Screen Printing of MWCNT-based Electrodes for Uric Acid Detection

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ABSTRACT

The detection of uric acid (UA) is critical due to its role in key physiological processes and its association with conditions like gout, kidney stones, and cardiovascular diseases. This study presents the fabrication and optimization of screen-printed multiwalled carbon electrodes modified with AuNPs for UA detection, achieving a high sensitivity and a detection limit of 6.25 μM using differential pulse voltammetry. These electrodes show promise for integration into wearable devices, enabling continuous UA monitoring for personal health management and clinical diagnostics. This advancement could enhance personalized healthcare through early intervention and improved management of UA-related conditions.

Keywords: Screen-printed carbon electrodes, uric acid, differential pulse voltammetry, wearable sensors, and electrochemical sensors.

1. INTRODUCTION

The detection of uric acid (UA) is crucial due to its significant role in various physiological and biochemical processes within the human body. UA, a metabolic product of purines, is regulated through renal and intestinal pathways. Abnormal levels, either hyperuricemia or hypouricemia, are linked to health conditions such as gout, kidney stones, cardiovascular diseases, and metabolic syndrome. Accurate measurement of UA is essential for early diagnosis and effective management of these conditions. Purines, integral to cellular energy metabolism, are metabolized into UA via intermediates hypoxanthine and xanthine, catalyzed by the enzyme xanthine oxidase. This process is particularly active in the liver (Johnson et al., 2018). UA levels are tightly regulated by the kidneys and intestines. The kidneys manage urinary excretion and reabsorption of UA, while the

intestines contribute through microbial metabolism (Brown et al., 2019, Wang et al., 2021). UA's biological role centers on its antioxidant activity and neuroprotective effects, reacting with free radicals to protect cells from oxidative stress and potentially aiding in neurological health (Sautin et al., 2016). Hyperuricemia, high UA levels, is clinically significant and linked to conditions such as gout, kidney stone formation, metabolic syndrome, and cardiovascular disease (Ames et al., 2018, Choi et al., 2007). Gout, characterized by UA crystal accumulation in joints, presents with severe pain and inflammation, typically in the big toe (Schlesinger et al., 2004). High UA levels also contribute to kidney stone formation, causing pain, urinary tract obstruction, and infection risk (Rule et al., 2011). Factors influencing urate stone formation include genetics, diet, water intake, and medical conditions. Treatment options range from medications to surgical interventions. UA levels are also associated with insulin resistance, obesity, hypertension, and dyslipidemia, components of metabolic syndrome, a strong risk factor for cardiovascular disease. UA may trigger inflammation, increasing cardiovascular disease risk through mechanisms such as oxidative stress and endothelial dysfunction (Feig et al., 2008). It may also increase insulin resistance and impair pancreatic beta cell function, elevating the risk of type 2 diabetes (Ames et al., 2018). Conversely, low UA levels, while rare, can lead to weakened antioxidant defenses and are linked to neurodegenerative diseases like Parkinson's disease (Sautin et al., 2016, Ames et al., 2018). In this study, we aim to develop, optimize, and evaluate flexible multiwalled carbon nanotube-based screen-printed carbon electrodes (SPCEs) for the electrochemical detection of UA. Multi-walled carbon nanotubes (MWCNTs) are extensively utilized in various areas of research, spanning from fabricating efficient conductive pathways for electronic systems to designing innovative conductive pastes used in sensors and (Sikora et al. 2015). The focus is on creating a reliable and sensitive method for UA detection, enhancing electrochemical performance through the deposition of gold nanoparticles. This research seeks to demonstrate the practical application of these sensors in wearable health monitoring devices, providing continuous, real-

time monitoring of UA levels in biological fluids. By contributing to electrochemical sensor technology, we aim to offer a robust, flexible, and highly sensitive platform for UA detection, facilitating timely diagnosis and management of health conditions related to uric acid levels.

2. MATERIALS AND METHODS

2.1. Materials

Ferrocenemethanol ($FcCH_2OH$) (Sigma-Alrich, USA), phosphate buffered saline (PBS) (Sigma-Alrich, USA), UA (Sigma-Alrich, USA), dopamine (DA) (Sigma-Alrich, USA), ascorbic acid (AA) (Sigma-Alrich, USA).

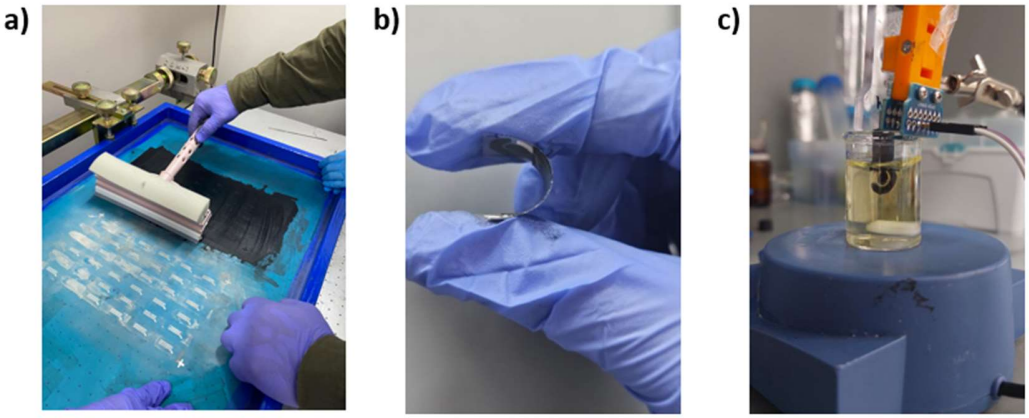

Fig. 1. Screen printing of flexible SPCEs. An image showing electrochemical measurement using an SPCE.

2.2. Fabrication and electrochemical characterization of SPCEs

A conductive paste was formulated by combining MWCNTs with acrylic paint and applied alongside silver paste (Ag paste) to screen-print SPCEs onto acetate paper (Şen et al., 2024). The conductive paste was utilized to print the upper sections of the working and counter electrodes, while the silver paste was used for the lower portions of these electrodes as well as the reference electrode (Fig. 1a). To define and insulate the sensor area of the flexible SPCE (Fig. 1b), electrical tape was applied. Finally, the SPCE surfaces were modified with AuNPs by electrodepositing them in an auric solution using chronoamperometry. The cyclic voltammetry curves of both bare and

AuNP coated SPCEs were obtained in 1 mM $FcCH_2OH$ by sweeping the potential from -0.1 to 0.5 V (E vs. Ag) at a scan rate of 50 mV/s (Fig. 1c) (Şen et al. 2014).

2.3. Electrochemical detection of UA

In the present study, electrochemical detection of UA with AuNP modified SPCEs was conducted using a potentiostat/galvanostat (Autolab PGSTAT204, Metrohm). The measurements were performed in the potential range 0.0 to 0.6 V vs. Ag using differential pulse voltammetry (DPV) due to the technique's high sensitivity for distinguishing closely spaced peaks of redox processes, hence giving a better detection for low UA concentrations in complex samples at a very high scan rate of 500 mV/s. The electrolyte was prepared by the dissolution of UA in PBS solution at pH 7.4. In this respect, various concentrations of UA in the range of 0-1000 µM were assessed, though a main concern of the oxidation currents is UA concentrations of 0, 50, 75, 100, 200, 300, 500, and 1000 µM to cover physiologic levels usually found in bio-samples (Oguz et al., 2024, Seven et al.). In each case of measurement, the working electrode was dipped in the UA solution, followed by DPV scanning. The obtained oxidation peak currents at each concentration were recorded and analyzed for a calibration curve (Aydin et al., 2017, Avcı et al., 2023, Şen et al., 2022).

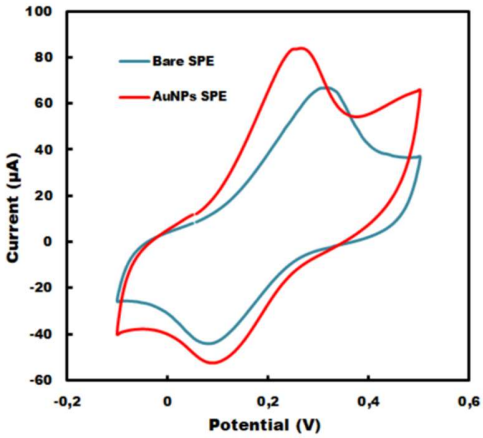

Fig. 2. CV curves of bare and AuNP coated SPCEs obtained in 1 mM $FcCH_2OH$.

3. RESULTS AND DISCUSSION

The fabricated SPCEs were modified with AuNPs via chronoamperometric deposition conducted at 0 V for 30 minutes. This modification was performed to enhance the surface properties of the electrodes, particularly their electrical conductivity and catalytic activity. The time-dependent current response observed during the deposition process verified the successful formation of a uniform layer of AuNPs on the electrode surface. The electrochemical performance of AuNP-modified electrodes was systematically evaluated and compared with that of unmodified (bare) electrodes using cyclic voltammetry. The resulting voltammograms demonstrated pronounced differences between the two electrode types. Specifically, the AuNP-modified electrodes exhibited markedly higher current responses and more distinct peaks compared to the bare electrodes (Fig. 2). The peak-to-peak potential separation also dropped from approx. 248 mV to 147 mV. These improvements can be attributed to the increased electroactive surface area and the superior catalytic properties conferred by the AuNPs, which facilitate stronger and more efficient interactions with the analytes. Next, the AuNP modified SPCEs were used for electrochemical detection of UA. Basically, DPV curves were recorded at different concentrations of UA. The DPV technique, as represented in Fig. 3a, is very sensitive and gives sharp and well-defined peaks at different concentration levels of UA. Peak currents obtained from these curves were plotted to get a calibration curve; it gave a linear relationship, shown in Fig. 3b. This quantitative analysis requires a linear relationship, so this proves the efficacy of the electrode. From the slope of the calibration curve, sensitivity was found to be 70.06 $\mu A \cdot mM^{-1} \cdot cm^{-2}$. The limit of detection (LOD) for UA was around 6.25 μM, which represented the capacity for very low UA concentration detection by the sensor and is rather critical in its early clinical detection.

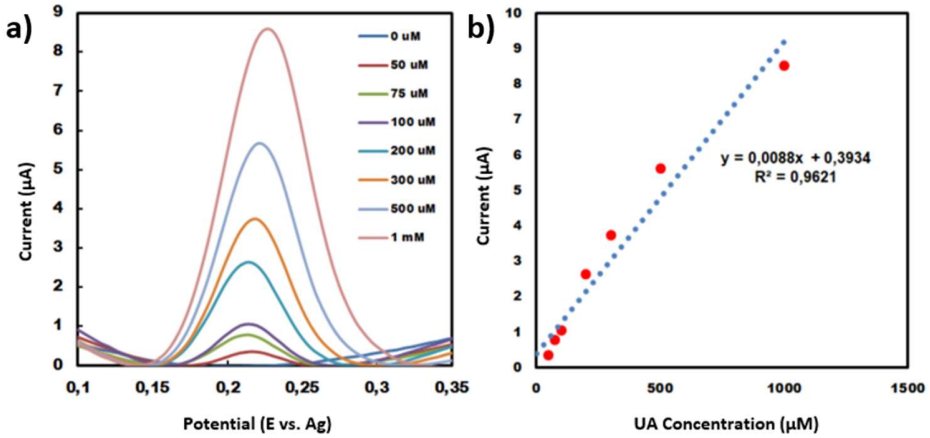

Fig. 3. DPV results showing the responses for different concentrations (a) and a calibration curve derived from the DPV measurements of UA at varying concentrations (b).

4. CONCLUSION

This study highlights the potential of SPCEs modified with AuNPs for the determination of uric acid (UA). The adopted fabrication approach for SPCEs was successfully implemented, and the modification with AuNPs significantly enhanced their electrochemical performance by improving electron transfer kinetics. The modified electrodes demonstrated high sensitivity (70.06 $\mu A \cdot mM^{-1} \cdot cm^{-2}$) and a low detection limit (6.25 µM) for UA detection. The integration of this technology into wearable devices offers exciting possibilities for revolutionizing personal health monitoring. Continuous monitoring of UA levels through portable and wearable sensors holds significant promise for personal health management and clinical diagnostics. Such advancements could play a critical role in personalized healthcare by enabling early interventions and improved management of conditions associated with abnormal UA levels.

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REFERENCES

Ames, B., and Cathcart, R. (2018). Protective effect of uric acid on neurological health. *Neurobiology of Disease, 104,* 349-361.

Aydin, V. K., and Şen, M. (2017). A facile method for fabricating carbon fiber-based gold ultramicroelectrodes with different shapes using flame etching and electrochemical deposition. Journal of Electroanalytical Chemistry, 799, 525-530.

Brown, E., and Green, F. (2019). Renal handling of uric acid. Kidney International, 88(4), 567-580.

Choi, H. K., and Ford, E. S. (2007). Prevalence of the metabolic syndrome in individuals with hyperuricemia. The American Journal of Medicine, 120(5), 442-447.

Feig, D. I., and Kang, D. H. (2008). Uric acid and cardiovascular risk. New England Journal of Medicine, 359(17), 1811-1821.

Johnson, C., and Williams, D. (2018). Role of xanthine oxidase in uric acid production. Biochemical Journal, 72(3), 205-218.

Oğuz, M., Aykaç, A., and Şen, M. (2024). A disposable sensor based on one-pot synthesized tungsten oxide nanostructure-modified screen-printed electrodes for selective detection of dopamine and uric acid. *Analytical Sciences, 40(2),* 301-308.

Rule, A. D., Krambeck, A. E., and Lieske, J. C. (2011). Chronic kidney disease in kidney stone formers. Clinical Journal of the American Society of Nephrology, 6(8), 2069-2075.

Sautin, Y., and Nakagawa, T. (2016). Uric acid and oxidative stress. American Journal of Physiology - Renal Physiology, 292(3), F78-F92.

Schlesinger, N. (2004). Management of acute and chronic gouty arthritis: Present state-of-the-art. Drugs, 64(21), 2399-2416.

Seven, F., Gölcez, T., and Şen, Mustafa, (2020). Nanoporous carbon-fiber microelectrodes for sensitive detection of H2O2 and dopamine. Journal of Electroanalytical Chemistry, 864, 114104.

Şen, M., and Avcı, I. (2023). A simple microfluidic redox cycling-based device for high-sensitive detection of dopamine released from PC12 cells. Journal of Electroanalytical Chemistry, 939, 117473.

Şen, M., Azizi, E., Avcı, İ., Aykaç, A., Ensarioğlu, K., Ok, İ., Yavuz, G.F., and Güneş, F. (2022). Screen printed carbon electrodes modified with 3D nanostructured materials for bioanalysis. *Electroanalysis, 34(9),* 1463-1471.

Şen, M., Ino, K., Inoue, K.Y., Suda, A., Kunikata, R., Matsudaira, M., Shiku, H. and Matsue, T. (2014). Electrochemical evaluation of sarcomeric α-actinin in embryoid bodies after gene silencing using an LSI-based amperometric sensor array. *Analytical Methods*, *6*(16), pp.6337-6342.

Şen, M., Oğuz, M., and Avcı., I. (2024). Non-toxic flexible screen-printed MWCNT-based electrodes for non-invasive biomedical applications. *Talanta, 268,* 125341.

Sikora, Aurélien, Javier Ramón-Azcón, Mustafa Sen, Kyongwan Kim, Hikaru Nakazawa, Mitsuo Umetsu, Izumi Kumagai, Hitoshi Shiku, Tomokazu Matsue, and Winfried Teizer. (2015). Microtubule guiding in a multi-walled carbon nanotube circuit. Biomedical Microdevices, 17, 1-6.

Wang, X., and Li, Q. (2021). Microbial metabolism of uric acid in the gut. Gut Microbes, 14(1), 45-58.