







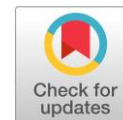
Electrochemical creatinine determination with metal-organic framework catalyst based on copper and acetylenedicarboxylic acid

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Abstract

Fast and accurate determination of creatinine is critical in kidney function diagnostics. This paper discusses the usage of the metal-organic framework based on copper(II) and acetylenedicarboxylic acid (CuADCA) as a catalyst of electrochemical oxidation of creatinine, glucose and urea. CuADCA was synthesized by deprotonation with triethylamine for the first time. Successful synthesis was confirmed by FTIR and EDS. The material was characterized by SEM, EIS, and CV. CuADCA forms laminated-like flakes with diameter from 1 μm to 20 μm , which is consistent with the polymer-like structure. CV and EIS analyses showed that CuADCA immobilized on GCE acts as a catalyst in electrooxidation reaction of glucose, urea, and creatinine. The sensitivity of creatinine detection, $1057 \pm 99 \mu\text{A}/\text{mM}$, was higher than the detection sensitivity of glucose and urea by more than 100 times with the limit of detection of 2 μM , so CuADCA is a promising material for further development of enzymeless sensors for creatinine.

Keywords

metal-organic framework
creatinine
voltammetry
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enzymeless determination

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1. Introduction

The determination of creatinine in urine and blood is critical in case of diagnosis of kidney and liver diseases. Modern methods for these purposes are chromatography, mass-spectrometry, and Jaffe reaction. Chromatography and mass-spectrometry require cumbersome devices highly qualified personnel and high-cost consumables. The Jaffe reaction, despite its simplicity and availability, is associated with using poisonous and explosive picric acid and low specificity, causing erroneously high creatinine results in the presence of proteins, glucose, acetoacetate, ascorbic acid, guanidine, acetone, cephalosporins, aminoglycosides, ketone bodies, α -keto acids, and other organic compounds. Thereby, the development of new simple, express, safe, and specific methods of creatinine determination is an urgent task in the field of medical diagnosis.

A promising approach for solving this problem involves electrochemical methods, especially voltammetry, due to its accuracy, high rate and low-cost of consumables and devices. However, analysis of organic compounds, including creatinine, on traditional electrodes (platinum, glassy

carbon, etc.) is difficult because of the absence of inherent electroactivity. There are a few ways of avoiding this drawback. One of them is using an electrochemical catalysts, which can reversibly oxidize or reduce and transfer electrons from non-electroactive molecule to electrode (or vice versa). The most popular electrochemical catalysts used in electrochemical sensors are metal (platinum, gold, palladium, etc.) and carbon nanomaterials, metal-organic complexes. During the past two decades, metal-organic frameworks (MOFs), also known as porous coordination polymers (PCPs), have experienced explosive growth. MOFs exhibit a wide variety of potential applications in catalysis, gas storage and separation, luminescence, and drug delivery, owing to their specific features, such as structural diversity, flexibility and tailorability, high porosity, large surface area, and extraordinary adsorption affinities [1]. In electrochemical biosensing MOFs were used for determination of cancer biomarkers [2], heavy metals [3], herbicides [4], H_2O_2 [5], bisphenol A [6] and other analytes.

There are several MOFs that are used to absorb creatinine in hemodialysis apparatus [7] and to detect creatinine: in the works [8, 9] the authors report a luminescent sensor

for detecting creatinine based on lanthanide-organic frameworks, but such sensors are non-reusable and require expensive equipment. Anyway, electrochemical creatinine sensors based on MOFs have not been described in the literature.

In the past, a lot of MOFs with different linkers and metal ions were synthesized and applied as sensing receptors in electrochemical sensors. Significant portion of these MOFs are based on copper(I) or (II) ions because of their high catalytic activity and low cost [1, 5, 6, 10–12]; besides, copper ions form a strong coordination bond with creatinine: from 2 to 4 creatinine molecules per one Cu^{2+} ion [13].

A variety of MOF forms and their characteristics are available due to using different linkers between metal ions. The main requirements for these molecules are the rigid structure, e.g., imidazole, benzene ring(s), acetylene group, etc., and the presents of two or more functional groups that can attach ions ($-\text{COOH}$, $-\text{NH}_2$, pyridines, etc.) [1]. One of the promising linkers for MOF synthesis is acetylenedicarboxylic acid (ADCA), which meets all these requirements [14]. Some amount of copper and ADCA containing CPs were synthesized to date [14, 15].

So, the aims of the present work were the synthesis of Cu^{2+} -acetylenedicarboxylic acid MOF (CuADCA) and the investigation of its electrochemical behavior towards creatinine in the presence of glucose and urea.

2. Materials and Methods

2.1. Materials

$\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, ethyl alcohol, dimethylformamide (DMF), acetylenedicarboxylic acid (ADCA, 95%, Sigma-Aldrich, USA), triethylamine (TEA, Sigma, USA), creatinine (Millipore, Germany), glucose (PanReac, Spain), urea (Sigma-Aldrich, USA), Na_2HPO_4 (Sigma-Aldrich, USA), KH_2PO_4 (Sigma-Aldrich, USA), KCl (Sigma-Aldrich, USA), NaCl (Sigma-Aldrich, USA), $\text{K}_4[\text{Fe}(\text{CN})_6]$ (Sigma-Aldrich, USA), $\text{K}_3[\text{Fe}(\text{CN})_6]$ (Sigma-Aldrich, USA). Deionized water (18.2 M Ω) was produced with Barnstead™ Pacific TII Water Purification System (Germany) and was used in all experiments. Phosphate buffer saline (PBS) pH = 7.4 was prepared by dissolving of 8.00 g of NaCl, 0.2 g of KCl, 1.44 g of Na_2HPO_4 and 0.24 g of KH_2PO_4 in 1 liter of water with further adjustment to the desired pH.

2.2. Apparatus

Voltammetric and electrochemical impedance spectroscopy (EIS) studies were performed using an Autolab PGSTAT302N potentiostat/galvanostat (Metrohm AG, The Netherlands). Three-electrode electrochemical cell was used: glassy carbon disk working electrode (GCE) with $S=0.07 \text{ cm}^2$, Ag/AgCl reference electrode and glassy carbon rod counter electrode (all – Metrohm AG, The Netherlands). Cyclic voltammetry (CV) measurements were carried out at room temperature in PBS. The electrode modification process was investigated by electrochemical impedance

spectroscopy (EIS), which was performed in 5.0 mM $\text{Fe}(\text{CN})_6^{3-/4-}$ solution containing 0.1 M KCl.

The IR spectra were recorded in KBr tablets on an ALPHA FTIR spectrometer manufactured by BrukerOptikGmbH (Germany).

SEM microphotographs and elemental analysis by energy-dispersive X-ray spectroscopy (EDS) were obtained with AURIGA CrossBeam (Carl Zeiss NTS, Germany).

2.3. Synthesis of CuADCA and working electrode modification

Scheme 1 represents the routes of CuADCA synthesis and GCE modification. Briefly, 0.33 mL of distilled water, 0.33 mL of ethyl alcohol, and 0.33 mL of DMF were added to a 1.5 mL Eppendorf tube. Next, the resulting mixture was divided into two equal parts of 0.5 mL. 0.54 mmol (0.0092 g) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ was dissolved in the first part, 0.02925 mmol (0.0034 g) ADCA was dissolved in the second part. After the dissolution of both components, the solutions were mixed and stirred for 10 minutes. Then 12.5 μL of triethylamine was added to the tube and stirred for 1.5 hours. The precipitated blue crystals were isolated by centrifugation and washed 3 times with water, ethyl alcohol and DMF and dried in air at 60 °C for 3 hours. Then the 5 μL of suspension of 1 mg of CuADCA per 1 mL of water prepared with ultrasonication was drop casted on GCE and dried in air. The modified electrode was named CuADCA@GCE.

2.4. Procedure of electrocatalytic creatinine detection using CuADCA@GCE as the electrocatalyst

The analytical procedure included the following stages:

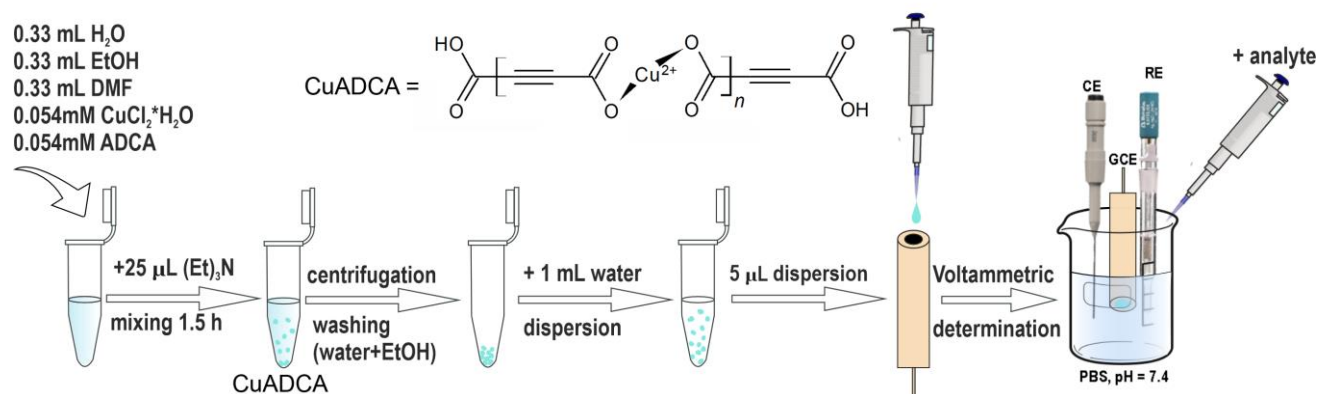
1. A cyclic voltammogram of CuADCA@GCE was registered in the working solution (10 mL of PBS), and anodic peak current was denoted as I_o .
2. 100 μL of standard creatinine solution in PBS (10 mM) was added to the working solution, and a cyclic voltammogram was registered. Anodic peak current was denoted as I_{st} .
3. 100 μL of analyzed creatinine solution in PBS (sample) was added to the working solution, and a cyclic voltammogram was registered. Anodic peak current was denoted as I_x .
4. The concentration of creatinine in the sample (C_x) was calculated as in Equation 1:

$$C_x = c_{st} \frac{I_{st}}{I_x} \quad (1)$$

3. Results and Discussion

3.1. Characterization of CuADCA

The CuADCA synthesis methods used in the past involved mixing a Cu^{2+} salt with ADCA with further slow water evaporation during several days [14]. To avoid long synthesis time, we use TEA as a deprotonating agent, so the reaction time reduces by up to 2 hours. The synthesis of the CuADCA can be explained by each ADCA ligand connecting to two Cu^{2+} ions metal nodes, forming the linear polymer-like structure [14].



Scheme 1 CuADCA synthesis and electrode modification.

The morphology, composition, and electrochemical properties of CuADCA were determined by SEM, EDS, FTIR, EIS and CV.

Figure 1 shows the SEM image of CuADCA. As can be clearly seen, CuADCA particles appear layered, which is consistent with the polymer-like structure. The dimensions of the flakes vary from 1 μm to 20 μm . Successful synthesis of CuADCA material is confirmed by EDS (Table 1) and FTIR (Figure 2): the spectra of CuADCA synthesized using triethylamine are identical to the spectra in the literature [16]. The spectra of ADCA have a characteristic peak at 1698 cm^{-1} (dimer between two carboxylic groups of the ADCA) that shifts to 1597 cm^{-1} in CuADCA spectra, which shows the pseudo-monodentate coordination of the anion.

Nyquist plots for bare GCE and CuADCA@GCE were registered in the solution containing 5 mM K₄[Fe(CN)₆]/K₃[Fe(CN)₆] and 0.1 M KCl at a potential of 0.25 V (Figure 3). Compared with the small semicircle of GCE, the R_{ct} of CuADCA@GCE was increased, indicating the successful modification of CuADCA nanoparticles on the GCE surface. The increased R_{ct} is due to the poor conductivity of CuADCA, which hinders, to some extent, the electron transfer through the electrode-solution interface.

3.2. Electrochemical behaviour of CuADCA in the presence of creatinine

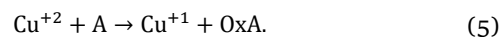
Figure 4a shows cyclic voltammograms of bare GCE and CuADCA@GCE registered in 0.1 M PBS pH = 7.4 in absence and in presence of different concentrations of creatinine. As seen, a couple of cathodic (at -0.4 V) and anodic (at -0.1 V) peaks in CuADCA@GCE are observed. To determine the number of electrons involved in the electrochemical reaction, Heyrovsky-Ilkovic equation (Equation 2) was used:

$$E = E_{1/2} + \frac{RT}{nF} \ln \left(\frac{I_d - I}{I} \right), \quad (2)$$

where R is the gas constant; T is the absolute temperature, K; F is the Faraday constant; n denotes the number of electrons taking part in the electrode reaction; $E_{1/2}$ is the half-wave potential, V; E is the potential applied, V; I is the current registered when E is applied, A; I_d is the limiting diffusion current (peak current), A. After rebuilding of voltammograms in the ranges of [(-0.20 V)-0 V] and

[(-0.26 V)-(-0.35 V)], the numbers of electrons involved in the electrochemical reaction were calculated as $n_a = 1.3$, $n_c = 0.4$. Deviations from a whole number can be explained as processes of reduction of Cu²⁺ and Cu⁺ to Cu⁰ and further oxidation of Cu⁰ to Cu⁺ occurring simultaneously.

The presence of creatinine, urea, or glucose in the working solution leads to the increase in the peaks currents, and the additional current depends linearly on the analyte concentration (Figure 4a, for creatinine). This fact can be explained as electrocatalytic processes represented by Equations 3-5:



Copper in form of Cu²⁺ binds with the analyte molecule (A) and then Cu²⁺ oxidizes the analyte molecule, is converted to Cu⁺ while oxidizing the analyte to form OxA, so CuADCA acts as a catalyst of electrochemical oxidation of analytes.

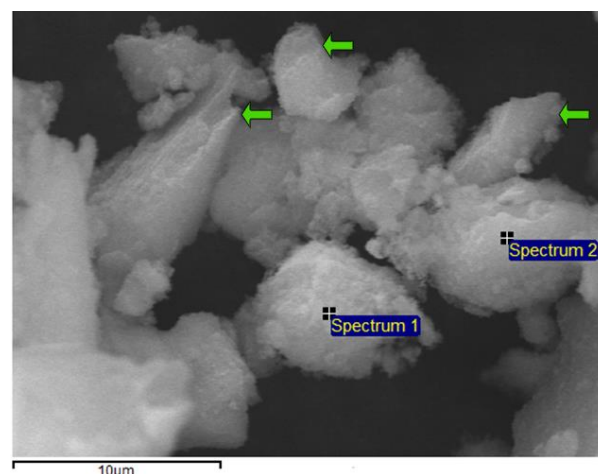


Figure 1 SEM microphotograph of CuADCA. Green arrows point to layered structure of microparticles.

Table 1 Elemental composition of CuADCA in atomic %, measured with EDS. Spectrum numbers correspond to points in Figure 1.

Spectrum number	C	O	Cl	Cu
Spectrum 1	54.3	11.6	2.7	31.3
Spectrum 2	57.7	18.4	4.2	19.7

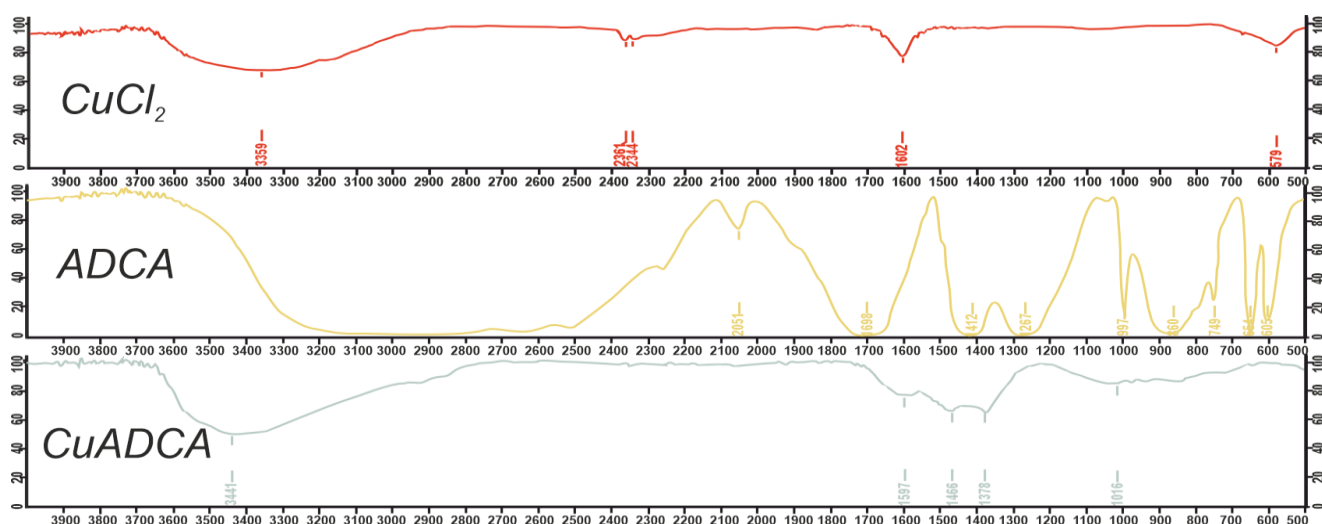


Figure 2 FTIR spectra of CuCl_2 , ADCA and CuADCA.

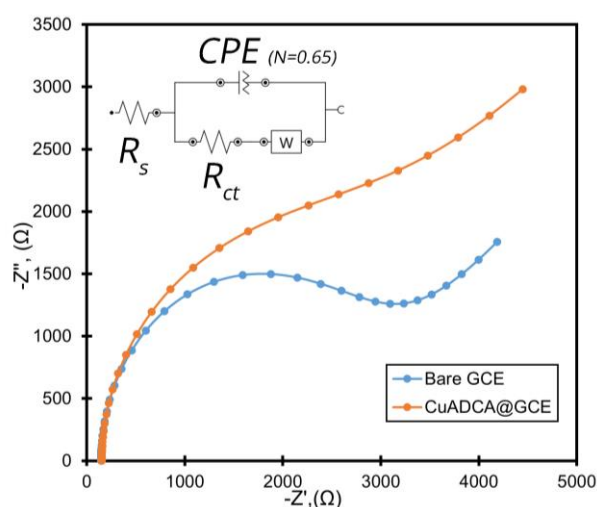


Figure 3 Nyquist plots at potential of 0.25 V for bare GCE and CuADCA@GCE registered in 5 mM $\text{K}_4[\text{Fe}(\text{CN})_6]/\text{K}_3[\text{Fe}(\text{CN})_6]$ + 0.1 M KCl; dots are experimental data and lines are fitted data. Inset: equivalent circuit.

Electrochemical transformations of CuADCA are processes that are controlled by diffusion of analyte to electrode-solution interface; the linear plots of the dependence of peak current on the square root of scan rate (Figure 4b) indicate this.

The analytical characteristics of urea, glucose, and creatinine determination were calculated from I vs. C_A dependences and are reflected in Table 2. As seen, the most linear dependences were obtained for the anodic peaks, and the highest sensitivity (the slope of I vs. C_A dependence) and the lowest limit of detection (LOD) were obtained for creatinine, which can be explained by the formation of strong complex between copper ions and creatinine molecules. This fact can be used in the future in the development of enzymeless electrochemical sensor for detection of creatinine in the presence of glucose and urea.

The developed creatinine determination system of CuADCA@GCE was compared with known enzymeless creatinine sensors (Table 3). It can be noticed that CuADCA@GCE is not inferior in sensitivity and LOD to the previously developed sensors.

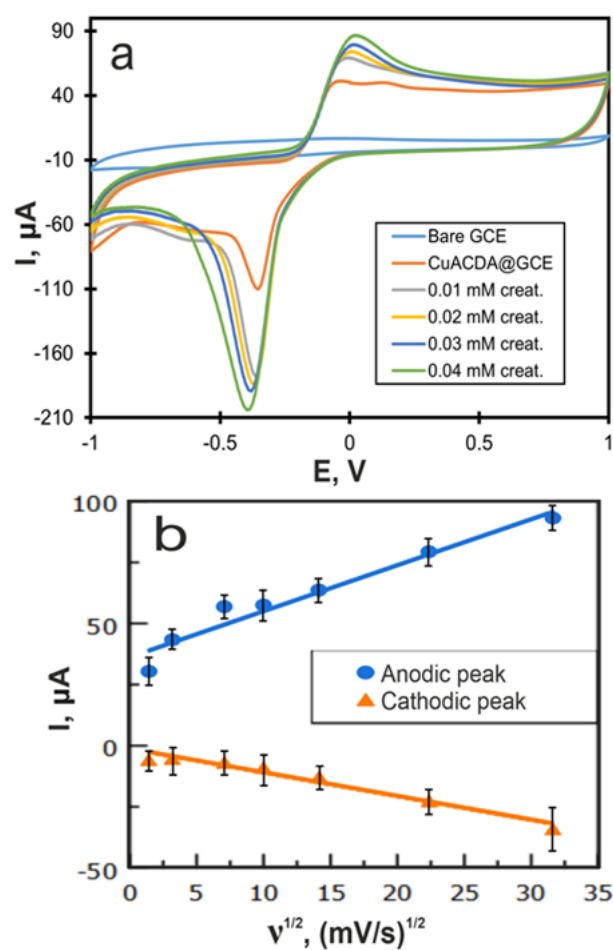


Figure 4 Cyclic voltammograms of bare GCE and CuADCA@GCE in absence and in presence of 10 μM , 20 μM , 30 μM and 40 μM of creatinine in 0.1 M PBS pH = 7.4. Scan rate: 0.1 V/s (a). The dependence of anodic and cathodic current peaks on square root of scan rate of CuADCA@GCE in 0.1 M PBS pH = 7.4 with 40 μM of creatinine (b).

4. Limitations

In this research, creatinine, urea and glucose were determined in model solutions imitating blood serum. In order to develop the enzymeless electrochemical sensor for creatinine, it is necessary to make investigations with real blood serum and whole blood.

Table 2 Analytical characteristics of urea, glucose, and creatinine determination with CuADCA@GCE as electrocatalyst ($n = 5$, $P = 0.95$).

Analyte	Sensitivity ($\mu\text{A}/\text{mM}$)		R^2		LOD (μM)	Linear range (mM)
	Anodic peak	Cathodic peak	Anodic peak	Cathodic peak		
Urea	1.0±0.1	5.0±0.4	0.973	0.891	1923	0–10
Glucose	13.0±1.1	116±10	0.969	0.874	228	0–0.4
Creatinine	1057±99	1756±150	0.966	0.649	2	0–0.1

Table 3 Comparing of CuADCA@GCE with previously developed electrochemical enzymeless sensors for creatinine determination systems.

System	Sensitivity, $\mu\text{A}/\text{mM}$	LOD, μM	Linear range, μM	Reference
CuADCA@GCE	1057±99	2	0–0.1	This work
Fe ₂ O ₃ /PANI-1@GCE	28.77	0,23	0.442–8840	[17]
CuO/IL@ERGO	1.02	0.2	0.01–2000	[18]
CB nanoparticles@SPE	16.7	8.6	370–3600	[19]

5. Conclusions

In this work we report enzymeless electrochemical determination of urea, glucose, and creatinine in PBS pH = 7.4 on the glassy carbon electrode modified with CuADCA synthesized with a simple and rapid method and characterized by SEM, FTIR, EIS and CV. Sensitivity and LOD were calculated. The results show that CuADCA immobilized on GCE acts as catalyst in electrooxidation reaction of glucose, urea, and creatinine. Since the sensitivity and LOD for creatinine detection were more than 100 times higher than for glucose and urea detection, CuADCA is a promising material for further development of an enzyme-free sensor for creatinine. As compared with the existing enzymeless sensors, CuADCA@GCE is not inferior in sensitivity and LOD.

• Supplementary materials

No supplementary materials are available.

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Formal Analysis: A.V.O., A.N.K.

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Investigation: A.A.I., Y.V.I.

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Supervision: A.V.O.

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• Conflict of interest

The authors declare no conflict of interest.

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References

- Yi F-Y, Chen D, Wu M-K, Han L, Jiang H-L. Chemical sensors based on metal-organic frameworks. *ChemPlusChem*. 2016;81(8):675–690. doi:[10.1002/cplu.201600137](#)
- Mohan B, Kumar S, Kumar V, Jiao T, Sharma HK, Chen Q. Electrochemiluminescence metal-organic frameworks biosensing materials for detecting cancer biomarkers. *TrAC Trends Anal Chem*. 2022;157116735. doi:[10.1016/j.trac.2022.116735](#)
- Chauhan S, Dahiya D, Sharma V, Khan N, Chaurasia D, Nadda AK, Varjani S, Pandey A, Bhargava PC. Advances from conventional to real time detection of heavy metal(loid)s for water monitoring: An overview of biosensing applications. *Chemosphere*. 2022;307136124. doi:[10.1016/j.chemosphere.2022.136124](#)
- Niu Z, Liu Y, Li X, Yan K, Chen H. Electrochemical sensor for ultrasensitive detection of paraquat based on metal-organic frameworks and para-sulfonatocalix[4]arene-AuNPs composite. *Chemosphere*. 2022;307135570. doi:[10.1016/j.chemosphere.2022.135570](#)
- Huang W, Xu Y, Wang Z, Liao K, Zhang Y, Sun Y. Dual nanozyme based on ultrathin 2D conductive MOF nanosheets intergraded with gold nanoparticles for electrochemical

- biosensing of H₂O₂ in cancer cells. *Talanta*. 2022;249123612. doi:[10.1016/j.talanta.2022.123612](https://doi.org/10.1016/j.talanta.2022.123612)
6. Ma J, Yuan J, Xu Y, Jiang Y, Bai W, Zheng J. Ultrasensitive electrochemical determination of bisphenol A in food samples based on a strategy for activity enhancement of enzyme: Layer-by-layer self-assembly of tyrosinase between two-dimensional porphyrin metal-organic framework nanofilms. *Chem Eng J*. 2022;446137001. doi:[10.1016/j.cej.2022.137001](https://doi.org/10.1016/j.cej.2022.137001)
 7. Li W, Li Y, Wen X, Teng Y, Wang J, Yang T, Li X, Li L, Wang C. Flexible Zr-MOF anchored polymer nanofiber membrane for efficient removal of creatinine in uremic toxins. *J Membr Sci*. 2022;648120369. doi:[10.1016/j.memsci.2022.120369](https://doi.org/10.1016/j.memsci.2022.120369)
 8. Wu N, Guo H, Peng L, Chen Y, Sun L, Liu Y, Wei X, Yang W. Three-step post-synthetic modification metal-organic framework as a ratiometric fluorescent probe for the detection of creatinine. *Microporous Mesoporous Mater*. 2022;338111989. doi:[10.1016/j.micromeso.2022.111989](https://doi.org/10.1016/j.micromeso.2022.111989)
 9. Luo L, Xie Y, Hou S-L, Ma Y, Zhao B. Recyclable luminescent sensor for detecting creatinine based on a lanthanide-organic framework. *Inorg Chem*. 2022;61(26):9990-9996. doi:[10.1021/acs.inorgchem.2c00850](https://doi.org/10.1021/acs.inorgchem.2c00850)
 10. Ma B, Guo H, Wang M, Li L, Jia X, Chen H, Xue R, Yang W. Electrocatalysis of Cu-MOF/graphene composite and its sensing application for electrochemical simultaneous determination of dopamine and paracetamol. *Electroana*. 2019;31(6):1002-1008. doi:[10.1002/elan.201800890](https://doi.org/10.1002/elan.201800890)
 11. Campbell MG, Sheberla D, Liu SF, Swager TM, Dincă M. Cu₃(hexaiminotriphenylene)₂: an electrically conductive 2D metal-organic framework for chemiresistive sensing. *Angew Chem Int Ed*. 2015;54(14):4349-4352. doi:[10.1002/anie.201411854](https://doi.org/10.1002/anie.201411854)
 12. Stassen I, Burtch N, Talin A, Falcaro P, Allendorf M, Ameloot R. An updated roadmap for the integration of metal-organic frameworks with electronic devices and chemical sensors. *Chem Soc Rev*. 2017;46(11):3185-3241. doi:[10.1039/C7CS00122C](https://doi.org/10.1039/C7CS00122C)
 13. Mitewa M. Coordination properties of the bioligands creatinine and creatine in various reaction media. *Coord Chem Rev*. 1995;1401-25. doi:[10.1016/0010-8545\(94\)01122-R](https://doi.org/10.1016/0010-8545(94)01122-R)
 14. Ntep TJMM, Gramm VK, Ruschewitz U, Janiak C. Acetylenedicarboxylate as a linker in the engineering of coordination polymers and metal-organic frameworks: challenges and potential. *Chem Commun*. 2022;58(64):8900-8933. doi:[10.1039/D2CC02665A](https://doi.org/10.1039/D2CC02665A)
 15. Xu W, Pan W-J, Zheng Y-Q. Syntheses and crystal structures of phthalato-, succinato-, maleato-, acetylenedicarboxylato-bridged [bis(2-pyridylcarbonyl)amide]copper(II) complexes. *J Coord Chem*. 2013;66(24):4415-4429. doi:[10.1080/00958972.2013.862789](https://doi.org/10.1080/00958972.2013.862789)
 16. Shershnev VA, Shilov GV, Dzhardimalieva GI, Pomogailo AD, Izydorzak M, Leonowicz M. Synthesis and characteristics of acetylenedicarboxylic acid salts as precursors for obtaining of nanocomposites. *Macromol Symp*. 2012;317-318(1):180-186. doi:[10.1002/masy.201100131](https://doi.org/10.1002/masy.201100131)
 17. Sriramprabha R, Sekar M, Revathi R, Viswanathan C, Wilson J. Fe₂O₃/polyaniline supramolecular nanocomposite: A receptor free sensor platform for the quantitative determination of serum creatinine. *Anal Chim Acta*. 2020;1137103-1137114. doi:[10.1016/j.aca.2020.09.004](https://doi.org/10.1016/j.aca.2020.09.004)
 18. Boobphahom S, Ruecha N, Rodthongkum N, Chailapakul O, Remcho VT. A copper oxide-ionic liquid/reduced graphene oxide composite sensor enabled by digital dispensing: Non-enzymatic paper-based microfluidic determination of creatinine in human blood serum. *Anal Chim Acta*. 2019;1083110-1083118. doi:[10.1016/j.aca.2019.07.029](https://doi.org/10.1016/j.aca.2019.07.029)
 19. Fava EL, Prado TM do, Garcia-Filho A, Silva TA, Cincotto FH, Cruz de Moraes F, Faria RC, Fatibello-Filho O. Non-enzymatic electrochemical determination of creatinine using a novel screen-printed microcell. *Talanta*. 2020;207120277. doi:[10.1016/j.talanta.2019.120277](https://doi.org/10.1016/j.talanta.2019.120277)