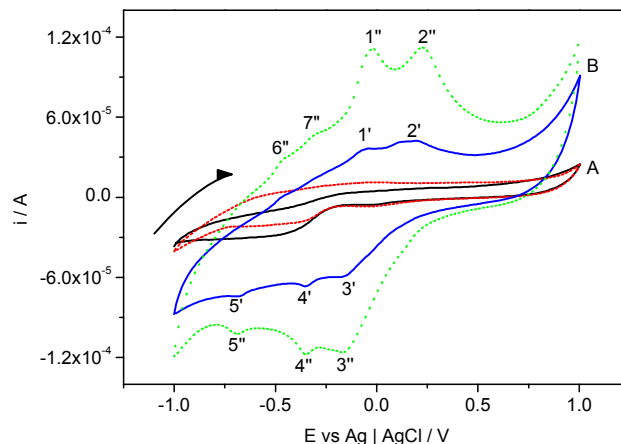
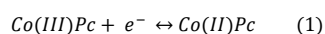


Figure 1. Electrochemical profiles obtained by cyclic voltammetry in the absence (A) and presence (B) of complex CoPc with addition of 4.8×10^{-4} mol L⁻¹ (curves red and green). Measurements performed using a 0.5 mol L⁻¹ NaOH solution (pH 12.0).

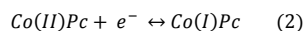
It can be noticed that in the absence of the complex there is no formation of a peak, and after cyanide addition the voltammogram practically not changes, showing a little increase of the current from close to -400 mV, probably because of the cyanide redox process in the electrode surface. On the other hand, in presence of the complex, is observed that the conductivity of the electrode increase, and can be explain consider that the complex have electrochemically active ion (Co²⁺) and functional groups in the phthalocyanine. This behavior is expected to sensors based on this class of macromolecules [48, 49, 50].

In order to explain the cyclic voltammogram presents by the proposed sensor, the studies carried out by Ouyang *et al* [51] and Song *et al* [52] were taken as reference. Thus, is possible to assign the peaks observed in the proposed sensor in absence of analyte. Thus, is observed two reversible redox couples, the first one at 160 mV and -150 mV (vs Ag|AgCl), corresponding to peaks 2' and 3', and the second at -7 mV and -350 mV (vs Ag|AgCl), corresponding to the peaks 1' and 4'; and other irreversible peak at -680 mV (5'), following the reactions below:

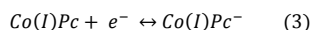
Peaks 2'/3'



Peaks 1'/4'



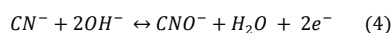
Peak 5'



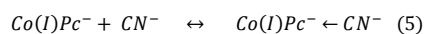
In the reaction (3) Pc^- represents the reduced ligand [52].

In presence of cyanide ion is possible to observe in the reverse scan the appearance of two small peaks (6'' and 7''), indicating the presence of new oxidized species, which possibly corresponding to partial and very-well known oxidation via two electrons of CN^- to CNO^- in alkaline media (pH 12) [53, 54].

Peaks 6'' and 7''



A plausible explanation to the sensor response is based on that the transition elements, as cobalt and iron, form stable complexes with cyanide, because they can use their d orbitals filled to form $d-\pi$ bonds, besides coordinated ligation σ of $\text{Co} \leftarrow \text{CN}^-$. This bond is similar to that happens with carbonyl. The negative charge on cyanide makes it a better σ donor than CO, but in contrast it reduces the cyanide efficiency like a receptor π [55]. In the proposed sensor, since the CN^- must not be reduced to other species, the increasing of the cathodic current in presence of CN^- can be explained considering that in the Co(I)Pc^- (generated in an electrochemical step at -680 mV, reaction 3) the metallic center is highly susceptible to interact with electron donors, such CN^- . In presence of analyte, the reaction (chemical step, 5) will allow the formation of the coordinated bond $\text{Co} \leftarrow \text{CN}^-$.



Thus, when the cyanide concentration increases, the reaction 5 shifts to the right, requiring that larger amount of CoPc is reduced by shifting reaction 3 to the Co(I)Pc^- production, and thereby increasing the reduction current observed.

In order to verify if the sensor response is in agreement with that described in the preceding paragraphs, firstly was verified if the sensor presents an electrochemical response controlled by diffusion. To confirm this, the sensor was evaluated at different scan rates and the Figure 2, shows a linear dependence between the cathodic current at -680 mV and the square root of the scan rate ($v^{1/2}$) for the v range between 50 and 325 mV s^{-1} , indicating that sensor response is controlled by the mass transport of CN^- to the sensor surface [56,57].

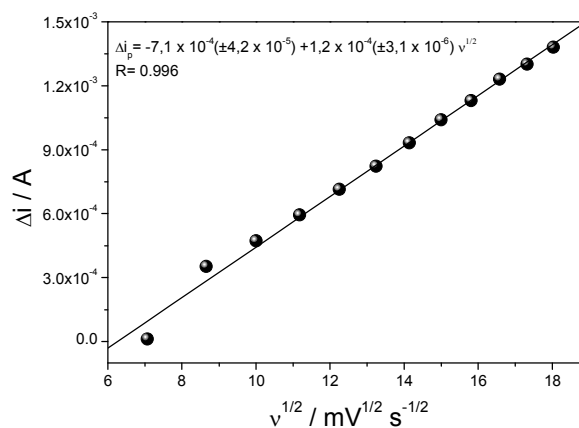


Figure 2. Linear profile of the variation of the current (Δi) as a function of the square root of the scan rate ($v^{1/2}$). Measurements carried out in 0.5 mol L^{-1} NaOH (pH 12.0) containing 1.0×10^{-3} mol L^{-1} of cyanide.

Then, when was plotted the graph scan rate-normalized by the square root of the current ($\Delta i v^{-1/2}$) vs v (Figure 3), is possible to observe than a typical graph of an EC process is obtained [49], characterized by an electrochemical process coupled with chemical step (EC). In these system the analyte chemically react with a product from electrochemical reaction, previously generated in the electrode surface [57, 58]. In addition, in these plots is expected, than the value of the ratio between the current and low scan rates will be high, and at high scan rates the current function to converge towards the slope of the curve i vs $v^{1/2}$ obtained in Figure 2 ($1.2 \times$

$10^{-4} \text{ A s}^{1/2} \text{ mV}^{-1/2}$) [59]. As can be observed, in this case, is evident than the maximum value of Figure 3, tends to the expected value.

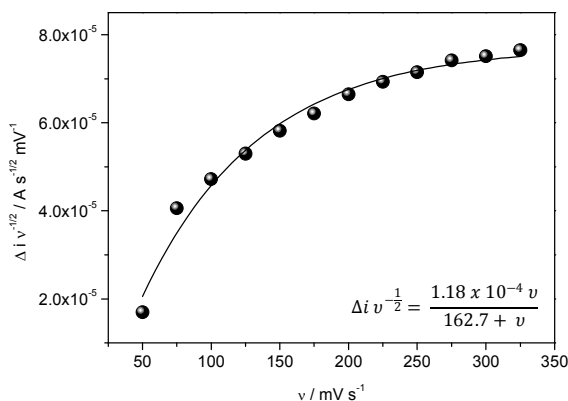


Figure 3. Plot of the current variation (Δi), normalized by the square root of the scan rate ($v^{1/2}$), as a function of the scan rate (v). Measurements carried out in $0.5 \text{ mol L}^{-1} \text{ NaOH}$ (pH 12.0) containing $1.0 \times 10^{-3} \text{ mol L}^{-1}$ of cyanide.

Thus, based on experimental evidences is possible to infer than the sensor response follow the EC proposed mechanism.

Finally, to be considered a biomimetic sensor, is expected that its response profile should be similar to the response profile of an enzymatic biosensor [48], since the complex used has a structure similar to the active site of the cytochrome P450 enzyme. In enzymatic biosensors, the signal initially increases linearly with the concentration of its substrate (analyte), then at higher concentrations of substrate, the active sites of the enzyme are completely filled, saturating it, and in this situation the current signal reaches its maximum value, characterizing the hyperbolic profile that follows the Michaelis-Menten kinetics [36, 47]. Thus, the proposed sensor presents a hyperbolic profile (data not shown) following the Michaelis-Menten kinetics. Then, this saturation curve allowed to plot the double reciprocal (or Lineweaver-Burker) graph (Figure 4) to estimate the constant apparent Michaelis-Menten (K_{MM}^{app}) with a value of $4.7 \times 10^{-5} \text{ mol L}^{-1}$. This value is consistent for K_{MM}^{app} of biosensors and biomimetic sensors [35, 60], since it represents the affinity of the catalyst (enzyme or biomimetic) by its

substrate, indicating that smaller this value higher is the affinity of catalyst (CoPC) by its substrate (CN⁻).

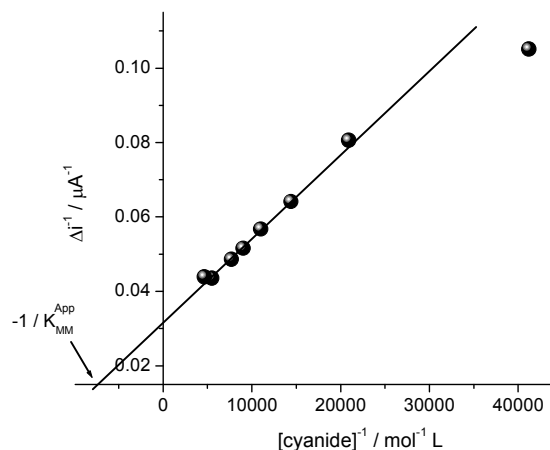


Figure 4. Lineweaver-Burk plot for the cyanide reduction catalyzed by the CoPc-based sensor.

3.2 Optimization of the analysis

Square wave voltammetry measurements were used to optimize the analytical parameters influencing the sensor response, with the values selected being based on the highest sensitivity as indicated by the respective analytical curves. The parameters evaluated were pH (between 8 and 13), concentration of the electrolyte solution ($0.1 - 0.5 \text{ mol L}^{-1}$), the amount of cobalt complex in the carbon paste (5 – 25% w/w), step potential (2 – 10 mV), frequency (10 – 25 Hz), and amplitude (10 – 150 mV). The results obtained are provided in Table 1.

3.3 Sensor Analytical Characteristics

The square wave voltammogram profile of the biomimetic sensor under optimized conditions is shown in the Figure 5.

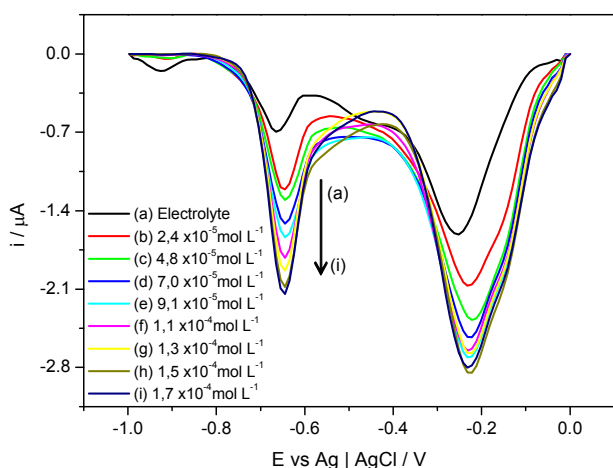


Figure 5. Typical square wave voltammogram obtained for successive additions of cyanide under optimized conditions.

A linear correlation coefficient of 0.996 was obtained, and the data in Figure 6 could be described by:

$$\Delta i / \mu\text{A} = 3,86 (\pm 0,25) + 69891 (\pm 2284) [\text{cyanide}]$$

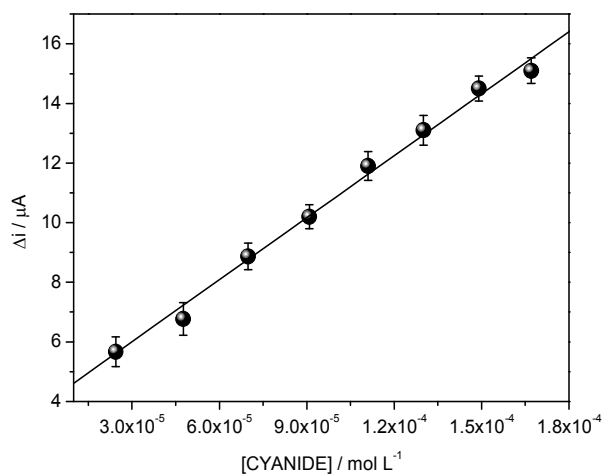


Figure 6. Typical analytical curve profile of the CoPc sensor for cyanide under optimized conditions (number of replicates=3).

Table 1. Parameters evaluated in the optimization of the biomimetic sensor for cyanide determination.

Variables	Parameters optimized
Amount of complex in the paste (% w/w)	15
Electrolyte concentration (mol L ⁻¹)	0.5
pH of the electrolyte	12
Frequency (Hz)	20
Amplitude (mV)	10
Step potential (mV)	10

The detection and quantification limits were calculated as suggested by the ANVISA recommendations [61]. The repeatability of the measurements was estimated by plotting five successive analytical curves in the corresponding linear range of the sensor. In this case, the repeatability intra-day and inter-day were defined in terms of the relative standard deviation (RSD). Finally, the sensor response time was also evaluated. The analytical parameters for cyanide were evaluated and are summarized in Table 2.

Table 2. Analytical parameters for cyanide determination on the proposed sensors based on carbon paste modified with [CoPc].

Parameters / unit	Response
Linear range	$2.4 \times 10^{-5} - 1.7 \times 10^{-4} \text{ mol L}^{-1}$
Sensitivity	$69891 \mu\text{A L mol}^{-1}$
R value	0.996
Detection limit	$3.6 \mu\text{mol L}^{-1}$
Quantification limit	$12 \mu\text{mol L}^{-1}$
Repeatability intra-day (RSD, n = 5 sensitivities of analytical curves)	4.8%
Inter-day repeatability (RSD, n = 5 sensitivities of analytical curves)	5.2%
Lifetime keeping 95% initial sign	5 days (or 378 measures)

These values are compared to the values reported by other research groups for cyanide obtained by electrochemical methods (Table 3). Analyzing the information of the Table 3, it can be deduced that the proposed sensor is easy to prepare [64], does not use toxic reagents, such as mercury [26,27,29], or more complex devices, such as rotating disk electrode [28], which compromises the portability of the sensor. In addition,

sensitivity may be improved by using carbonaceous nanomaterial, such as carbon nanotubes or graphene, since the carbon paste is feasible to modifications.

, MoO_4^{2-} , NO_3^- , Cl^- and of all ions analyzed, only CN^- had electrochemical response used the proposed sensor.

3.5 Application

The acceptable recovery values (Table 4) for the river water samples and mineral water enriched with $1.0 \times 10^{-3} \text{ mol L}^{-1}$ of cyanide demonstrate that the sensor can be successfully used for the direct analysis of ion. The method used in the determination of cyanide in the matrices analyzed was the standard addition.

Table 3. Comparison of the efficiency of some methods in the determination of cyanide.

Electrode	Technique	Linear range (mol L^{-1})	L. D. (mol L^{-1})	Ref.
Copper with adenine complex on the mercury electrode	AdSV	$5.0 \times 10^{-8} - 8.0 \times 10^{-7}$	1.0×10^{-8}	[26]
Chemically modified carbon-paste mercury-sensitive electrode	DPV	$0.3 \times 10^{-6} - 1.9 \times 10^{-6}$	3.5×10^{-5}	[27]
Rotating silver disk electrode	DPV and SWV	-	3.5×10^{-7} and 1.2×10^{-6}	[28]
EDTA/ Cu(II)/ hanging mercury drop electrode	DPV	$6.5 \times 10^{-8} - 3.8 \times 10^{-6}$	6.5×10^{-8}	[29]
AgI/Ag ₂ S/paraffin	Pot	$2.0 \times 10^{-5} - 2.9 \times 10^{-3}$	-	[62]
Tetrakis-4-chlorophenylporphyrinato-iron(III) chloride/PVC/graphite	Pot	$6.3 \times 10^{-7} - 1.2 \times 10^{-2}$	4.0×10^{-7}	[63]
Carbon paste/Carbon Nanotubes/ ion-imprinted polymer	Pot	$1.0 \times 10^{-6} - 1.0 \times 10^{-1}$	8.0×10^{-7}	[64]
Carbon paste modified with [CoPc]	SWV	$2.4 \times 10^{-5} - 1.7 \times 10^{-4}$	1.1×10^{-5}	This work

L.D: Detection limit, AdSV: Adsorptive stripping voltammetry, DPV: Differential pulse voltammetry, SWV: Square Wave voltammetry, Pot: Potentiometric.

3.4 Study of selectivity and interferences

The selectivity/interference of the proposed sensor was confirmed electrochemically with the square wave voltammetry evaluate the response of the proposed sensor in nine ions which are soluble in water (Supplementary material). The ions are Na^+ , Ca^{2+} , NH_4^+ , Pb^{2+} , H_3CCOO^- , $\text{B}_4\text{O}_7^{2-}$.

Table 4. Recoveries of cyanide added to river water and mineral water samples.

Samples	Value found	Recovery
	[CN ⁻] x 10 ⁻⁵ (mol L ⁻¹)	
Jacaré-Pepira river	2.3 ± 0.5	95%
Chibarro river	2.5 ± 0.8	102%
Mineral water	2.4 ± 0.3	98%

4. Conclusions

This work describes an alternative methodology for the determination of cyanide, using a sensitive and selective voltammetry sensor based on a carbon paste modified with [CoPc] complex that could be considered a biomimetic catalyst. The sensor was satisfactorily applied in analyses of mineral water and river water samples as well as being inexpensive, simple, portable, precise, accurate and rapid determination.

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