

Electrochemical Treatment of Gout in the Presence of Sherry Vinegar

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Abstract

This study focuses on evaluating the analytical performance and chelation capabilities of SV, using specialized NPM-CPE sensors designed for Ca²⁺ ion detection. The research context centres on addressing analytical and therapeutic challenges in conditions like gout, where CaC₂O₄ dissolution plays a critical role. The findings demonstrate that SV exhibits a remarkable ability to chelate Ca²⁺ ions in a solution, resulting in the formation of stable complexes. A combination of electrochemical techniques, including SWV, CV and EIS, to characterize SV's chelation capacity, and the presence of Ca²⁺ metals, was employed. Through these electrochemical methods, valuable insights on the efficacy of SV in chelating Ca²⁺ ions were gained, which offered significant implications for conditions associated with CaC₂O₄ deposition, such as gout. This study addresses the need to tackle analytical and therapeutic challenges posed by gout and related disorders, and proves a novel approach to understanding and potentially treating these conditions. Detailed results of the research, which include the successful chelation of Ca²⁺ ions by SV, can be found in the main body of the paper, offering a comprehensive account of the findings.

Keywords: chelation; electrochemical methods; gout; SV.

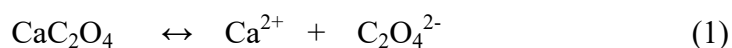
Introduction*

Gout is the most common disease in recent decades, characterized by inflammatory arthritis induced by hyperuricemia, and the subsequent deposition of monosodium urate crystals in joints and other tissues [1]. The prevalence of gout is steadily increasing worldwide. Gout constitutes the formation of small crystals that accumulate in the joints, leading to excruciating pain, swelling and redness in affected areas. Often, it primarily affects the big toe base [3]. Gout exhibits two

* The abbreviations list is in page 8.

primary forms: hyperuricemia and pseudogout. In hyperuricemia, uric acid crystals accumulate in the joints. Pseudogout results from pyrophosphate crystals deposits in the joints [2]. Various factors contribute to gout attacks, including genetic and environmental elements. Common risk factors include hyperuricemia, obesity, high blood pressure, alcohol consumption, dietary choices, inflammatory cytokines, genetic predisposition, certain drug treatments and exposure to lead [4-6].

Conventional treatments for gout mainly involve medications to reduce uric acid levels in the bloodstream. While these drugs have shown effectiveness in managing gout, several epidemiological and animal studies have raised concerns on their carcinogenic potential [7-11]. CaC_2O_4 is a naturally occurring chemical compound in the human body that can form crystals, leading to joint symptoms alike those seen in gout, such as calcium pyrophosphate arthritis (pseudogout) or other joint-related conditions. CaC_2O_4 crystals can also develop in tendons and connective tissues. This study focused on the development of modified electrodes designed to monitor CaC_2O_4 solubility reactions, proposing a local intervention to facilitate its dissolution. Given the perpetual equilibrium between CaC_2O_4 and Ca^{2+} ions, the primary aim was to chelate the latter and subsequently promote the dissolution of the former.



This research endeavoured to contribute to a better understanding of gout electrochemical treatment, particularly in SV presence, and its potential for mitigating the effects of this painful condition. To achieve this goal, C and rock phosphate were chosen as key electrode materials. The rationale behind these selections will be elaborated upon in the subsequent sections of this paper.

Experimental

Electrochemical measurement

In this section, the details of the electrochemical measurements conducted during this study are presented, focusing on the characterization of SV's chelation effect on Ca^{2+} ions using NPM-CPE sensors.

Reagents and chemicals

All chemicals used in the experiments were of the highest quality. Graphite powder (spectroscopic grade RWB, Rings Dorff-Werke GmbH, Bonn-Bad Godesberg, Germany) was obtained from Aldrich, and used without further purification. CaCl_2 was procured from Merck chemicals, and deionized water was used to prepare all solutions. SV was freshly prepared from the Sherry.

Electrochemical apparatus

Electrochemical experiments were done using a Voltalab potentiostat (PGSTAT 100, Eco Chemie B.V., Utrecht, Netherlands) controlled by general-purpose electrochemical systems data processing software (Voltalab Master 4 software). A standard one-compartment three-electrode cell was used in all experiments. The reference electrode was SCE, while the counter electrode was Pt. All

electrode potentials were referenced to SCE. Modified CPE was the working electrode.

Electrode preparation

CPE was prepared by mixing paraffin oil with C powder. To create NPM-CPE, the same amount of C powder was substituted with natural phosphate. Then, paraffin oil was added. The mixture was meticulously hand-mixed in a mortar and pestle. The resulting paste was packed into the electrode, and the surface was smoothed [12].

Electrochemical measurement and characterization

To evaluate the modified electrodes electrochemical behaviour, and study SV's chelation capacity for Ca^{2+} ions, a series of electrochemical measurements was conducted. These measurements included CV, SWV and EIS. These techniques were instrumental in characterizing the interactions and redox reactions of Ca^{2+} ions with SV and the modified electrodes.

Results and discussion

CV experiments

The characteristic CV of the two elaborate electrodes (Fig. 1 (a)), CPE and NP-CPE (Fig. 1 (b)), were recorded in an electrolytic medium.

As seen, the CV recorded at the NP-CPE has changed in its shape, which corresponds to a surface morphology alteration [13]. Electrical current densities were very high, and C had a very large specific surface, which promoted phosphate dispersion.

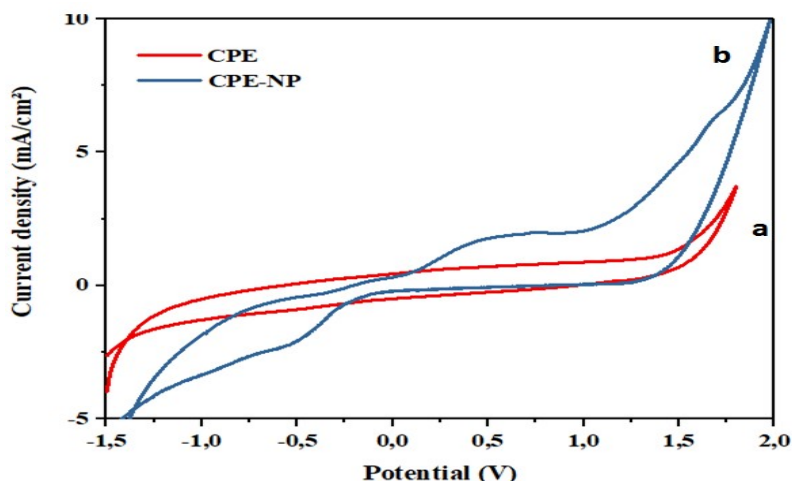


Figure 1: CV recorded in a Na_2SO_4 solution, at **a-** CPE and **b-** NP-CPE, with a SR of 50 mV/s.

Behavior of NP-CPE electrode towards Ca^{2+} ions

CV recorded at the surface of unmodified CPE, in an electrolytic medium containing Ca^{2+} ions (Fig. 2), seems passive towards Ca ions, and no peak was observed.

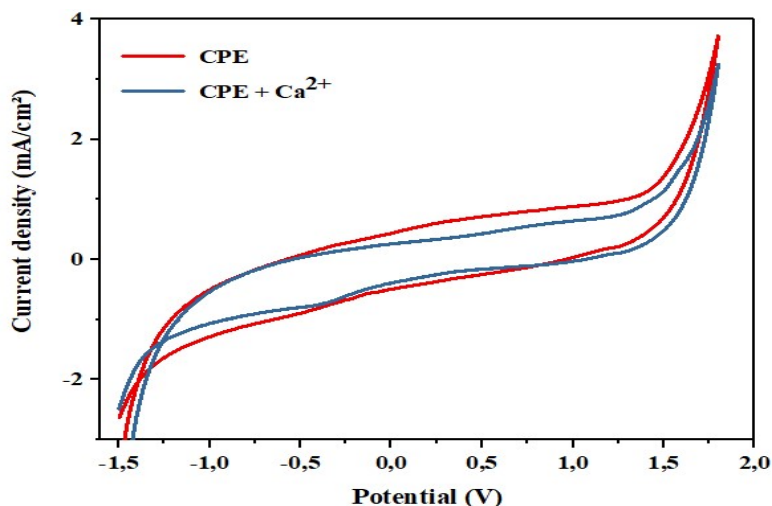


Figure 2: CV recorded in Na_2SO_4 , **a-** without and **b-** with Ca^{2+} ions, at CPE, with a SR of 50 mV/s.

Ca^{2+} ions presence in the electrolytic medium is manifested on the CV recorded for NP-CPE electrode, by the appearance of two well-defined redox peaks (Fig. 3): the first in the cathode scanning direction, towards its end, around -0.2 V, which corresponds to Ca^{2+} ions reduction; and the second of an anodic nature, at 0.7 V, which is due to metallic Ca oxidation. The anodic peak is relatively broad, because it represents Ca oxidation on the electrode surface, which was trapped in the natural phosphate matrix.

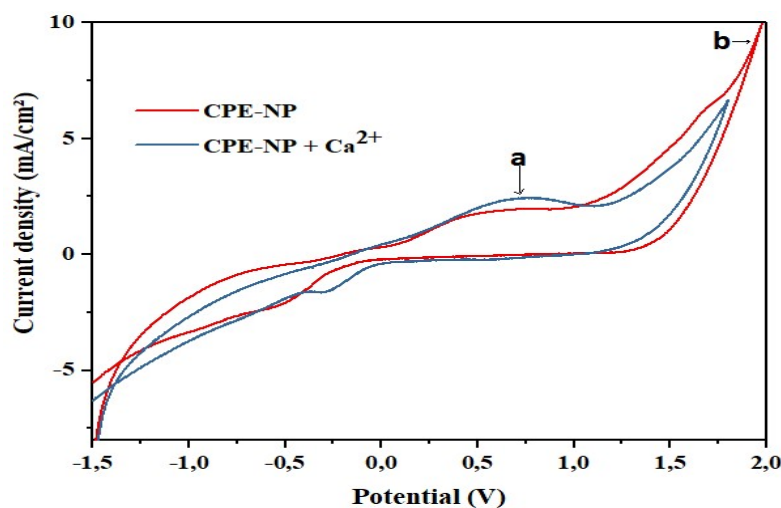


Figure 3: CV recorded in Na_2SO_4 , **a-** without and **b-** with Ca^{2+} ions, at NP-CPE, at a SR of 50 mV/s.

Fig. 4 shows the electrochemical impedance diagrams, recorded at the NP-CPE electrode surface, in Na_2SO_4 without (curve a) and with (curve b) defined Ca^{2+} ions concentration. The two curves have the shape of a half-loop, the diameter of which is reduced in Ca^{2+} ions presence (curve a), which means that their redox reaction was favoured by natural phosphate.

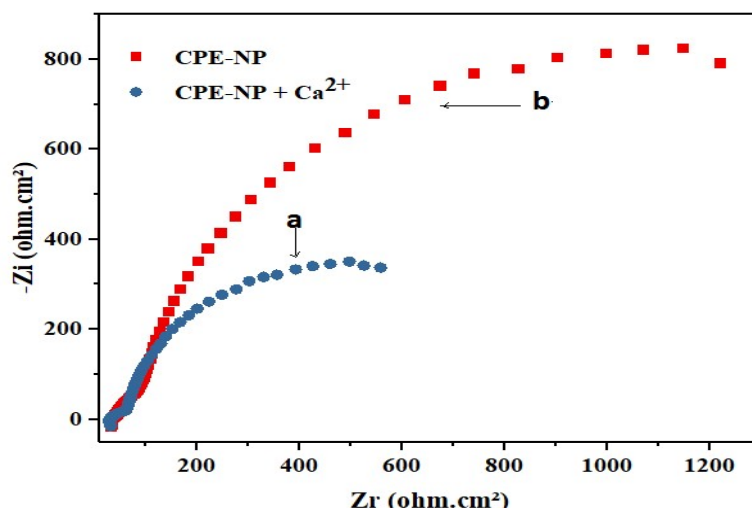


Figure 4: EIS recorded at NP-CPE in Na_2SO_4 solutions, **a-** without and **b-** with Ca^{2+} ions.

The effect of Ca^{2+} ions concentration on CV, recorded at the NP-CPE electrode surface, was studied (Fig. 5). It is seen an increase in Ca^{2+} ions that caused higher electric current densities, and the anodic peak displacement towards potential higher values. This suggests that the electrode surface contained an infinite number of active sites.

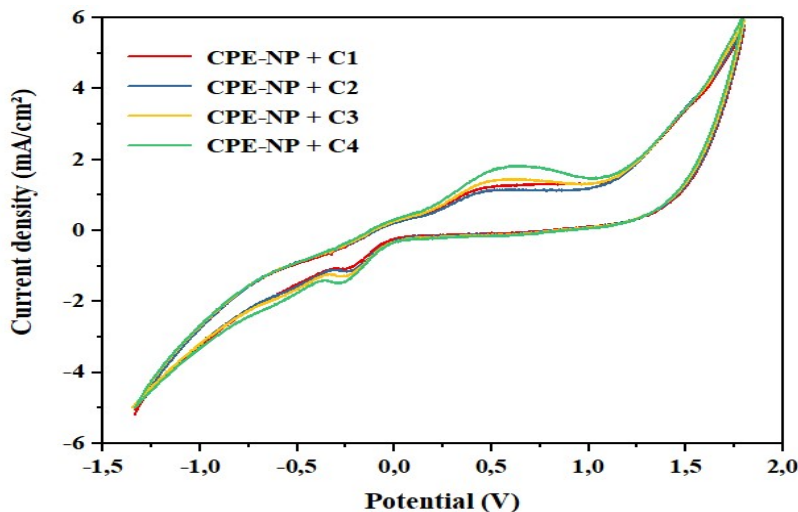


Figure 5: CV recorded at NP-CPE in a Na_2SO_4 solution with Ca^{2+} , at the SR of 50 mV/s.

SV chelation effect on Ca^{2+} ions

In this experiment, SV was introduced into the Na_2SO_4 medium with Ca^{2+} ions, and subsequently, CV were recorded on the NP-CPE surface (Fig. 6). Notably, SV addition to Na_2SO_4 with Ca^{2+} ions caused their redox peaks disappearance in the CV. This observation strongly suggests that SV effectively chelated Ca^{2+} ions.

Figs. 3(b) and 6(a) depict CV of the CPE-NP electrode with Ca^{2+} ions, under similar conditions. The apparent differences in the shapes of these CV may be due to variations in the experimental conditions or to the specific characteristics of the studied systems. The observed differences in CV between Figs. 6(a-b) suggest the possibility of effective Ca^{2+} ions chelation when SV was added, although the oxidation potential mentioned in Fig. 3 was approximately 0.7 V.

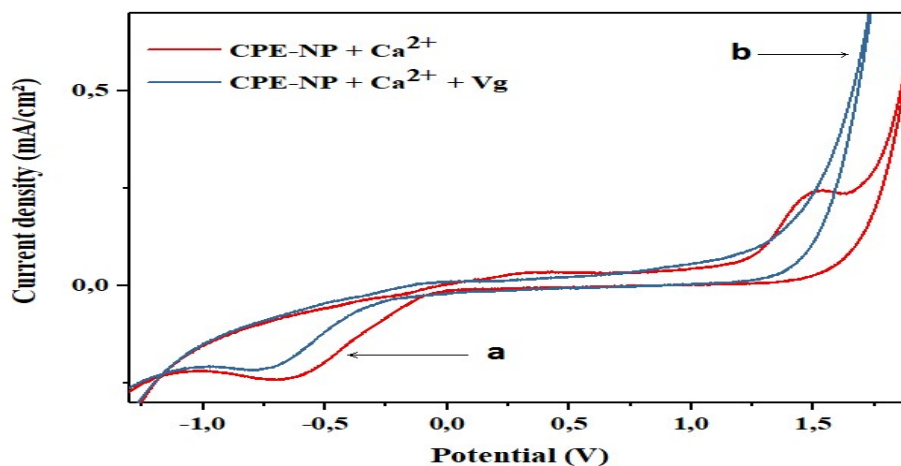


Figure 6: CV recorded in Na_2SO_4 solutions, **a-** with Ca^{2+} and **b-** with Ca^{2+} ions and Vg, at a SR of 50 mV/s.

SWV confirmed SV's effect on Ca^{2+} ions, showing distinct Ca^{2+} ions redox reaction peak (Fig. 7 (a)), which almost entirely disappeared with SV addition (Fig. 7 (b)).

The peak disappearance around 1.2 V in the CV with SV is indeed a notable observation. This phenomenon can be explained by the fact that the peak appearance at 1.2 V may be due to certain electrochemical reactions occurring in SV presence, which warrant further investigation. Indeed, oxidation potential in Fig. 3 was around 0.7 V, and the reduction potential was approximately -0.2 V.

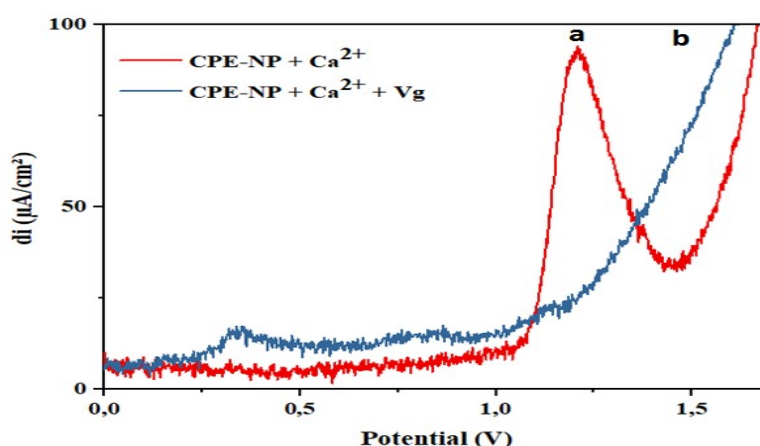


Figure 7: SWV recorded at NP-CPE in Na_2SO_4 solutions-, **a-** with Ca^{2+} and **b-** with Ca^{2+} ions and Vg.

Ca^{2+} ion chelation by the SV solution was also studied by EIS (Fig. 8). It is seen that, in SV presence, the half loop diameter (curve b), which corresponds to the electron transfer resistance, becomes greater, indicating Ca^{2+} ions disappearance.

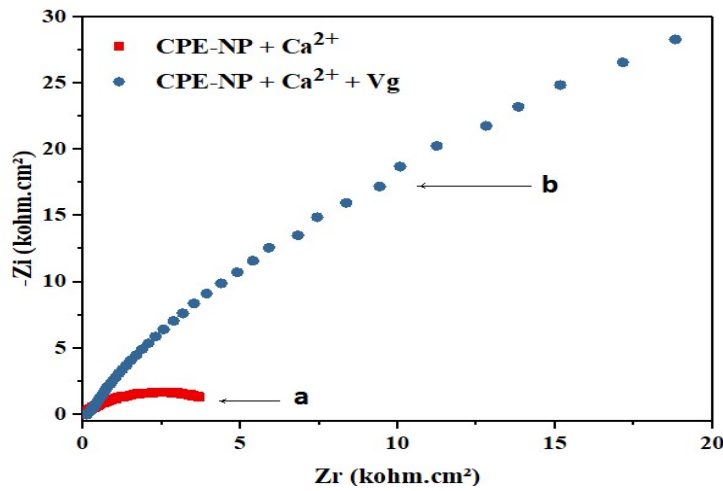


Figure 8: EIS recorded at NP-CPE in Na_2SO_4 solutions, **a-** with Ca^{2+} and **b-** with Ca^{2+} ions and Vg.

Fig. 9 shows the impact of varying SV amounts, represented as V1, V2, V3, and V4, which range from which range from low to high concentrations, on EIS diagrams. EIS data analysis reveals a notable trend: with higher SV concentrations, there was a corresponding increase in the electron transfer resistance.

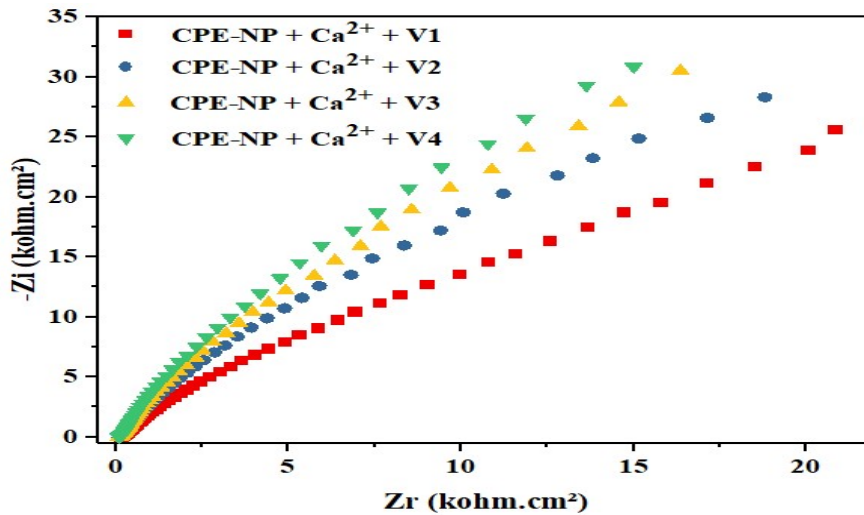


Figure 9: EIS recorded at NP-CPE in Na_2SO_4 solutions, **a-** with Ca^{2+} and **b-** with Ca^{2+} ions and Vg.

Conclusion

In this study, several significant milestones were achieved. Firstly, NPM-CPE was successfully developed, showcasing its exceptional efficiency in detecting

Ca²⁺ ions within Na₂SO₄ solutions. Additionally, electrochemical methods to explore SV chelation capabilities concerning Ca²⁺ ions were employed, revealing an impressive chelating strength by SV.

The primary goal outlined in the introduction, which aimed to establish an electrode for monitoring CaC₂O₄ solubility, and propose an instrument based on local materials for knowing CaC₂O₄ dissolution, has been effectively done through the methodologies employed in this study. While the primary focus centred on Ca²⁺ ions detection and chelation, these findings directly contribute to a deeper understanding of CaC₂O₄ dissolution. The electrochemical techniques have proficiently monitored Ca²⁺ ions behaviour, providing invaluable insights into their dissolution process.

Revisiting the scientific problem addressed in this study, the goal was to contribute to the understanding and potential treatment of conditions related to CaC₂O₄, particularly gout. The methodological approach in here presented, including CPE modification and Ca²⁺ ions electrochemical investigation, has proven to be highly effective in addressing this issue. By detecting and chelating Ca²⁺ ions, essential processes linked to CaC₂O₄ dissolution, a critical scientific concern within the realm of gout and related conditions, have been clarified.

In conclusion, this research not only established a robust electrochemical tool for Ca²⁺ ion detection, but also advanced the comprehension of CaC₂O₄ dissolution, a pivotal factor in gout-related conditions. The electrochemical methods and materials introduced in this study hold great promise for further advancements in the field, potentially paving the way for innovative treatments and interventions targeting gout and related disorders.

Authors' contributions

M. Bouha: conceptualization; experimental investigation; data analysis; writing - original draft preparation, review and editing. **M. Oubaouz:** conceptualization. **R. Maallah:** experimental investigation. **S. Zahid:** experimental investigation. **Y. Tahiri:** experimental investigation. **M. Oukbab:** conceptualization. **A. Zaroual:** data analysis. **S. El Qouatli:** data analysis. **M. Echajia:** data analysis; methodology; supervision. **A. Chtaini:** conceptualization; methodology; writing - original draft preparation, review and editing; supervision.

Abbreviations

Ca²⁺: calcium cation

CaC₂O₄: calcium oxalate

CPE: carbon paste electrode

CV: cyclic voltammetry

EIS: electrochemical impedance spectroscopy

NPM-CPE: natural phosphate-modified carbon paste electrode

SCE: saturated calomel electrode

SR: scan rate

SWV: square wave voltammetry

SV: sherry vinegar

References

1. Roddy E, Doherty M. Epidemiology of gout. *Arthritis Res Ther.* 2010;12:223. <https://doi.org/10.1186/ar3199>
2. Kuo CF, Grainge MJ, Zhang W et al. Global epidemiology of gout: prevalence, incidence and risk factors. *Nat Rev Rheumatol.* 2015;(11)11:649-662. <https://doi.org/10.1038/nrrheum.2015.91>
3. Chen-Xu M, Yokose C, Rai SK et al. Contemporary prevalence of gout and hyperuricemia in the United States and decadal trends: the National Health and Nutrition Examination Survey, 2007–2016. *Arthrit Rheumatol.* 2019;(71)6:991-999. <https://doi.org/10.1002/art.40807>
4. Schlesinger N. Treatment of acute gout. *Rheum Dis Clin.* 2014;(40)2:329-341. <https://doi.org/10.1016/j.rdc.2014.01.008>
5. Bleyer AJ, Hart TC. Genetic factors associated with gout and hyperuricemia. *Advances in chronic kidney disease.* 2006;(13)2:124-130. <https://doi.org/10.1053/j.ackd.2006.01.008>
6. Pascual E, Andrés M, Vázquez-mellado J et al. Severe gout: strategies and innovations for effective management. *Joint Bone Spine.* 2017;(84)5:541-546. <https://doi.org/10.1016/j.jbspin.2016.10.004>
7. Chen C-J, Hsieh M-C, Liao W-T et al. Allopurinol and the incidence of bladder cancer: a Taiwan national retrospective cohort study. *Euro J Cancer Prev.* 2016;25:216-23. <https://www.jstor.org/stable/48504587>
8. Shih H, Kao M, Tsai P et al. Long-term allopurinol use decreases the risk of prostate cancer in patients with gout: a population-based study. *Prost Canc Prostat Dis.* 2017;20:328-33. <https://doi.org/10.1038/pcan.2017.14>
9. Wang CY, Hayashida S, Pamukcu AM et al. Enhancing effect of allopurinol on the induction of bladder cancer in rats by N-[4-(5-nitro-2-furyl)-2-thiazolyl] formamide. *Canc Res.* 1976;36:1551-5. <https://pubmed.ncbi.nlm.nih.gov/1268818/>
10. Fukushima S, Hagiwara A, Ogiso T et al. Promoting effects of various chemicals in rat urinary bladder carcinogenesis initiated by N-nitroso-n-butyl-(4-hydroxybutyl) amine. *Food Chem Toxicol.* 1983;21:59-68. [https://doi.org/10.1016/0278-6915\(83\)90269-7](https://doi.org/10.1016/0278-6915(83)90269-7)
11. Ito N, Fukushima S, Shirai T et al. Effects of promoters on N-butyl-N-(4-hydroxybutyl) nitrosamine-induced urinary bladder carcinogenesis in the rat. *Environ Health Perspect.* 1983;50:61. <https://doi.org/10.1289/ehp.835061>
12. Valery, HG, Ngono TR, Saâdane H et al. Evaluation of Carbon Paste Electrodes Modified with Organic Molecules for the Analysis of Heavy Metals by Square Wave Voltammetry. *Pharmaceut Analyt Acta.* 2013;(4)271:2. <https://doi.org/10.4172/2153-2435.1000271>
13. Mohamed O, Imane S, Raja M et al. Zinc Modified Carbon Paste Anode for Microbial Fuel Cells. *J Xid Univ.* 2022;(16):11. <https://doi.org/10.37896/jxu16.11/058>