

Sustainable Copper Electrochemical Stripping onto a Paper-Based Substrate for Clinical Application

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Cite This: <https://doi.org/10.1021/acsmeasuresciau.1c00059>

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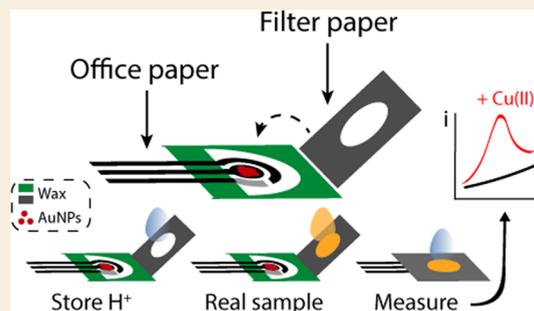


Supporting Information

ABSTRACT: The electroanalytical field has exploited great advantages in using paper-based substrates, even if the word “paper” might be general. In fact, the mainly adopted paper-based substrates are often chromatographic and office ones. They are characterized by the following main features (and drawbacks): chromatographic paper is well-established for storing reagents/treating samples, but the sensitivity compared to traditional screen-printed ones is lower (due to porosity), while office paper represents a sustainable alternative to plastic (with similar sensitivity), but its porosity is not enough to load reagents. To overcome the limitations that might arise due to the adoption of a type of individual paper-based substrate, herein, we describe for the first time the development of a two-dimensional merged paper-based device for electrochemical copper ion detection in serum. In this work, we

report a novel configuration to produce an integrated all-in-one electrochemical device, in which no additional working medium has to be added by the end user and the sensitivity can be tuned by rapid preconcentration on porous paper, with the advantage of making the platform adaptable to real matrix scenarios. The novel architecture has been obtained by combining office paper to screen-print a sustainable and robust electrochemical strip and a chromatographic disk to (1) store the reagents, (2) collect real samples, and (3) preconcentrate the analyte of interest. The novel sensing platform has allowed us to obtain a detection limit for copper ions down to 4 ppb in all the solutions that have been investigated, namely, standard solutions and serum, and a repeatability of ca. 10% has been obtained. Inductively coupled plasma-mass spectrometry measurements confirmed the satisfactory correlation.

KEYWORDS: electrochemical sensor, screen-printed electrodes, paper-based, office paper, chromatographic paper, gold nanoparticles, copper ions, serum



INTRODUCTION

Copper (Cu) is as an essential metal playing a crucial role in various biochemical reactions as a cofactor of many metalloenzymes and in physiological regulations. The majority of copper ions (65–90%) are tightly bound to serum proteins, i.e., ceruloplasmin, albumin, and transcuprein. Even if the protein-free copper level is lower than the total serum copper concentration,¹ it has been highlighted that abnormal levels of unbound copper ions could be related to tissue injury due to pro-oxidant effects and depletion of antioxidant reserves.² The normal range of value of free copper for healthy people is ca. 20–25 ppb,³ and significant changes in serum could reflect pathological disorders like neurodegenerative and oxidative stress-related diseases and diseases related to abnormal ceruloplasmin levels, e.g., Wilson’s disease (WD) and Menkes’ syndrome.⁴ Regarding WD, which is an autosomal-recessive disorder of copper metabolism, the serum copper level ranges from that of hypocupremia (lower than 12 μM) to that of fulminant Wilson’s hepatitis (higher than 22 μM).⁵ In WD, a gene mutation leads to an accumulation of copper in the liver, brain, eyes, and kidneys, while in Menkes’ disease, a gene mutation leads to failure of copper efflux from the intestines,

resulting in low blood absorption.⁶ In addition to this, free copper ions are involved in the development of some chronic degenerative diseases whose pathophysiology is largely attributed to oxidative stress, e.g., Alzheimer’s disease.^{7,8}

The determination of copper in its unbound form is of particular interest because of its high toxicity: from an analytical point of view, copper ions (and metals in general) are detected through atomic absorption spectrometry (AAS) and inductively coupled plasma-mass spectrometry (ICP-MS).^{9,10} Although these techniques display the advantages of sensibility and selectivity, they are strictly related to skilled personnel, sophisticated instruments, and time-consuming procedures.¹¹ In view of these experimental limitations, it is important to develop easy-to-use and portable methods for decentralizing analyses. In this context, the development of

Received: December 20, 2021

Revised: January 4, 2022

Accepted: January 5, 2022

portable analytical devices represents a hot topic in the analytical chemistry field because it allows developing miniaturized, sustainable, and low-cost devices, to be exploited for on-site measurements. In this direction, decentralized systems have demonstrated a great potential in recent years and thus have arisen as proposed analytical tools for effective monitoring in most of the fields, from clinical to environmental through agri-food ones. In particular, paper-based analytical devices have been highlighted as excellent and versatile substrates for developing point-of-care tests (POCT).¹² Due to its valuable features such as porosity, sustainability, abundance, affordability, lightness, and biodegradability, paper has been combined with colorimetric and electrochemical sensors for metal determination. It should be noted how the choice of paper-based substrates represents a low-risk environmentally friendly substrate material over the plastic ones, as the toxicity implications of microplastics in the environment have not been fully evaluated.¹³ As reported in the literature, although paper-based substrates have been used for determining various species as heavy metals, ions, pH, proteins, etc., paper-based substrates are not completely inert.^{14–16} The main issue is mainly due to nonspecific adsorption and the presence of impurities in paper that can represent a limitation in real-settings analysis. However, pretreatments may be applied to reduce the metal ion interaction between the standard/sample/paper substrates, as reported for heavy-metal detection.^{17,18}

In particular, different approaches have been reported for colorimetric copper sensing in diverse matrices with the use of paper-based devices: the group of Dungchai¹⁹ developed a silver nanoparticle-modified paper-based tool for the visualization of copper ions down to micromolar in pond and tap water; another approach has exploited the combination of microspheres to absorb copper ions, with a metal ion indicator as the detector, an SPE column, and waxed paper to determine copper in spring waters;²⁰ copper ions have been also colorimetrically visualized down to 15 μM with the use of ZnO@ZnS core–shell nanoparticles onto a paper-based platform.²¹ Colorimetric approaches offer a valuable alternative to traditional analytical methods; however, these novel approaches need to be developed together with ad hoc settings for avoiding interference from light exposure.²² In addition to this, an effect that should be taken into account is the possibility to analyze colored matrices that are among the most limiting factors for colorimetric analyses. An alternative in sensing and biosensing is represented by the combination between paper-based substrates and electrochemistry, which has enforced the ASSURED criteria that have been established by the WHO.²³ The advantage of electrochemical detection over the colorimetric ones is mainly represented by the absence of interference due to the color of the matrix, especially for biological ones. Paper-based screen-printed electrodes have been reported by many research groups, utilizing various substrates (e.g., chromatographic, office, and nanocellulose) for different fields of application, including clinical, pharmaceutical, environmental, and agri-food.^{24–27} With regard to the electrochemical detection of copper ions, Bagheri et al. reported a paper-based Au-decorated platform on chromatographic paper for detection of copper ions in biological fluids,²⁸ and another approach has exploited the use of a gold screen-printed electrode for the simultaneous determination of copper, mercury, and lead in the Amazon river,²⁹ characterized by the detection limit and the linear

range equal to 3 and 1.5 ppb and 400 and 300 ppb, respectively.

Even if paper-based substrates represent an established alternative to plastic-based ones for realizing portable electro-analytical tools, the aim of the proposed work is to highlight that the use of papers of different porosities is capable to enhance analysis of biological samples. It should be noted that the use of paper-based devices is usually limited to the adoption of this support to replace plastic-based ones, but this is limitative. In this work, we took advantage, for the first time, of a 2D mixed paper-based device for copper ion detection in serum samples. The sensitive detection of copper ions has been achieved by employing office paper to realize the printed electrochemical strips^{30–32} and filter paper to (1) store the reagents, (2) collect real samples, and (3) preconcentrate the analyte of interest.^{33–35} In this work, we report a novel configuration to produce an integrated all-in-one electrochemical device, in which no additional working medium has to be added by the end user and the sensitivity can be tuned by rapid preconcentration on porous paper. The combination of two different paper-based supports represents a sustainable advancement. In fact, (1) the use of office paper allows reducing costs of ca. 40% with respect to polyester-based manufacturing,³⁶ and also, the group led by Whitesides reported a decrease in the cost from 0.5 to 0.014 \$/strip by replacing the plastic with chromatographic paper,³⁷ (2) paper can be incinerated and disposed with easier procedures with respect to plastic-based ones (especially in remote areas), and (3) the loading of all the reagents in filter paper provides a user-friendly ultimate device (everyone is able to use). It should be noted that only the reported architecture is capable to merge the sensibility of office paper (detecting copper ions) and the storing capacity of chromatographic paper (store reagents, remove interferences, and preconcentrate the matrix).

EXPERIMENTAL SECTION

Reagents and Equipment

Hydrochloric acid, acid solution (nitric acid, sulfuric acid, and trifluoroacetic acid), and serum samples were purchased from Sigma-Aldrich. Copper, lead, and cadmium standard solutions (1000 mg/L) were purchased from Fisher Scientific (Italy, Milan). Nickel(II) nitrate hexahydrate and iron(III) chloride hexahydrate were purchased from Sigma-Aldrich. Subsequent dilutions were obtained using 0.1 M HCl. All of the solutions were prepared in double distilled water. All the electrochemical measurements were carried out using portable and battery-powered instrumentation, EmStat Blue (PalmSens, The Netherlands, Utrecht), connected to a laptop. Currents can be recorded and displayed on a laptop by using a dedicated app, e.g., PStouch, which can be used with all PalmSens and EmStat potentiostats.

Fabrication of a Paper-Based Platform

The homemade production of paper-based screen-printed electrodes (SPEs) started with the choice of the paper used as a substrate, office paper (Copy 2, 80 g/m², Fabriano, Italy, Fabriano) characterized by a thickness of ca. 90 μm and prepared using an ECF (elemental chlorine-free) technique, acid-free warranties, and described as ash-free. As reported in Figure S1 (Supporting Information), SEM images show that the porosity of office paper was lower if compared with that of the chromatographic one. Regarding paper-based substrates, their porosity can represent a source of electrical noise due to diffusion of aqueous samples to the connector: to avoid this, the testing area was surrounded with a hydrophobic layer, melted wax, that prevents liquid flow toward the undesired portion of the strip. This was obtained through wax-printing. First, the wax pattern was drawn using a

drawing software (Adobe Illustrator). Then, a wax ink layer was opportunely waxed with a solid-ink printer, ColorQube 8580 from Xerox (USA, CT, Norwalk). Successively, wax-printed office paper was thermally cured at 100 °C for 2 min. High-temperature curing (>100 °C) allowed wax to melt forming a hydrophobic barrier. Then, the three-electrode system was manually screen-printed using a squeegee and two masks, one for the Ag/AgCl ink (Electrodag 477 SS, Acheson, Italy, Milan), which was used to print the connections and the reference electrode, and one for the carbon ink (Electrodag 421, Acheson, Italy, Milan), which was used to print the working and counter electrodes. Thermal curing, at 60 °C for 15 min, was necessary to make the printed ink stable for electrochemical measurements. Depending on the quality of paper, in particular the porosity and the conductive inks, the relative position of the waxed paper and ink can be easily tuned as reported in our recently published protocol on paper-based strips.³⁸

AuNPs Synthesis

The AuNPs synthesis started with the cleaning of all glassware and the magnetic stir bar used with aqua regia (HCl/HNO₃ of 3:1, v/v), rinsed with ultrapure water and then cleaned with piranha solution (H₂SO₄/H₂O₂ of 7:3, v/v) and rinsed again with ultrapure water before use. Each procedure should be repeated two times. Then, we added 9 mL of double distilled water and 1 mL of the 10 mg/mL HAuCl₄ solution (30 mM) into the flask placed on the magnetic plate. Then, we added 2 mL of the 10 mg/mL trisodium citrate dihydrate solution (34 mM) and finally added 500 μL of the 0.8 mg/mL NaBH₄ solution (21 mM) drop by drop. The reaction was left under stirring overnight at room temperature.^{39,40}

Cu(II) Measurements

The electroanalytical technique adopted to measure Cu(II) was linear sweep–anodic stripping voltammetry (LS-ASV) using a AuNPs-modified paper-based SPE. In particular, 0.1 M HCl was used as the working solution, and the method parameters were optimized as follows: a deposition potential of −0.4 V was applied for 300 s, in a potential range from 0.1 to 0.6 V, with an *E* step of 0.01 V and a scan rate of 0.5 V/s.

ICP-MS Measurements

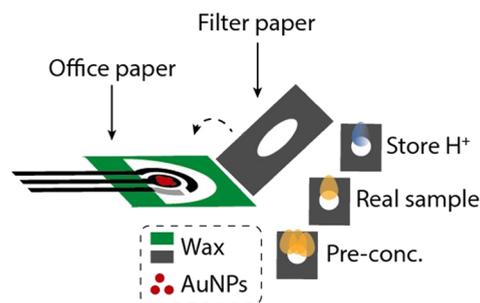
Samples were mineralized as follows: 250 μL was transferred into a 7 mL Pyrex container. Concentrated nitric acid and hydrochloric acid were added to each sample (in the ratio of 1:3). The reaction was conducted for 16 h at a temperature of 90 °C. The samples after digestion were diluted to 15 mL with Milli-Q water and were transferred into an ICP-MS vial for analysis. Measurements were performed with an Agilent 7700 ICP-MS instrument (Agilent Technologies) equipped with a frequency-matching radio frequency (RF) generator and a third-generation octopole reaction system (ORS3) operating with helium gas in the ORF. The following parameters were used: RF power, 1550 W; plasma gas flow, 14 L/min; carrier gas flow, 0.99 L/min; He gas flow, 4.3 mL/min.¹⁰³Rh was used as an internal standard (final concentration of 50 ppb). Copper concentrations were measured with three replicates.

Protocol for an All-in-One Configuration

In order to obtain an integrated paper-based device, the office paper-based electrode has been coupled with a waxed filter paper. The filter paper was designed and printed with a solid-ink printer, in order to obtain a multitask paper capable to (1) store reagents (hydrochloric acid), (2) treat a real matrix (serum), and (3) preconcentrate copper ions. In particular for the loading of hydrochloric acid, it was performed in order to make the final platform reagent-free. In this way, when the sample to be analyzed was added onto the filter paper, it was capable to make the solution acidic (0.1 M) in order to perform the measurements. Acidity was retained,⁴¹ and it was needed because stripping analysis, as reported in the literature, is performed in the presence of acidic media, which are necessary to have metals in their oxidized forms. Briefly, the chromatographic paper was loaded with 10 μL of 1 M HCl. After the paper was dried, 10 μL of the sample (serum in this case) was added onto the same paper. After the paper

was dried, 100 μL of ultrapure water was added on the same porous area, all the dry reagents were released, and the measurements were performed with LS-ASV in combination with the office-paper based electrode. The scheme of the device is reported in the following Scheme 1.

Scheme 1. Representation of the Combination between Office Paper and Chromatographic Paper to Obtain a Synergic Platform



RESULTS AND DISCUSSION

Optimization of the Platform

The first study has been focused on the selection of the substrate for printing the conductive strips. The choice of the substrate should reflect the final application of the analytical device: a plastic-based substrate would be more suitable for application where flexibility and resistance are required, and perhaps, paper-based ones could represent a good compromise between sustainability and sensitivity. For this occasion, three substrates have been investigated, namely, plastic, office paper, and filter paper. As shown in Figure 1A, the same electrode configuration has been printed on the three substrates; 2 μL of the AuNP dispersion has been drop cast, and metal determination has been performed using a 200 ppb standard solution of copper ions.

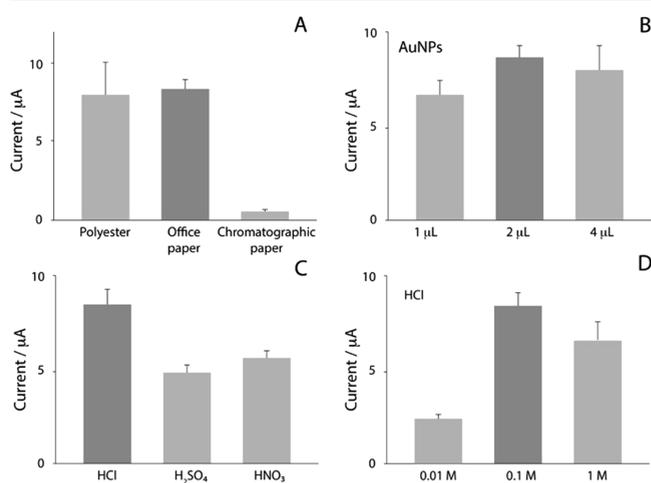


Figure 1. (A) Choice of the substrate (polyester, office paper, and chromatographic paper), (B) evaluation of the amount of the AuNPs to be drop cast (1, 2, and 4 μL), (C) optimization of the acid used to conduct stripping analysis (hydrochloric acid, sulfuric acid, and nitric acid), and (D) evaluation of the concentration of hydrochloric acid (0.01, 0.1, and 1 M). Each vertical bar is the results of three different paper-based devices.

As shown in Figure 1A, the current intensity obtained with office paper and polyester is roughly the same, while the current intensity obtained at the porous filter paper-based electrodes is low. It is attributable to the fact that with filter paper-based electrodes, the electrochemical cell is represented by the paper itself, and two phenomena need to be considered: (1) AuNPs are drop cast on top of the working electrode and they are not in contact with the working solution, and (2) the analyte should diffuse within the paper and it is reflected with a lower resulting signal.⁴² Regarding polyester-based and office paper-based electrodes, because of the poor porosity of office paper (within the experimental conditions, i.e., time and volume) and the same working electrode area that has been screen-printed, the current intensity was similar within the experimental errors. Due to the possibility of developing a more sustainable platform, office paper has been chosen for further studies. Consequently, the amount of AuNPs has been also evaluated as shown in Figure 1B. The amount of 2 μL (equivalent to ca. 2.5 nmol) has been chosen as the optimum, considering the responses obtained by modifying the electrodes with 1 and 4 μL . During deposition, copper is reduced onto the gold layer that has been drop cast onto the carbon electrode. It should be noted that, in the absence of AuNPs onto the graphite-based electrode, the signal due to copper was absent. What has been observed was that an amount of AuNPs higher than 2 μL had not produced a significant improvement in terms of current (that depends on the copper that is reduced at the working electrode surface). This could be ascribable to the fact that a higher concentration of AuNPs might lead to a thick surface, without producing a higher number of sites for copper deposition. In fact, with increasing the volume of AuNPs drop cast to 4 μL , the maximum of the current did not increase further. AuNPs have been used also in combination with carbon black nanoparticles (to improve the area), but in this case, it did not represent any recorded current improvement. Another investigated variable was the type and concentration of acid to be used as the supporting electrolyte for copper quantification. As displayed in Figure 1C,D, the best results have been obtained with the use of 0.1 M hydrochloric acid. This is in accordance with other works that have been reported in the literature,^{29,42} and it might be due to the different counterions that can affect the availability of copper ions within the working solution.

Electrochemical Parameter Optimization

After having optimized the parameters related to the printing substrates, AuNPs, and acidity of the working solution, optimization of the electrochemical parameters has been taken into account. According to the electrochemical detection technique that has been used, i.e., LS-ASV, the three most relevant factors have been optimized: the deposition potential, the deposition time, and the scan rate of the stripping wave, as shown in Figure 2. All the experiments have been carried out in the presence of 200 ppb copper ions in 0.1 M hydrochloric acid.

The deposition potential, required to reduce Cu^{2+} to Cu, has been studied from -0.6 to -0.2 V, as reported in Figure 2A. Thus, -0.4 V has been chosen as the optimal deposition potential because of its better repeatability with respect to another potential, -0.2 V, having the recorded current similar. Then, the deposition time has been evaluated from 100 to 400 s. This time is necessary to allow copper ions to reach the working electrode surface, and in the absence of stirring

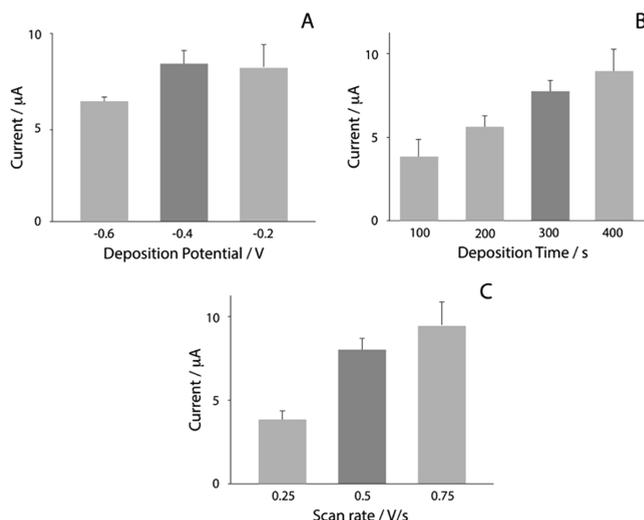


Figure 2. (A) Optimization of the deposition potential (-0.6 , -0.4 , and -0.2 V), (B) choice of the deposition time between 100 and 400 s, and (C) scan rate of the linear sweep (0.25, 0.5, and 0.75 V/s). Each vertical bar is the results of three different paper-based devices.

procedures, only diffusion of copper ions occurs. A deposition time of 300 s represented the optimal compromise between response, analysis time, and repeatability (the percentage errors are 7.7 and 15%, respectively, for 300 and 400 s depositions). Finally, the scan rate of the anodic stripping has been considered, and in the range between 0.25 and 0.75 V/s, 0.5 V/s has represented the optimal compromise between signal current and repeatability of the measurements, as shown in Figure 2C.

Analytical Performance of Office Paper toward Copper Ions

Once both the printed platform and the electrochemical method have been optimized, the office paper-based sensor has been tested for determination of copper ions within the 0–300 ppb range in standard solution as reported in the following Figure 3.

As shown in the inset i of Figure 3, a linear correlation has been obtained between the height of the current peaks and the concentration of copper ions. The relationship is described by the following equation: $y = 0.047x + 0.723$ (where y represents the current difference between copper and the blank and x represents the copper level expressed in ppb), $n = 5$ ($R^2 = 0.995$). The detection limit, calculated as $3\sigma\text{B}/\text{slope}$ (σB represents the standard deviation calculated for blank measurements, and slope is the slope of the calibration curve), has been calculated to be equal to ca. 4 ppb, and the limit of quantification has resulted in ca. 12 ppb, with a repeatability of 11% (calculated on five replicates). As reported in the inset ii of Figure 3, the signal due to interfering species has been evaluated using the same experimental conditions. In particular, stripping measurements of solution containing 100–200 ppb zinc, nickel, lead, cadmium, and iron ions demonstrated the absence of significant interference, even when copper ions were measured in binary mixtures (inset iii of Figure 3).

Serum Measurements

The analytical efficacy of the developed electrochemical sensor for the determination of copper ions has been also demonstrated by applying it to the determination of copper

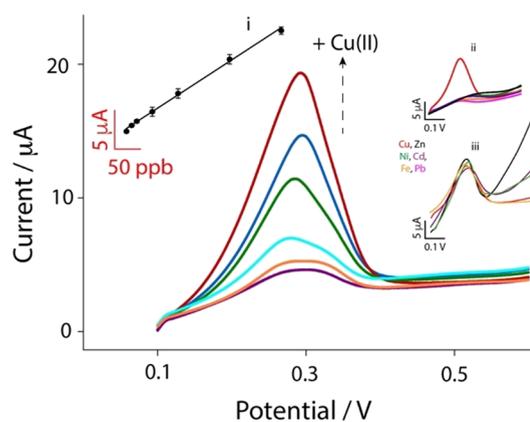


Figure 3. Recorded LS-ASV from 0 to 300 ppb Cu(II) in 0.1 M HCl (standard solution) using an office paper-based platform. Inset i: calibration curve in a linear range up to 300 ppb ($n = 5$). Inset ii: measurements in the presence of copper (red), zinc (black), nickel (green), cadmium (violet), iron (orange), and lead (pink) at the ppb level in 0.1 M hydrochloric solution. Inset iii: measurements in the presence of mixed-metal solutions, including copper and other metal ions (same as reported in inset ii). Experimental parameters: $E_{\text{dep}} = -0.4$ V; $t_{\text{dep}} = 300$ s; $E_{\text{begin}} = 0.1$ V; $E_{\text{end}} = 0.6$ V; $E_{\text{step}} = 0.01$ V; scan rate = 0.5 V/s.

ions in serum. A potential issue is given by the adsorption of proteins that are contained in serum, and a possible strategy to limit this possibility is the porosity of the paper itself and/or the combination of paper-based substrates with AuNPs.^{43,44} However, it should be noted that for the present study, an all-in-one approach has been adopted. The serum sample has been drop cast onto a chromatographic paper and not on the office paper where the electrodes are printed. Briefly, a chromatographic paper-based substrate has been used to load 10 μL of 1 M hydrochloric acid and also to preconcentrate the sample by dropping it on the wax-patterned filter paper increasing the amount of the sample to be measured. Depending on the dilution factor, different amounts of serum and the working solvent (water) can be used. For instance, to measure serum with a 90% dilution factor, the following procedure can be followed: (1) 10 μL of 1 M HCl is drop cast onto the chromatographic spot, and the solution is allowed to dry at room temperature; (2) 10 μL of serum is drop cast onto the same spot, and the solution is allowed to dry at room temperature; (3) reagents and samples are redissolved with the addition of 100 μL of water; (4) measurement is performed with the use of the optimized stripping parameters. It should be noted that the volume of reagents/samples to be drop cast can be customized depending on the experimental conditions. In fact, a 10 μL volume can be drop cast through five 2 μL additions, 10 1 μL additions, and so on. In our cases, steps of 2 μL additions have been used.

The first study has involved the evaluation of the matrix effect (inset ii of Figure 4).

It should be noted that the presence of this complex matrix has produced a decrease in the sensitivity due to the presence of species like proteins that can foul the electrode surface by adsorption phenomena. As the consequence of this evaluation, the optimal dilution of commercial serum has been selected to be equal to 90% dilution due to the highest sensitivity results. The relationship is described by the following equation: $y = 0.056x - 0.071$, $n = 5$ ($R^2 = 0.994$). Consequently, the serum sample has been spiked with copper ion levels up to 300 ppb.

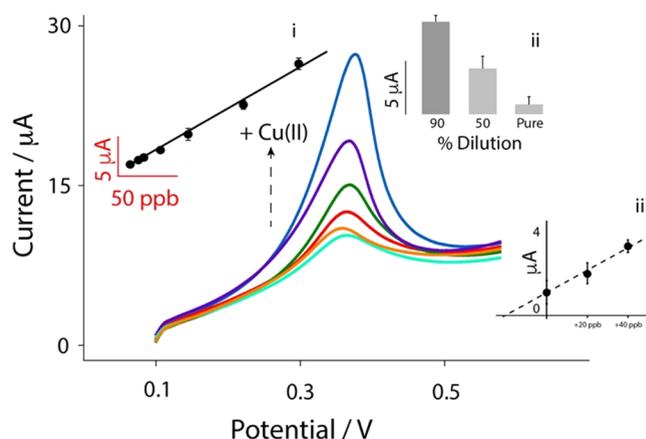


Figure 4. LS-ASV recorded while performing in serum using the all-in-one paper-based platform. Inset i: calibration curve in a linear range up to 300 ppb ($n = 5$). Inset ii: evaluation of the effect of the matrix with the use of 0.1 M hydrochloric acid (90%, 50%, and untreated). Inset iii: recovery studies in the presence of 20 ppb spiked serum samples. Experimental parameters: $E_{\text{dep}} = -0.4$ V; $t_{\text{dep}} = 300$ s; $E_{\text{begin}} = 0.1$ V; $E_{\text{end}} = 0.6$ V; $E_{\text{step}} = 0.01$ V; scan rate = 0.5 V/s.

As shown in the inset i of Figure 4, a good linearity has been obtained, in good agreement with the results that have been obtained in standard solution, and the detection limit in serum has been calculated to be equal to 4 ppb. It should be noted that the same sensitivity of the platform has been obtained by using both the traditional office-paper based configuration (where all the reagents are applied directly onto the testing area) and with the use of the all-in-one device (merging office paper for sensing and chromatographic paper for loading reagents/sampling/diluting). As reported in the literature, depending on its porosity, a paper-based substrate can be used to work with whole blood samples, by exploiting the advantage in filtering interferences, e.g., blood cells.^{45–47}

By comparing these analytical results with those obtained by analyzing copper at different platforms, it should be noted how the combination of office paper and chromatographic paper allows us to remove tasks for the end user. In fact, even if the analytical performance obtained at the different printed electrochemical systems appears roughly the same (Table 1), this approach provides a new route to develop an all-in-one method.

Nonporous substrates like polyester, polyethylene, wire, foil, etc. depend strongly on the necessity of adding reagents for quantification. Porous substrates, i.e., filter papers, are characterized by a lower sensitivity and are often associated to relevant matrix treatment. Instead, the combination of different paper-based substrates allows us to differentiate tasks, e.g., sensing at office paper and matrix treatment at chromatographic paper.

In order to evaluate the accuracy of the method, recovery studies have been carried out at two different levels of copper ions, namely, 20 and 50 ppb, obtaining 81 and 84% recoveries, respectively (the inset iii of Figure 4 shows a 20 ppb recovery). In addition, the satisfactory accuracy of the reported paper-based architecture has been confirmed by comparing the results obtained with the standard addition method on two real serum samples, with those obtained through the use of ICP-MS, and the results are reported in Table 2.

Table 1. Comparison with Electrochemical Portable Methods for Copper Detection

platform	sensing mechanism	LOD (ppb)	range (ppb)	matrix	method	ref.
filter paper	AuNPs synthesized within paper	3	10–400	serum, sweat	external dilution with strong acid (serum/sweat)	28
Whatman No. 1	dimethylamino pyridine-sintered AuNPs	50	up to 1000	std	10' accumulation in ammonium acetate buffer (pH = 7.0) of cysteine Au sensors	48
Au μ wire	lab-on-tip	6	20–300	river		49
polyester	AuNPs	1.6	20–300	std	stirring in 0.1 M acetate buffer (pH = 4.5)	50
aluminum foil	thiophene-based conducting polymer	4	6–600	std	stirring in 0.1 M acetate buffer and EDTA	51
polyethylene	phenanthroline/Nafion-carbon pencil	1	up to 400	PM aerosol	microwave-assisted digestion	52
office paper /Whatman No. 1	AuNPs	4	up to 300	serum		this work

Table 2. Recoveries and Comparison with Measurements Performed by ICP-MS

sample	spiked level	recovery
serum #1	20 ppb	81%
serum #2	50 ppb	84%

sample	ICP-MS measurement	SPE measurement	accordance (ICP-MS/SPE)
serum #3	10.7 ppb	12.0 ppb	89%
serum #4	23.5 ppb	25.8 ppb	91%

CONCLUSIONS

This work demonstrates the development of a simple and sustainable method for detecting copper ions in a biological matrix like serum. Screen-printed electrodes were easily produced onto office paper and effectively customized with gold nanoparticles by a drop casting procedure. The detection limit of the platform has been approximately calculated to be equal to 4 ppb in both standard and serum solutions. In addition, it should be noted that an ulterior filter paper-based platform has been used to preload the reagents and preconcentrate real samples, with the advantage of making the platform adaptable to real matrix scenarios. We demonstrate that filter paper can act in combination with office paper to avoid tasks for the end user, i.e., acidification. The utilization of double paper-based substrates allows us to use chromatographic paper to load reagents and collect real samples and to use office paper to perform electroanalysis. The tasks required for the end user are minimal; in fact, one just needs to cast serum and add water to perform the analysis. The satisfactory comparison with ICP-MS measurements has demonstrated good accuracy of the proposed approach. The next challenge will be focused on the development of a customized 3D-printed case that will make the platform integrated and ready to market, and this approach could be easily expanded to different fields of action as the environmental and pharmaceutical ones.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsmeasuresciau.1c00059>.

SEM micrographs of office and filter papers (PDF)

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Author Contributions

All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

S.C. acknowledges the MIUR Grant “Dipartimento di Eccellenza 2018-2022” to the Department of Pharmacy of University of Naples “Federico II”.

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