A new microconductometric sensor based on a PVC membrane including an o -COSAN ion-pair complex for the detection of caffeine

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Abstract

Caffeine is a central nervous system (CNS) stimulant and is the most routinely used drug in the world. It is present in coffee, tea, in soft drinks. It is responsible for bitterness in coffee and tea. A new microconductometric sensor for the detection of caffeine was designed, based on a PVC liquid membrane including a [*o*-COSAN]$^-$/caffeine ion-pair complex deposited on interdigitated electrodes. This caffeine sensor presents de dynamic range from 10^{-6} M to 10^{-1} M and a limit of detection of 0.3 µM. The sensor presents good reproducibility (RSD 3%) and repeatability (RSD 8%). The shelf-life time of the sensor was more than three months. The sensor is selective versus interfering components present in the different matrices (coke, tea, and coffee) and was used successfully for the detection of caffeine in these matrices.

Keywords: caffeine; [*o*-COSAN]$^-$/caffeine ion-pair complex; microconductometric sensor; liquid membrane;

1. Introduction

Caffeine (1,3,7-trimethylpurine-2,6-dione) (CF) is a purine alkaloid that is composed of two heterocyclic rings: a pyrimidinedione ring, and an imidazole ring. It is a white crystalline compound found in the seeds, fruits, nuts, and leaves of trees and plants native of Africa, East Asia, and South America. It is one of the substances responsible for the bitterness of tea and coffee [1]. CF is a central nervous system (CNS) stimulant, and is the most routinely used drug in the world, with 87% of Americans consuming caffeinated products ≥ 1 time/week, at an average of 165 ± 1 mg/day [2,3]. Among caffeinated products, coffee is

the most consumed (68%), followed by sodas (42%). While low to moderate doses of caffeine (≤ 400mg a day for healthy adults [4,5]) can be beneficial for enhancing cognitive function, higher doses can lead to cardiovascular symptoms, gastrointestinal problems, anxiety, insomnia, musculoskeletal symptoms, pulmonary symptoms, and other side effects [5-8]. Some have indicated that after a dose of around 1g per day, toxic symptoms begin to manifest, a dose of 2g per day requires hospitalization, while higher doses (typically 5g per day or more) could result in death [5,7], most commonly due to tachycardia, renal failure, ventricular fibrillation, and arrhythmia [8,9]. Subsequently, determining the concentration of caffeine is necessary to ensure safe caffeine consumption through quality control.

A variety of techniques have been used to date for CF detection, such as High-Performance Liquid Chromatography (HPLC), Gas Chromatography (GC), Liquid Chromatography-Mass Spectrometry (LC-MS), Thin Layer Chromatography (TLC), Enzyme-Linked Immunosorbent Assay (ELISA), Spectrophotometry, Capillary Electrophoresis (CE), and Biosensors [9-15]. However, there are also several problems with these techniques. Although they are efficient, LC-MS and GC can be expensive and require complicated equipment. Additionally, the portability of LC-MS and GC devices limits their usefulness in the field, particularly for industrial monitoring.

Electrochemical sensors were selected due to their low cost, easy operability, portability, and rapid response. Voltammetric detection, based on pulsed methods, of caffeine is the main way of detection, around fifteen papers are published each year about this topic. The oxidation process of caffeine molecule involves four electrons and four protons. The use of bare carbon electrodes with a wide range of polarizability is necessary. On bare boron-doped diamond (BDD) electrodes, presenting a large range of polarizability (2.8 V), the oxidation peak appears at 1.4 V vs Ag/AgCl [16]. Moreover, these electrodes present anti-fouling properties which allows their excellent reusability. Several works were carried out on this type of bare electrode [17,18]. A comparison between the electrochemical detection of caffeine on BDD and on screen-printed carbon electrodes (SPCE) was carried out [19], the detection limit obtained on BDD (0.4 mg/L) was lower than that obtained on SPCE (1.7 mg/mL) in the same conditions. To decrease the detection limits, the modification of electrodes with different types of nanomaterials was carried out. Chalcogenides such as SnSe [20], MoS_2 [21] were used and the obtained detection limits were respectively 6.5 nM, and 51 nM. Several metallic oxides were used such as 3D $ZnCo_2O_4$ [22], $Gd_2(MoO_4)_3$ [23], ZnO [24], TiO_2 [25], the obtained detection limits were respectively 11.4 nM, 4.1 nM, 150 nM, 3.3 µM. Some other compounds were used for the sensitive detection of caffeine: phenantroline Cu(II) [26], Cu-MOF [27] and porphyrin [28] leading to respective detection limits 10.2 nM, 19 nM and 14.06 µM. A potentiometric sensors was also designed for the

caffeine detection. PVC membrane including tetradecylammonium bromide and dihydroxybenzoic acid was the recognition part of potentiometric sensor working in comparison with a reference solution containing tartaric acid [1]. The detection limit of caffeine was found to be 300 µM.

Several potentiometric sensors based on PVC membrane were designed for sulphapyridine [29], amphetamine [30], aminoacids [31] including the θ-shaped molecule [3,3'-Co(1,2-$C_2B_9H_{11})_2]^-$ ([*o*-COSAN]$^-$). This negatively charged molecule was able to form ion-pair complexes with positively charged molecules, such as molecules including any type of amine group. These complexes are highly insoluble in water and very soluble in many organic solvents. Detection limits were in the range of 10^{-6} M. Caffeine can be protonated on N9 in acidic media, with a pK of 0.18 [32]. It could then be a candidate for the formation of an ion-pair complex with [*o*-COSAN]$^-$ and its inclusion in a PVC membrane. This work presents for the first time, this synthesized [*o*-COSAN]$^-$/caffeine ion-pair complex (Fig. 1).

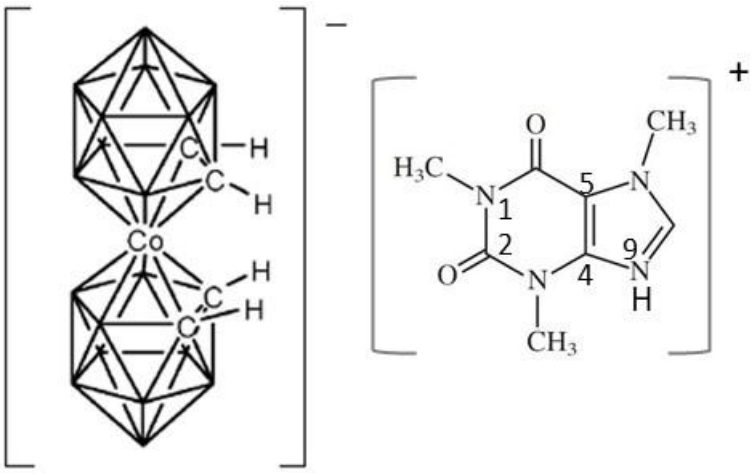

Figure 1. Molecular structure of [*o*-COSAN]$^-$/caffeine ion-pair complex

In contrast with voltammetric and potentiometric sensors, conductometric sensors do not require any reference electrode, which simplifies the fabrication process. Conductometric microtransducers offer several other advantages: (1) Thin-film interdigitated electrodes are suitable for miniaturization and large-scale production using inexpensive technology such as the printed circuit technology; (2) differential mode measurements allow cancellation of many interferences, (3) the driving voltage is sufficiently low (few mV) to have a low power consumption [33]. This type of transducer was used for the sensitive detection of cationic surfactants with a PVC membrane including sodium tetraphenylborate as a carrier [34].

A PVC membrane including the ion-pair complex with [*o*-COSAN]$^-$/caffeine was drop-casted on interdigitated electrodes in to obtain for the first time a caffeine microconductometric

sensor. After the determination of its analytical performance, the caffeine microconductometric sensor was validated for the detection of caffeine in some soft drinks.

2. Experimental

2.1. Chemicals

Caffeine, quinine, hydrochloric acid (37%), phosphate buffered saline (PBS), polyvinylchloride (PVC), bis(2-ethylhexyl)sebacate were provided by Merck (Saint-Quentin-Fallavier, France). [*o*-COSAN]$^-$ was purchased from Katchem Spol.sro (Praha, Czech Republic).

Ultra-pure water (UPW) (resistivity > 18 MOhm.com) was produced by a Millipore System.

2.2. Microconductometric chip

For reasons of manufacturing cost, we turned to printed circuit technology which would not provide as fine a resolution as microelectronics technology [35] but which was worth testing as a low-cost sensor. The electrodes were made of copper (approximately 42 µm) covered with a layer of Nickel (3 to 6 µm) and then with a layer of Gold (50 to 120 nm). The interdigitated gold electrodes, deposited on a PCB support, have widths of 100 µm and interelectrode distances of 100 µm (Fig. 2). The diameter of each sensor (one pair of interdigitated electrodes) was 6 mm. On each chip, there is a working sensor and a reference sensor.

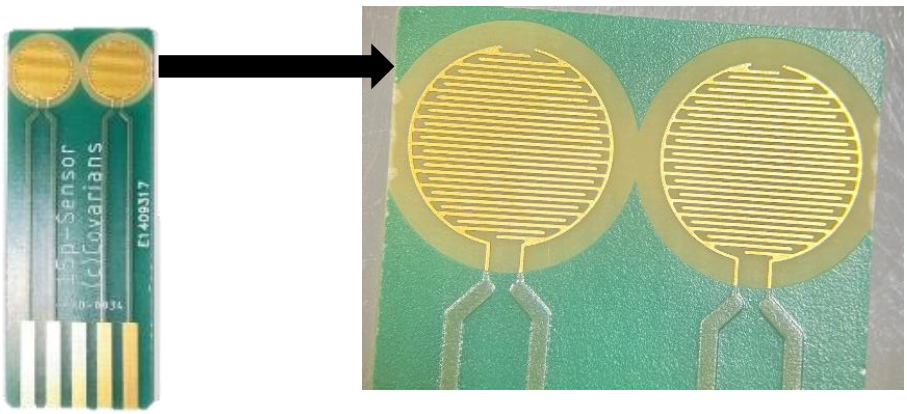

Figure 2. Interdigitated electrodes fabricated by the printed circuit technology: working sensor and reference sensor

2.3 Synthesis of [*o*-COSAN]$^-$/caffeine ion-pair complex

Caffeine (40 mg, 0.20 mmol) was dissolved in diluted hydrochloric acid (~25 mL). After agitating and obtaining a clear solution, Na [3,30-Co(1,2-C2B9H11)2] (0.20 mmol) in 10 mL

of diluted hydrochloric acid (3 M) was added. Almost instantly an orange precipitate appeared. The mixture was stirred for 5 min and left to rest for an additional period of 15 min. The orange solid was isolated through a Buchner funnel. The resulting solid was rinsed first with 10 mL of diluted hydrochloric acid (0.1 M) and then 2 x10 mL of deionized water and then carefully removed and placed in a round bottom flask with a ground glass joint for active 0.1–0.01 mm vacuum at room temperature. The solid was collected after a constant mass to remove all kinds of solvents. The solid was then ready for the membrane preparation.

For the characterization of the [*o*-COSAN]$^-$/caffeine ion pair complex, FTIR spectrum was recorded on at room temperature using a Nicolet Continuum microscope coupled with Nexus infrared spectroscopy in specular reflectance mode equipped with an MCT detector. Recordings were obtained with a resolution of 4 cm^{-1}, a spectral width between 690 and 4000 cm^{-1} and signal processing through Happgenzel apodization (256 scans).

2.4 Preparation of the caffeine microconductometric sensor

The liquid membrane was prepared as follows [30]. 43 mg of PVC were dissolved by stirring in 1.5 mL of tetrahydrofuran (THF) until a viscous but clear solution was obtained. Then, 10 mg of [*o*-COSAN]$^-$/caffeine ion-pair complex and 90 mg of plasticizer (bis(2-ethylhexyl)sebacate) were added. 2 µL of this liquid was deposited on the working sensor. The liquid membrane for the reference sensor was prepared by dissolving 13 mg of PVC and 90 mg of plasticizer in 1.5 mL of tetrahydrofuran, without ion-pair complex and 2 µL were drop-casted on the reference sensor. The caffeine sensors were stored at room temperature for future use.

2.5. Microconductometric measurements

Conductometric detection was achieved by applying to each pair of interdigitated electrodes (working sensor and reference sensor) a small-amplitude sinusoidal voltage (10 mV peak-to-peak at 0 V) at a 10 kHz frequency generated by "VigiZMeter" conductometer (Covarians (91190 Gif-sur-Yvette, France)). The conductance response, in the differential mode, was recorded as a function of time. Caffeine was injected in a 10^{-3} M PBS buffer, the pH value being adjusted at 2.5 by the addition of drops of a diluted HCl solution. The response time (**tRes**) describes the time necessary to reach 90% of the total change of conductance.

3. Results and Discussion

3.1. FTIR characterization of the [*o*-COSAN]$^-$/caffeine ion pair complex

The FTIR spectrum is presented in Fig. 3. The FTIR spectrum of [*o*-COSAN]$^-$/caffeine displays a strong and characteristic ν(B-H) frequency in the infrared range 2556 cm^{-1} in which no other frequencies of organic compounds appear. The FTIR spectrum displays the ν (O-H) stretching vibration at 3617 cm^{-1}; ν(N-H - caffeine; O-H) at 3411-3617 cm^{-1}; ν(C-H) at 3050 cm^{-1}; ν(C=O amide - caffeine; C=C; C=C aromatic - caffeine; N-H - caffeine) at 1451-1663cm^{-1}; ν(C-H) at 1325-1451 cm^{-1}; ν(C-O; CC; C-N - caffeine) at 1019-1325 cm^{-1}; ν(C-H; C=C) at 723-983 cm^{-1}.

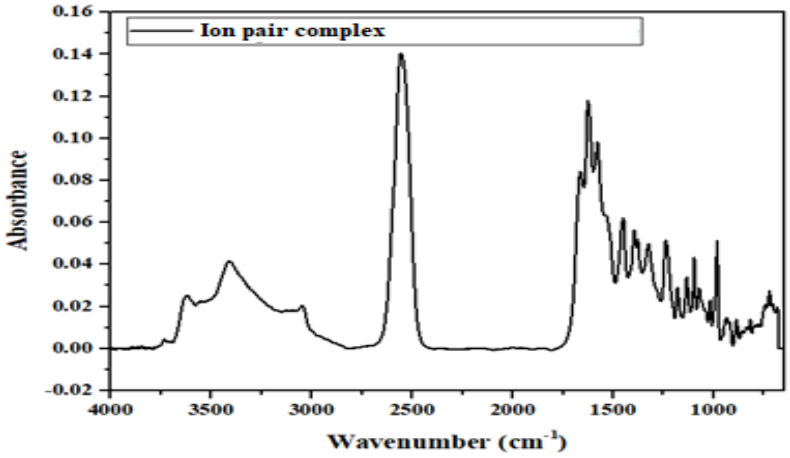

Figure 3. FTIR spectrum of the [*o*-COSAN]$^-$/caffeine ion pair complex

3.2. Analytical performance of the caffeine sensor

The conductance response of the caffeine sensor as a function of time, when increasing concentrations of caffeine are injected, is presented in Fig. 4. When the concentrations of caffeine in contact with the sensor increases, the conductivity of the liquid membrane increases. This type of response was observed only when the pH value was low enough (pH = 2.5). At this pH, the exchange between the protonated form of caffeine can occur with the [*o*-COSAN]$^-$/caffeine ion pair complex in the membrane. When the pH value becomes 2 or lower, no variation of the conductivity is observed, due to a two-high value of ionic strength in the solution. This increase in conductivity when the concentration of the specific analyte increases was also observed with microconductometric transducers modified with a plasticized PVC membrane including a specific complex for the detection of ionic species (NH_4^+ [36] and K^+ [37]), and of a cationic surfactant [34], due to the exchange of the charged specie with the complex in the membrane.

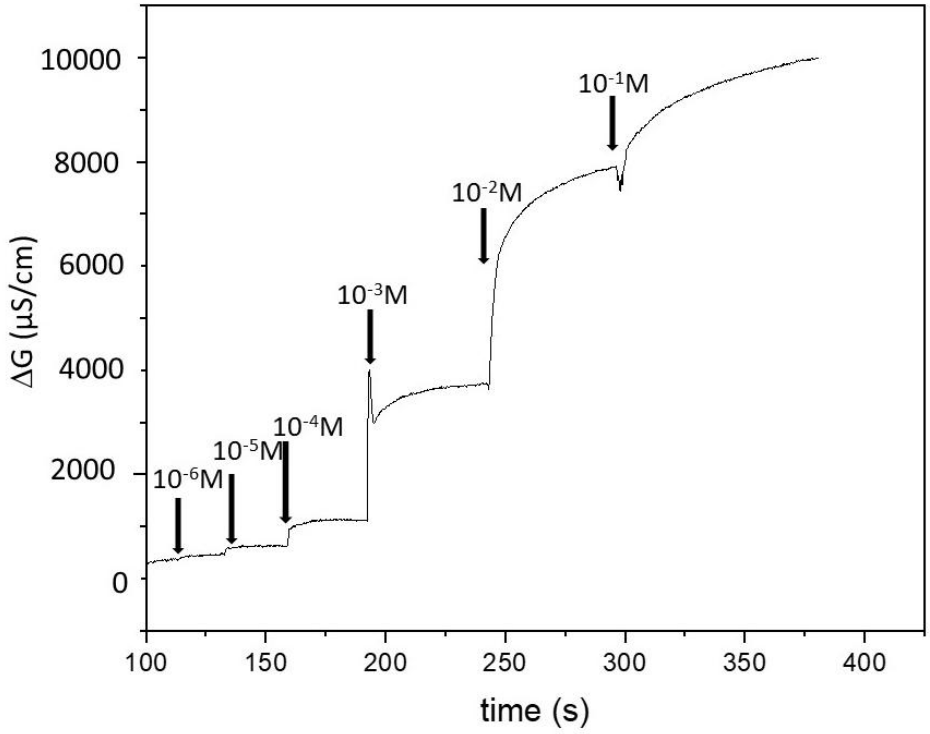

Figure 4. Conductance response of the caffeine microsensor as a function of time. Measuring conditions: differential mode, 10^{-3} M PBS buffer, pH 2.5

The response time of the caffeine microsensor varies from 10 s to 50 s from lower concentrations to higher concentrations. The saturation appears at 10^{-1} M.

The calibration curve of the caffeine microsensor is presented in Fig. 5. The slope of the curve DG versus log [caffeine] is 3280 μS/cm, in the high concentration range (10^{-4}M – 10^{-1}M) and 353 μS/cm for the lower concentration range (10^{-6}M – 10^{-4}M). The limit of detection calculated from the formula 3s/S (where s is the RSD on the background and S is the sensitivity) is equal to 0.3 μM. The relative standard deviation for the same sensor was 3%, the measurements being repeated three times. The sensor retained its detection sensitivity for three months when kept dry in a fridge at 4°C between measurements. The inter-sensor reproducibility obtained for five sensors is 8%. When comparing the analytical performance of this conductometric sensor to that of the previously published sensors, the detection limit is lower than that of the potentiometric sensor [1] and of the voltammetric sensor on bare BDD [19]. Nevertheless, the voltammetric detection of caffeine in the presence of nanomaterials leads to a lower detection limit, in the range of nM [22-27].

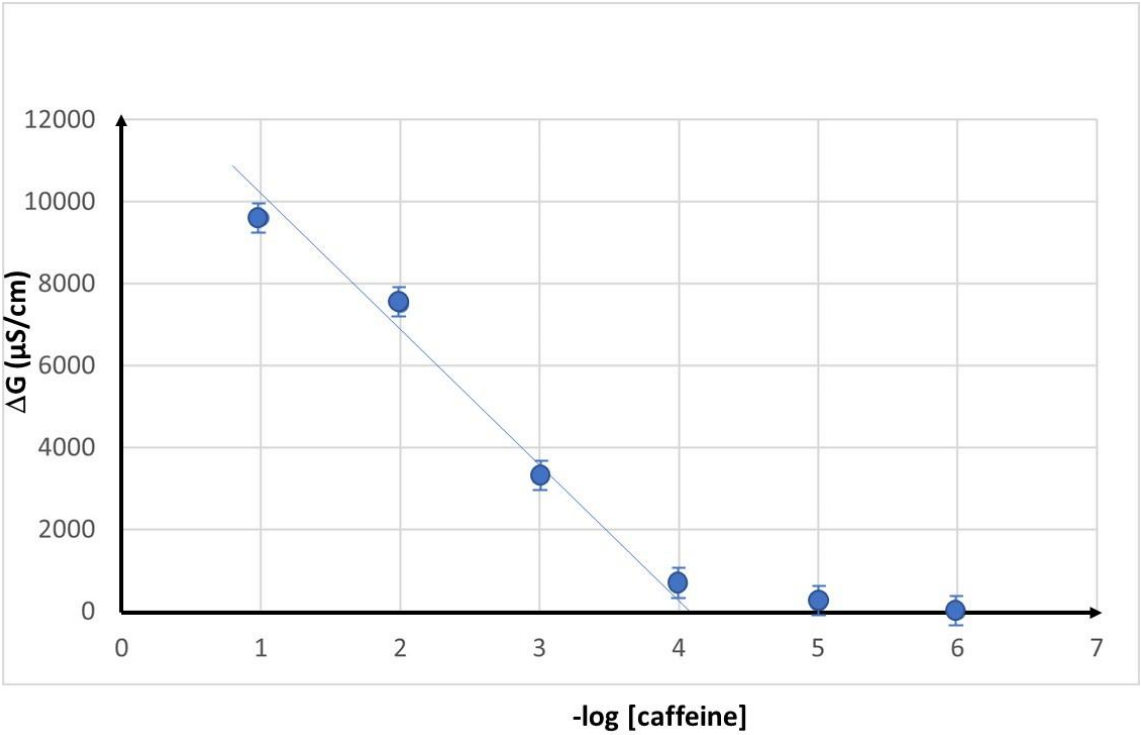

Figure 5. Calibration curve of the caffeine microsensor. Measuring conditions : differential mode, 10^{-3} M PBS buffer, pH 2.5

The specificity of detection was verified versus several molecules contained in coke (caffeic acid, citral, limonene, vanillin), in coffee (quinine, caffeic acid, quinic acid), and in tea (quinine, caffeic acid, quinic acid); among them, caffeine and quinine are responsible for bitterness [38] (Fig. 6). The sensitivity for quinine was 11.6 times lower than that of caffeine. For the other molecules, their sensitivity was 3 times (caffeic acid and quinic acid) and 5 times lower (citral, limonene, and vanillin).

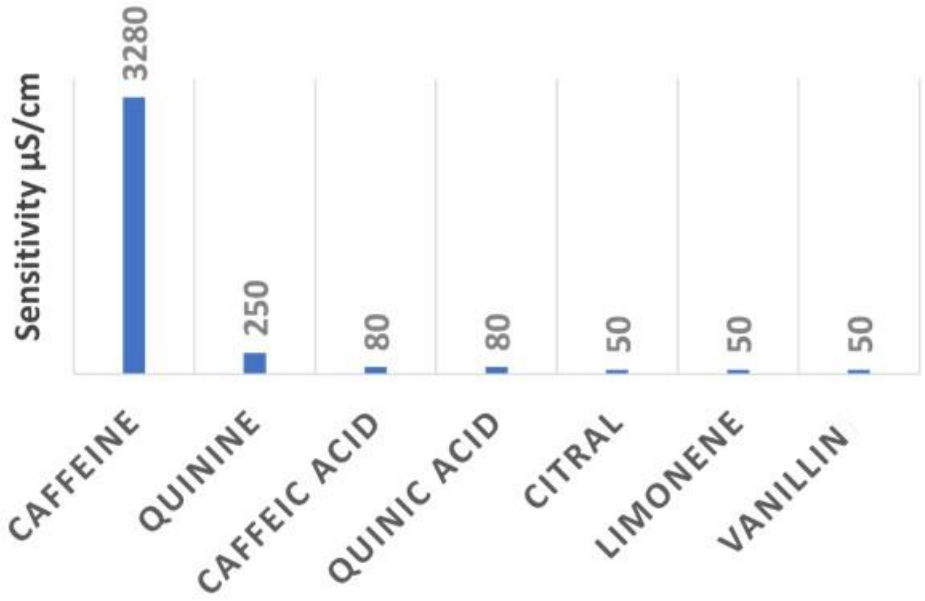

Figure 6. Comparison of the sensitivity of detection of caffeine and of quinine, caffeic acid, quinic acid, citral, limonene, vanilline. Measuring conditions : differential mode, 10^{-3} M PBS buffer, pH 2.5

The detection of caffeine in a soft drink (Coke), in Ceylan black tea, in arabica coffee and in robusta coffee was carried out using this microconductometric sensor, through the standard addition method. The obtained results are reported in Figure 7. For Coke, the curve is shifted to a value of 3300 µS/cm from that obtained in the buffer, showing that the initial concentration of the soft drink should be 0.40±0.02 mM. The given value for the provider was 8 mg for 100 g corresponding to 0.41 mM. For Ceylan black tea, the curve is shifted by a value of 3777 µS/cm, corresponding to 1.13±0.04 mM. The given value was 220 mg/L (2 spoons in 300 mL), corresponding to 1.1 mM. For arabica coffee, the curve is shifted by a value of 4526 µS/cm, corresponding to 2.02±0.08 mM. The given value was 394 mg/L (4 g in 150 mL), corresponding to 2.0 mM. For robusta coffee, the curve is shifted by a value of 5578 µS/cm, corresponding to 3.94±0.12 mM. The given value was 766 mg/L (4 g in 150 mL), corresponding to 3.9 mM.

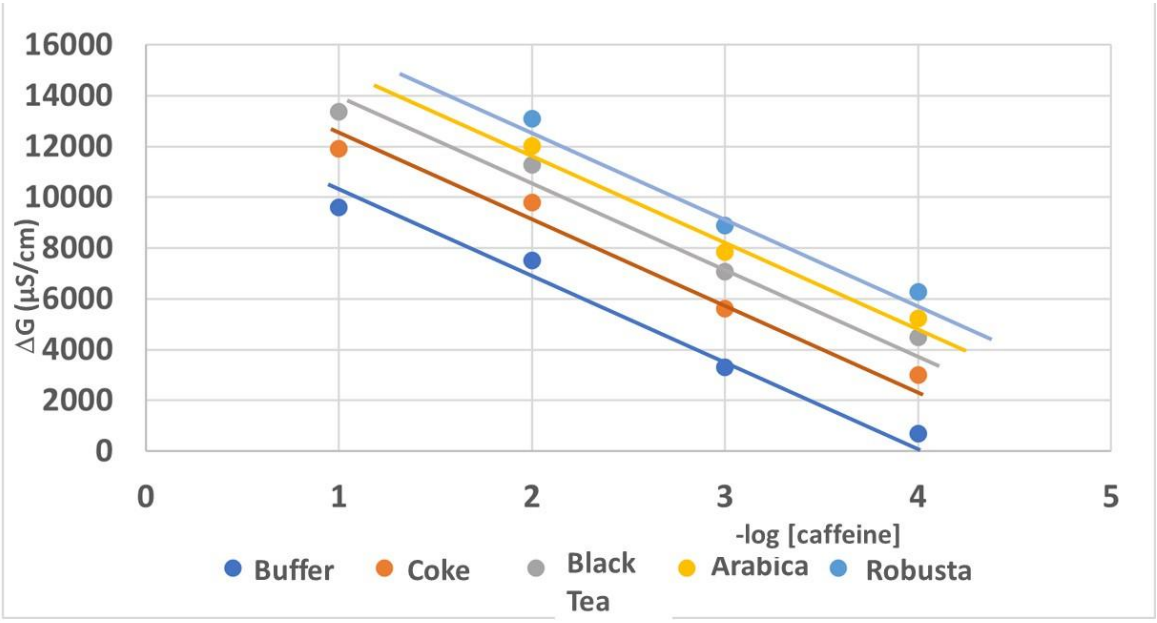

Figure 7. Calibration curves in 10^{-3} M PBS buffer, pH 2.5 (dark blue), in Coke (orange), in Ceylan black tea (grey), in arabica coffee (yellow), and in robusta coffee (light blue), in the differential measurement mode.

4. Conclusion

A new microconductometric sensor for the detection of caffeine was designed, based on a liquid PVC membrane, including a [*o*-COSAN]$^-$/caffeine ion pair complex. The response time of the sensor was from 10 s to 50 s for lower (< 10^{-4} M) to higher concentrations (until 10^{-2}

M). The obtained detection limit was 0.3 µM, which is low compared to other electrochemical sensors such as potentiometric or voltammetric on bare BDD electrodes. The sensor was shown to be selective versus other molecules present in Coke, tea, and coffee and was successfully used for the detection of caffeine in these drinks. A long shelf-life time of three months was observed for this sensor. This sensor could be used for the routine detection of caffeine in drinks or in pharmaceutical drugs. The membrane-based [*o*-COSAN]$^-$/caffeine ion pair complex could be also adapted to another type of transducer such as potentiometric (ISEs or ISFETs) for the detection of caffeine or the detection of bitterness in electronic tongues.

Acknowledgements

The authors thank C. Viñas and Dr F. Teixidor for fruitful discussions.

The authors acknowledge the financial support of the EU H2020 WIDESPREAD Program entitled Bionanosens grant agreement # 951887. High Ministry of Education and Research in Tunisia is acknowledged for financial support through POLYAM project. CNRS is acknowledged for the IRP NARES. Campus France is acknowledged for its financial support through PHC Maghreb EMBISALIM.

References

[1] J. Yoshimatsu, K. Toko, Y. Tahara, M. Ishida, M. Habara, H. Ikezaki, H. Kojima, S. Ikegami, M. Yoshida, T. Uchida, *Sensors*, **2020**, *20*, 3455. https://doi.org/10.3390/s20123455.

[2] J.J. Knapik, R.A. Steelman, D.W. Trone, E.K. Farina, H.R. Lieberman, *Nutr. J.,* **2022**, *21*, 22. https://doi.org/10.1186/s12937-022-00774-0

[3] D.C. Mitchell, C.A. Knight, C. A., J. Hockenberry, R. Teplansky, T.J. Hartman, *FCT,* **2014**, *63*, 136-142. https://doi.org/10.1016/j.fct.2013.10.042

[4] C. Willson, *Toxicol. Rep*., **2018**, *5*, 1140-1152. https://doi.org/10.1016/j.toxrep.2018.11.002

[5] S. Kerrigan, T. Lindsey, *Forensic Sci. Int*., **2005**, *153*, 67-69. https://doi.org/10.1016/j.forsciint.2005.04.016

[6] P. Banerjee, Z. Ali, B. Levine, D.R. Fowler, *J. Forensic Sci,* **2014**, *59*, 865-868. https://doi.org/10.1111/1556-4029.12387

[7] G. Bioh, M.M. Gallagher, U. Prasad, *BMJ Case Reports*, **2013**, *2013*. http://dx.doi.org/10.1136/bcr-2012-007454

[8] S. Cappelletti, D. Piacentino, V. Fineschi, P. Frati, L. Cipolloni, M. Aromatario. *Nutrients*, **2018**, *10*, 611. https://doi.org/ 10.3390/nu10050611

[9] S.H. Ashoor, G.J. Seperich, W.C. Monte, J. Welty, *J. Assoc. Off. Anal. Chem*. **1983**, *66*, 606-609. https://doi.org/10.1093/jaoac/66.3.606

[10] T. Hirai, H. Kondo, *Analytical Sciences*, **1985**, *1*, 191-194. https://doi.org/10.2116/analsci.1.191

[11] D. Perrone, C. Marino Donangelo, A. Farah, *Food Chem.* **2008**, *110*, 1030-1035. https://doi.org/10.1016/j.foodchem.2008.03.012

[12] C. Palacios, M.L.F. Salatino, A. Salatino, *World J. Chem. Educ.*, **2017**, *5*, 148-152. https://doi.org/ 10.12691/wjce-5-5-1

[13] T. Ohmichi, T. Kasai, M. Shinomoto, J. Matsuura, T. Koizumi, F. Kitani-Morii, H. Tatebe, H. Sasaki, T. Mizuno, T. Tokuda, *Front. Neurol*. **2020**, *11*, 580127. https://doi.org/10.3389/fneur.2020.580127

[14] S.A. Bhawani, S.S. Fong, M.N.M. Ibrahim, *Int. J. Anal. Chem*. **2015**, *2015*, 170239. https://doi.org/10.1155/2015/170239

[15] E.D. Conte, E.F. Barry, H. Rubinstein. *J. Chem. Educ.* **1996**,*73*, 1169. https://doi.org/10.1021/ed073p1169

[16] L. Svorc, *Int. J. Electrochem. Sci.* **2013**, *8*, 5755-5773. https://doi.org/10.1016/S1452-3981(23)14720-1

[17] O. Sarakhman, A. Benkova, L. Svorc, *Microchem. J.*, **2022**, *175*, 107132. https://doi.org/10.1016/j.microc.2021.107132

[18] A. Wong, A. M. Santos, M.H.A. Feitosa, O. Fatibello-Filho, F.C. Moraes, M.D.P.T. Sotomayor, *Biosensors* **2023**, *13*, 690. https://doi.org/10.3390/bios13070690

[19] K. Cortes, J.J. Trivino, V. Arancibia, *Electroanalysis*, **2023**, *35*, e202200484. https://doi.org/10.1002/elan.202200484

[20] E. Murugan and K. Kumar, *ACS Omega* **2022**, *7*, 35486−35495. https://doi.org/10.1021/acsomega.1c07306

[21] E. Murugan, A. Dhamodharan, *Diam. Relat. Mater.* **2022**, *128*, 109268. https://doi.org/10.1016/j.diamond.2022.109268

[22] A.J. Jesu Amalraj, N.M. Umesh, S.F. Wang, *J. Ind. Eng. Chem.* **2022**, *106*, 205–213. https://doi.org/10.1016/j.jiec.2021.10.026

[23] G. Singh, A. Kushwaha, M. Sharma, *Mater. Today Commun.* **2022**, *31*, 103390. https://doi.org/10.1016/j.mtcomm.2022.103390

[24] A.M. Madhusudhana, K.N.S. Mohana, M.B. Hegde, N.K. Swamy, S. A. Shivamurthy, *Diam. Relat. Mater.* **2022**, *130*, 109531. https://doi.org/10.1016/j.diamond.2022.109531

[25] A. Nema, M. Bano, M. Rai, K. Shrivastava, S. S. Dangi, F. Khan, *ChemistrySelect* **2023**, *8*, e202204572. https://doi.org/10.1002/slct.202204572

[26] A. Wagnew, A. Kassa, A. Abebe, T. Asmellash, Y. Beyene, A. Tesfaye, M. Amare, *Arab. J. Chem*. **2022**, *15*, 103458. https://doi.org/10.1016/j.arabjc.2021.103458

[27] V. Saravanakumar, V. Rajagopal, M. Kathiresan, V. Suryanarayanan, S. Anandan, K.C. Ho, *J. Taiwan Inst. Chem. Eng.* 2022, 133, 104248. https://doi.org/10.1016/j.jtice.2022.104248

[28] U. Güzel, G. Can, Y. T. Büyüksünetçi, O. Hakli, G. Oylumluoglu, Ü. Anik, *Mater. Chem. Phys* 2023, 307, 128129. https://doi.org/10.1016/j.matchemphys.2023.128129

[29] A. Saini, I. Fuentes, C. Viñas, N. Zine, J. Bausells, A. Errachid, F. Teixidor, *J. Organomet. Chem.* **2019**, *893*, 32–38. https://doi.org/10.1016/j.jorganchem.2019.04.030

[30] J. Gallardo-Gonzalez, A. Saini, A. Baraket, S. Boudjaoui, A. Alcácer, A. Streklas, F. Teixidor, N. Zine, J. Bausells, A. Errachid, *Sens. Actuators B Chem.* **2018**, *266*, 823–829. https://doi.org/10.1016/j.snb.2018.04.001

[31] A.I. Stoica, C. Viñas, F. Teixidor, *Chem. Commun*. **2009**, 4988. https://doi.org/10.1039/b910645f

[32] R.L. Benoit, M. Frechette, Can. J. Chem. **1985**, *63*, 3053-3056. https://doi.org/10.1139/v85-506

[33] N. Jaffrezic-Renault, S. Dzyadevych, *Sensors* **2008***, 8*, 2569-2588. https://doi.org/10.3390/s8042569

[34] M. Hnaien, S. Dzyadevych, F. Lagarde, N. Jaffrezic-Renault, *Electroanalysis* **2012**, *24*, 1441 – 1445. https://doi.org/10.1002/elan.201200055

[35] A. Madaci, G. Raffin, M. Hangouet, C. Pages, C. Jose, M. Martin, H. Ferkous, A. Bouzid, J. Bausells, A. Alcacer, A. Errachid, N. Jaffrezic-Renault, J. Mater. Sci.: Mater. Electron. 2021, 32, 17752-17763. https://doi.org/10.1007/s10854-021-06311-9

[36] B. Khadro, P. Namour, F. Bessueille, D. Leonard, N. Jaffrezic-Renault, *Int. J. Environ. Anal. Chem*. **2009**, *89*, 11-19. https://doi.org/10.1080/03067310802339785

[37] M. Braiek, M.A. Djebbi, J.F. Châteaux, N. Jaffrezic-Renault, *Sens. Actuators B Chem.* **2016**, *235,* 27-32. http://dx.doi.org/10.1016/j.snb.2016.05.050

[38] D.R. Reed, G. Zhu, P.A. Breslin, F.F. Duke, A.K. Henders, M.J. Campbell, G.W. Montgomery, S.E. Medland, N.G. Martin, M.J. Wright, *Hum. Mol. Genet.* 2010, 19, 4278-85. https://doi.org/10.1093/hmg/ddq324.