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A phenyl glycinol appended calix[4]arene film for chiral detection of ascorbic acid on gold surface



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derivative coated QCM sensor.

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ARTICLE INFO	A B S T R A C T				
Keywords:	This paper describes the synthesis of new chiral calix [4]arene derivative having (R)-2-phenylglycinol moiety				
Ascorbic acid	(compound 6), and its chiral recognition studies for ascorbic acid (AA) enantiomers by using Quartz Crystal				
Calixarene	Microbalance (OCM). Initial experiments indicated that the outstanding selective chiral recognition (a) was				
Chiral detection	observed as 2.61 for <i>i</i> -enantioner of AA. The sensitivity (S) and the limit of detection (LOD) values for L-AA were				
Quartz crystal microbalance sensor	calculated as 0.0226 Hz/µM and 0.63 µM, respectively. Furthermore, the sorption behavior and mechanism of				
Sensing	AA onto compound 6 film were evaluated and the sorption data exhibited a good correlation with the Freundlich				
	isotherm models. The maximum uptake of L-AA by the sensor was found as 5895.76 mg/g. In conclusion, chiral				
	recognition of AA enantiomers as real-time, sensitive, selective and effective was performed by a calixarene				

1. Introduction

Ascorbic acid (AA) is an indispensable component in terms of teeth, bone and skin health. Also, it is a carbohydrate-like chemical substance that participates in metabolic functions such as absorption of iron, collagen synthesis, and maintenance of the structure of blood vessels, the formation of some amino acids, hormone synthesis and secretion of the adrenal glands. Ascorbic acid has two isomers which are called *L*ascorbic acid and *p*-ascorbic acid. Although *p*-isomer is in an inactive form, the *L*-isomer is in a biologically active form and it also is known as vitamin C. Chiral recognition of biomolecules and drugs such as AA is an essential phenomenon for various areas of chemistry and life sciences. Therefore, designing efficient analytical methods is an essential task for sufficient sensitive and selective recognition of AA enantiomers. For the determination of AA, several methods like chromatographic [1], spectroscopic [2], electrochemical [3] have been developed and used. However, this kind of methods may have some disadvantages such as over time-consuming, expensive investment cost and analysis, and qualified staff requirement. In recent years, the sensor devices and methods which are acoustic systems have been widely used for investigation of sensor-analyte interaction in sensor applications [4]. Quartz Crystal Microbalance (QCM) system, which is one of the acoustic sensor systems, is based on piezoelectric and its usage is gradually increasing due to easy, rapid and cheap detection of the analyte. Additionally, it allows detecting a mass change even at a nanogram level by interactions between analyte and sensing material in both dry and aqueous conditions. Advantages of the QCM technique are high sensitivity and selectivity for the sensing of biologic analytes such as carbohydrates, antibiotics, bacteria, and DNA [5–8].

In the literature, some macromolecules, polymers, and nanoparticles have been widely used for the determination of biological molecules [9–11]. Among macromolecules, calixarenes, which are organic macromolecule having a cyclic structure by phenolic units are interconnected each other and can be designed with various functional groups easily and have excellent interaction ability [12]. These macromolecules which are conical shaped consist of upper and lower rims and, an annulus. Calixarenes as the promising materials have received great attention for the sensor applications due to their outstanding sensing properties [13–15]. In past recent years, many chiral calixarenes which were functionalized with chiral residues at either the lower or upper rim have been used in past recent years as chiral receptors or catalysts [16–23].

To best of our knowledge, using the calixarenes as sensor materials for the chiral recognition of AA enantiomers by QCM system has never been encountered in current literature. Therefore, in this study, we reported a simple and quick chiral discrimination strategy for AA enantiomers (Fig. 1) using QCM sensor which is modified the new chiral calix [4]arene building block bearing chiral phenyl glycinol moiety on

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Fig. 1. Used chiral ascorbic acid (AA) derivatives in the current study.

its lower rim and also thiol moiety on its upper rim (compound **6**) (Scheme 1). The chiral calix [4]arene film on QCM gold surface exhibited good and more than doubled selectivity towards *L*-AA. Significantly, the chiral discrimination factor (α) [24] of the sensor was specified by the evaluation of sensor response [25]. Accordingly, the limit of detection (*LOD*) [26] and sensitivity (*S*) [27] of the sensor were calculated from the analyte concentration studies to elucidate the sensing property of the sensor. Langmuir and Freundlich isotherm models that were also evaluated to fit the experimental data indicated the sorption phenomena of AA enantiomers by the sensor. Furthermore, the reproducibility of chiral calix [4]arene film on QCM gold surface was also studied.

2. Materials and methods

2.1. Reagents and instrumentations

Melting points were measured on a Stuart-SMP3 melting point apparatus. NMR spectra were taken on a Varian 400 MHz NMR spectrometer. FTIR spectra were recorded on a PerkinElmer 100 FTIR spectrometer. Elemental analyses were performed on a Leco CHNS-932 analyzer. Analytical TLC was carried out using precoated silica gel plates (SiO₂ Merck F_{254}). All reagents used in the experiments were of standard analytical grade from Merck, Sigma-Aldrich, Fluka and used without further purification.

A time-resolved QCM 200 system which is 5-MHz AT-Cut quartz crystals (1 inch) with gold electrodes on both sides were commercially available and purchased from SRS (California, USA) to measure the frequency change of quartz crystals between gold electrodes. The QCM crystals were ultrasonically cleaned using an Isolab ultrasonic bath. The QCM sensor surface which was modified with chiral calix [4]arene was characterized by an NT-MDT atomic force microscope (AFM, NTEGRA Spectra, Russia) and contact angle instrument (DSA 25, Krüss, Germany). We constructed the flow system with a peristaltic pump (An ISM940E from Ismatech, Wertheim, Germany) to transfer the solutions of AA on the sensor surface. The sensing experiments were performed in a glove box unit (Labconco-5220120, Kansas City, USA).

2.2. Synthesis

Compounds 1-4 were prepared according to literature methods [28–31]. Other calix [4]arene compounds 5 and 6 were synthesized for the first time using the known procedures (please see supplementary data for synthesis procedures).

2.3. Fabrication of sensor and sensing studies

According to Sauerbrey equation (Eqn. (1)) [32], the working principle of QCM sensor system is based on the response (ΔF) that took

Scheme 1. Synthetic route for compound 6 (i) Dry toluene, phenol, AlCl₃, room temperature, 4 h, 78% (ii) Acetone, K₂CO₃, methyl bromoacetate, reflux, 24 h, 75% (iii) Toluene-methanol (1:2), (*R*)-(-)-2-phe-nylglycinol, 120 h, reflux, 82% (iv) CHCl₃, SnCl₄, chloromethyl methyl ether, 1 h, -10 °C, 65% (v) MeCN, thiourea, KOH/H₂O, reflux, 24 h, 55%.



place according to mass change on quartz crystal (Δm).

$$\Delta f(Hz) = -(56.6 \, Hz \, cm^2/\mu g) \times \Delta m(\mu g) \tag{1}$$

Initially, QCM crystal surface was properly cleaned in the ultrasonic bath by chloroform before use to eliminate all impurities on gold surface and then taken out and coated with compound **6**. For deposition of compound **6**, the QCM crystal was immersed into baker containing compound **6** solution in chloroform (3 μ L, 1.0 mM) and chloroform (3 mL) at room temperature and the solvents evaporated overnight [33]. AFM analysis was performed to evaluate the morphology and surface roughness of compound **6** film on QCM gold surface. Furthermore, the existence of compound **6** film on QCM gold was characterized by contact angle measurement. The coating frequency of the film was estimated by measuring the frequency shift before and shortly after deposition of the sensing layer [34]. Besides, the mass change on the QCM sensor was calculated by Eqn. (1).

The chiral discrimination ability of compound 6 film on QCM gold surface was performed according to the following procedure respectively. The QCM sensor was placed in a QCM flow cell. After the frequency reached the steady state during circulation of deionized water (DW) into the QCM flow cell, the frequency shifts corresponding to the analyte-sensor interaction by injecting 1000 µM of AA enantiomers solutions in DW were measured for determination chiral discrimination ability of the QCM sensor. Frequency changes of the QCM sensor were recorded by the frequency counter and then the shifting on a frequency was monitored from the frequency-time curve during the circulation of AA enantiomer solutions in sensing system [35]. A home-made liquid phase sensing system (please see supplementary data, Fig. S1) consisted of a compound 6 film on QCM gold surface, a flow cell, an oscillator and a OCM controller connected to a personal computer. It was observed that the interaction between AA enantiomers and as-prepared QCM sensor at first led to frequency shifts. After the frequency shift reached the steady state, DW was circulated into the QCM cell to break down the interaction between analyte and sensor. The completing of the desorption process has been understood by reaching of frequency response to its initial level.

2.4. Modeling of adsorption phenomena

The sensing process of compound **6** film towards AA enantiomers was evaluated in terms of adsorption phenomena. As known, adsorption isotherms are generally used to describe the adsorption mechanism. For this reason, there are various adsorption models which are reported to describe the adsorption phenomena in the literature. Among them, Langmuir and Freundlich isotherm models are frequently used in adsorption studies. Langmuir isotherm is represented by the following equation [36]:

$$C_e/q_e = (1/q_0b) + (C_e/q_0)$$
⁽²⁾

where C_e is the equilibrium concentration (mg L⁻¹) in solution, q_e is the adsorption capacity (mg g⁻¹) at equilibrium, q_0 indicates the adsorption capacity (mg g⁻¹) and *b* is a constant related to the adsorption energy (L mmol⁻¹).

To determine whether the adsorption processes of AA enantiomers by the current QCM sensor are favorable or not to the Langmuir type adsorption process, the favorable nature of adsorption can be expressed in terms of dimensionless equilibrium parameter [37]:

$$R_L = 1/(1 + bC_0) \tag{3}$$

where *b* is Langmuir constant (L mmol⁻¹). The values of R_L indicates the type of the isotherm: $R_L > 1$, unfavorable; $R_L = 1$, linear; $0 < R_L < 1$, favorable; $R_L = 0$, irreversible.

The Freundlich isotherm was also applied for the adsorption of AA enantiomers by the current QCM sensor. Freundlich isotherm model is given by the following equation [38]:

$$logq_e = logK_f + (1/n)logC_e$$
(4)

where K_f and n are Freundlich sorption isotherm constants related to adsorption capacity and adsorption intensity, respectively.

3. Results and discussion

3.1. Synthesis and characterization

In this work, a chiral phenyl glycinol-based thiol calix [4]arene (compound **6**) was synthesized in order to investigate its chiral recognition abilities towards AA enantiomers through the QCM method. The synthesis of compound **1–4** was carried out according to previous literature methods [28–31]. The newly synthesized compound **5** and **6** were characterized by a variety of spectroscopic techniques such as FT-IR, ¹H and ¹³C NMR. Their spectroscopic information was given in supplementary data in detailed.

3.2. Analysis of the sensor film

Thiol moieties of the sensing materials can be strongly adsorbed on the gold surface to afford stable and ordered layers due to the high affinity of thiol groups to a metal surface such as gold [39]. For this reason, newly synthesized thiol functionalized compound 6 was coated on the QCM gold surface by the soaking method. For the characterization of compound 6 film, topographies of QCM sensors were taken using AFM to evaluate the changes on their surface morphologies after deposition of compound 6 on a bare gold surface. Topographies of bare gold surface and compound 6 coated QCM sensor were given in Fig. S7 (please see supplementary data), respectively. The bare gold surface seems to be almost smooth and homogenous (Fig. S7a) whereas it was monitored that there are different surface morphologies occurred on the sensor surfaces due to forming disulfide bonds between compound 6 molecules and gold surface after the coating [40]. So, the coated sensor surface (Fig. S6b) has a number of large peaks which are the same height and wideness. This means that compound 6 molecules may have been irregularly coated on the sensor surface or may have overlapped each other. The average roughness (S_a) increased from 1.66 nm (for bare crystal surface) to 3.62 nm after deposition of compound 6 molecules. Furthermore, the increase of peak-to-peak height (S_v) from 27.91 nm to 73.08 nm indicated the formation of compound 6 film on OCM gold surface.

Contact angles (CA) measurements were performed for determination of wettability properties or the evidence to deposition of compound **6** molecules on the bare gold surface. Wettability properties of sensor surface can be classified as high wettability (θ «90°) or low wettability (θ »90°) [41]. The CA of the bare gold surface was 68° (Fig. S6a, please see supplementary data). After deposition of compound **6** molecules, the surfaces of gold became hydrophobic. So, CA of the coated sensor surface has been determined as 84.9° (Fig. S6a, please see supplementary data). Hence, the increases at CA values due to the hydrophobic moieties of calix [4]arene molecules confirmed that the deposition of compound **6** molecules was performed on a bare gold surface.

3.3. Real-time chiral discrimination and quantification of AA enantiomers

The compound **6** film on QCM gold surface was employed for recognition assays of AA enantiomers as demonstrated in methods. Fig. 2 illustrated the frequency-response curves of the sensor towards the AA enantiomers. As is seen in Fig. 2, the frequency responses of the QCM were decreased quickly and reached equilibrium within 5 min after AA enantiomers were injected into the QCM flow cell. The decreasing of frequency responses indicated that interactions between AA enantiomers and compound **6** molecules. The affinity of compound **6** to *L*-AA enantiomer was approximately more than doubled when it was compared with *D*-AA enantiomer which depends on their



Fig. 2. Individual sensing curves of AA enantiomers $(1000\,\mu\text{M})$ by the QCM sensor.



Fig. 3. Calibration curves of the QCM sensor towards AA enantiomers in different concentrations. The inset figure depicts the changing of the chiral discrimination factors corresponding concentrations of AA enantiomers.

Table 1

Compariso	n of	the	recently	reported	methods	for	AA	detection.	

Methods	Analyte	Linear range	LOD	Ref.
Electrochemical Electrochemical UV–Vis Fluorescent Colorimetric AgNPs-HPLC	AA AA AA AA AA AA	10-800 μM 50 μM - 7.4 mM 12.5-100 μM 1-100 μM 0.01-100 μM 25-150 μM	9.6 μM 20.0 μM 1 μM 0.59 μM 2 nM 14.63 μM 0.27 (0.62 μM	[48] [49] [50] [51] [52] [53] This work
AgNPs-HPLC QCM	AA D/L-AA	25–150 μM 100–1000 μM	14.63 μM 0.27/0.63 μM	[53] This work

stereochemistry [24]. According to the "Lock-and-Key Principle", the difference in recognition ability of the QCM sensor for AA enantiomers may be explained with the size-fit concept, three-dimensional structures of molecules, steric effects and interaction between moieties of the sensible film layer and analyte molecules such as hydrogen bonding interactions [42–44]. Therefore, it is believed that the hydrophobic cavity of compound **6** and stereochemically position of phenyl glycinol moieties on compound **6** preferred *L*-enantiomer to *D*-enantiomer of AA.

The effectiveness of the QCM sensor can be well specified by the chiral discrimination factor a_{sens} , which is defined as [45];

$$\alpha_{sens} = \left| \frac{\Delta f_L}{\Delta f_D} \right| \tag{5}$$

Here, $\Delta f_{\rm L}$ and $\Delta f_{\rm D}$ denote frequency changes of the QCM sensor towards the same concentration of respective enantiomers of AA, respectively. The α_{sens} for compound **6** film towards AA enantiomers was calculated by Eqn. (5) as 2.61 which indicated that AA enantiomers were easily discriminated by the sensor [24].

In further experiments, sensing performance of the QCM sensor was tested towards AA solutions having different concentrations (100, 250, 500 and 1000 μ M). The frequency responses increased proportionally to the increase of AA concentrations. These changes on frequency responses of the QCM sensors towards AA enantiomers were given in Fig. S8 and Fig. S9 (please see supplementary data), respectively. Additionally, the calibration curves for frequency responses of the QCM sensor towards AA enantiomers are plotted in Fig. 3. Both the QCM sensor responses and the chiral discrimination factor (inset of Fig. 3) increased by the increasing of AA concentrations.

Sensor sensitivity (*S*) was determined as 0.0226 (for *L*-AA) and 0.0083 (for *D*-AA) Hz/ μ M by the ratio of frequency changes (Hz) versus AA solutions in different concentrations (μ M) which is the slope of calibration curves (Fig. 3) [46]. Limit of detection (*LOD*) of the QCM sensor was determined as 0.63 μ M and 0.27 μ M towards *L*-AA and *D*-AA enantiomers, respectively [47]. The limit of detections of the QCM sensor towards AA enantiomers was compared with their linear range in the literature (Table 1).

3.4. Adsorption evaluation for AA sensing

The Langmuir and Freundlich isotherm models were used to specify the adsorption mechanism. For this reason, the C_e/q_e versus C_e was plotted for Langmuir isotherms using the sensing results of AA enantiomers (please see supplementary data, Fig. S10). The constants of Langmuir isotherm model, q_0 and b, were calculated as 5895.76 mg/g and 0.0284 (for *L*-AA) L/mmol from the slope and intercept of the linear plots, respectively and were given in Table 2. These results suggested that the adsorption of *L*-AA onto compound **6** film occurred with the formation of a monolayer and that the weak force (small value for the parameter *b*) between the adsorbent and the adsorbate is the result of physical interaction [54]. Furthermore, dimensionless equilibrium parameters were calculated and given in Table 2. These values were between zero and one at the range of 100 and 1000 μ M initial AA concentrations indicating favorable adsorption.

The values of K_f and n were calculated from the intercept and slope of the plots of $log q_e$ versus $log C_e$ (please see supplementary data, Fig. S11). Freundlich isotherm data were also given in Table 2. On the

Table 2

Equilibrium adsorption parameters of AA enantiomers according to Langmuir and Freundlich models.

Enantiomers	Langmuir		Freundlich				
	q ₀ (mg/g)	b (L/mmol)	R^2	R_L	K_f	n	R^2
D-AA L-AA	223.08 5895.76	0.3917 0.0284	0.8393 0.8332	$0 < R_L < 1 \\ 0 < R_L < 1$	0.776 0.982	1.175 1.011	0.9993 0.9999



Fig. 4. The repeatability test of compound 6 film towards L-AA enantiomer ([L-AA]: 1000 µM).

comparison of the R^2 values, it can be concluded that Freundlich equations represent the better fit to the experimental data in adsorption of AA enantiomers onto the surface of compound **6** film. The maximum adsorption capacity of compound **6** is higher than other adsorbents for *L*-AA in the literature [55–58]. As known, the polymeric materials were widely used in adsorption applications. For this reason, a polymeric derivative of compound **6** may be useful adsorbent for AA adsorption applications in aqueous media.

3.5. Repeatability of the sensor

One of the most important parameters of sensors is well known as repeatability. In order to examine the repeatability of compound **6** film on the gold surface (it was prepared again which has 110 Hz mass loading) towards *L*-AA, it was exposed to a solution of *L*-AA (1000 μ M) at least five times and the changes on frequency responses of the sensor was recorded and given in Fig. 4. After every adsorption progress, desorption processes were performed *via* DW injection into the QCM system. The results showed that the differences in the responses of the qCM sensor remained almost constant after each process. This demonstrated that the compound **6** film on gold sensor showed a superior reproducibility in sensing of *L*-AA.

4. Conclusion

In summary, a simple and quick chiral discrimination strategy for AA enantiomers was first reported using calixarene-based QCM sensor. The compound **6** film on gold surface exhibited outstanding chiral recognition as 2.61 for AA enantiomers. It was considered that the "Lock-and-Key Principle", size-fit concept, three-dimensional structures of molecules, steric effects and complexing interaction between moieties of the sensible film layer and analyte molecules such as hydrogen bonding interactions were major factors during sensing process. Moreover, it has been determined that compound **6** film on QCM sensor for detection of *L*-AA enantiomer has shown good analytical performance in terms of the sensitivity (0.0226 Hz/ μ M) and limit of detection (0.63 μ M). Furthermore, the maximum adsorption capacity for compound **6** film towards *L*-AA was found to be 5895.76 mg/g, far higher than the reported adsorbents in literature. Finally, compound **6** film indicated that it exhibited strong potential for repeatability. Thus, a

film was produced on the QCM sensor surface of compound 6 which has outstanding properties such as real-time, sensitive, effective and selective chiral detection for AA enantiomers, durable and easily recoverable with distilled water.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ab.2019.113373.

References

- T.Z. Attia, Simultaneous determination of rutin and ascorbic acid mixture in their pure forms and combined dosage form, Spectrochim. Acta A Mol. Biomol. Spectrosc. 169 (2016) 82–86.
- [2] A. Vishnikin, Y. Miekh, T. Denisenko, Y. Bazel, V. Andruch, Use of sequential injection analysis with lab-at-valve and an optical probe for simultaneous spectrophotometric determination of ascorbic acid and cysteine by mean centering of ratio kinetic profiles, Talanta 188 (2018) 99–106.
- [3] L. Fu, A. Wang, G. Lai, W. Su, F. Malherbe, J. Yu, C.-T. Lin, A. Yu, Defects regulating of graphene ink for electrochemical determination of ascorbic acid, dopamine and uric acid, Talanta 180 (2018) 248–253.
- [4] Y.Q. Fu, J.K. Luo, N.T. Nguyen, A.J. Walton, A.J. Flewitt, X.T. Zu, Y. Li, G. McHale, A. Matthews, E. Iborra, H. Du, W.I. Milne, Advances in piezoelectric thin films for acoustic biosensors, acoustofluidics and lab-on-chip applications, Prog. Mater. Sci. 89 (2017) 31–91.
- [5] R.-Z. Hao, H.-B. Song, G.-M. Zuo, R.-F. Yang, H.-P. Wei, D.-B. Wang, Z.-Q. Cui, Z. Zhang, Z.-X. Cheng, X.-E. Zhang, DNA probe functionalized QCM biosensor based on gold nanoparticle amplification for Bacillus anthracis detection, Biosens. Bioelectron. 26 (2011) 3398–3404.
- [6] P. Jearanaikoon, P. Prakrankamanant, C. Leelayuwat, S. Wanram, T. Limpaiboon, C. Promptmas, The evaluation of loop-mediated isothermal amplification-quartz crystal microbalance (LAMP-QCM) biosensor as a real-time measurement of HPV16 DNA, J. Virol Methods 229 (2016) 8–11.
- [7] N. Karaseva, T. Ermolaeva, B. Mizaikoff, Piezoelectric sensors using molecularly imprinted nanospheres for the detection of antibiotics, Sens. Actuators B Chem. 225 (2016) 199–208.
- [8] Z. Pei, J. Saint-Guirons, C. Käck, B. Ingemarsson, T. Aastrup, Real-time analysis of

the carbohydrates on cell surfaces using a QCM biosensor: a lectin-based approach, Biosens. Bioelectron. 35 (2012) 200–205.

- [9] N. Asai, T. Shimizu, S. Shingubara, T. Ito, Fabrication of highly sensitive QCM sensor using AAO nanoholes and its application in biosensing, Sens. Actuators B Chem. 276 (2018) 534–539.
- [10] H.F. El-Sharif, H. Aizawa, S.M. Reddy, Spectroscopic and quartz crystal microbalance (QCM) characterisation of protein-based MIPs, Sens. Actuators B Chem. 206 (2015) 239–245.
- [11] B. Sonmez, S. Sayin, E.E. Yalcinkaya, D.A. Seleci, H.B. Yildiz, D.O. Demirkol, S. Timur, Calixarene modified montmorillonite: a novel design for biosensing applications, RSC Adv. 4 (2014) 62895–62902.
- [12] M. Tabakci, B. Tabakci, A.D. Beduk, Synthesis and application of an efficient calix [4]arene-based anion receptor bearing imidazole groups for Cr(VI) anionic species, Tetrahedron 68 (2012) 4182–4186.
- [13] T. Sarkar, S. Srinives, Single-walled carbon nanotubes-calixarene hybrid for subppm detection of NO2, Microelectron. Eng. 197 (2018) 28–32.
- [14] X.Q. Pham, L. Jonusauskaite, A. Depauw, N. Kumar, J.P. Lefevre, A. Perrier, M.-H. Ha-Thi, I. Leray, New water-soluble fluorescent sensors based on calix[4]arene biscrown-6 for selective detection of cesium, J. Photochem. Photobiol. A Chem. 364 (2018) 355–362.
- [15] F. Temel, E. Özçelik, A.G. Türe, M. Tabakci, Sensing abilities of functionalized calix [4]arene coated QCM sensors towards volatile organic compounds in aqueous media, Appl. Surf. Sci. 412 (2017) 238–251.
- [16] Y.-S. Zheng, C. Zhang, Exceptional chiral recognition of racemic carboxylic acids by calix[4]arenes bearing optically pure α,β-amino alcohol groups, Org. Lett. 6 (2004) 1189–1192.
- [17] W. Guo, J. Wang, C. Wang, J.-Q. He, X.-w. He, J.-P. Cheng, Design, synthesis, and enantiomeric recognition of dicyclodipeptide-bearing calix[4]arenes: a promising family for chiral gas sensor coatings, Tetrahedron Lett. 43 (2002) 5665–5667.
- [18] N. Natarajan, M.-C. Pierrevelcin, D. Sémeril, C. Bauder, D. Matt, R. Ramesh, Chiral calixarene and resorcinarene derivatives. Conical cavities substituted at their upper rim by two phosphito units and their use as ligands in Rh-catalysed hydroformylation, Catal. Commun. 118 (2019) 70–75.
- [19] J. Yang, Z. Li, W. Tan, D. Wu, Y. Tao, Y. Kong, Construction of an electrochemical chiral interface by the self-assembly of chiral calix[4]arene and cetyltrimethylammonium bromide for recognition of tryptophan isomers, Electrochem. Commun. 96 (2018) 22–26.
- [20] F. Temel, S. Erdemir, B. Tabakci, M. Akpinar, M. Tabakci, Selective chiral recognition of alanine enantiomers by chiral calix[4]arene coated quartz crystal microbalance sensors, Anal. Bioanal. Chem. 411 (2019) 2675–2685.
- [21] F. Temel, S. Erdemir, E. Ozcelik, B. Tabakci, M. Tabakci, Rapid and real-time detection of arginine enantiomers by QCM sensor having a Calix[4]arene receptor bearing asymmetric centers, Talanta 204 (2019) 172–181.
- [22] E. Ozcelik, F. Temel, S. Erdemir, B. Tabakci, M. Tabakci, QCM sensors coated with calix[4]arenes bearing sensitive chiral moieties for chiral discrimination of 1-phenylethylamine enantiomers, J. Inclusion Phenom. Macrocycl. Chem. (2019).
- [23] N.A. De Simone, R. Schettini, C. Talotta, C. Gaeta, I. Izzo, G. Della Sala, P. Neri, Directing the cation recognition ability of calix[4]arenes toward asymmetric phasetransfer catalysis, Eur. J. Org. Chem. (2017) 5649–5659 2017.
 [24] W.C. Su, W.G. Zhang, S. Zhang, J. Fan, X. Yin, M.L. Luo, S.C. Ng, A novel strategy
- [24] W.C. Su, W.G. Zhang, S. Zhang, J. Fan, X. Yin, M.L. Luo, S.C. Ng, A novel strategy for rapid real-time chiral discrimination of enantiomers using serum albumin functionalized QCM biosensor, Biosens. Bioelectron. 25 (2009) 488–492.
- [25] F. Temel, M. Tabakci, Calix[4]arene coated QCM sensors for detection of VOC emissions: methylene chloride sensing studies, Talanta 153 (2016) 221–227.
- [26] G.L. Long, J.D. Winefordner, Limit of detection a closer look at the iupac definition, Anal. Chem. 55 (1983) 712A–724A.
- [27] I.A. Koshets, Z.I. Kazantseva, A.E. Belyaev, V.I. Kalchenko, Sensitivity of resorcinarene films towards aliphatic alcohols, Sens. Actuators B Chem. 140 (2009) 104–108.
- [28] C.D. Gutsche, B. Dhawan, K.H. No, R. Muthukrishnan, Calixarenes. 4. The synthesis, characterization, and properties of the calixarenes from p-tert-butylphenol, J. Am. Chem. Soc. 103 (1981) 3782–3792.
- [29] C.D. Gutsche, M. Iqbal, D. Stewart, Calixarenes. 19. Syntheses procedures for *p-tert*butylcalix[4]arene, J. Org. Chem. 51 (1986) 742–745.
- [30] E.M. Collins, M.A. McKervey, E. Madigan, M.B. Moran, M. Owens, G. Ferguson, S.J. Harris, Chemically modified calix[4]arenes. Regioselective synthesis of 1,3-(distal) derivatives and related compounds. X-Ray crystal structure of a diphenoldinitrile, J. Chem. Soc. Perkin Trans. 1 (1991) 3137–3142.
- [31] E. Kocabaş, A. Karaküçük, A. Sırıt, M. Yılmaz, Synthesis of new chiral calix[4]arene diamide derivatives for liquid phase extraction of α-amino acid methylesters, Tetrahedron: Asymmetry 17 (2006) 1514–1520.
- [32] G. Sauerbrey, The use of quartz crystal oscillators for weighing thin layers and for microweighing applications, Z. Phys. 115 (1959) 206.
- [33] L. Sartore, M. Barbaglio, L. Borgese, E. Bontempi, Polymer-grafted QCM chemical

sensor and application to heavy metal ions real time detection, Sens. Actuators B Chem. 155 (2011) 538–544.

- [34] V.I. Kalchenko, I.A. Koshets, E.P. Matsas, O.N. Kopylov, A. Solovyov, Z.I. Kazantseva, Y.U.M. Shirshov, Calixarene-based QCM sensors array and its response to volatile organic vapours, Mater. Sci. 20 (2002) 73–88.
- [35] Z. Zhang, J. Fan, J. Yu, S. Zheng, W. Chen, H. Li, Z. Wang, W. Zhang, New poly(N,Ndimethylaminoethyl methacrylate)/polyvinyl alcohol copolymer coated QCM sensor for interaction with CWA simulants, ACS Appl. Mater. Interfaces 4 (2012) 944–949.
- [36] W.J. Weber, Physicochemical Processes for Water Quality Control, Wiley-Interscience, 1972.
- [37] K.U. Ahamad, R. Singh, I. Baruah, H. Choudhury, M.R. Sharma, Equilibrium and kinetics modeling of fluoride adsorption onto activated alumina, alum and brick powder, Groundw. Sustain. Dev. 7 (2018) 452–458.
- [38] M. Rao, A.V. Parwate, A.G. Bhole, Removal of Cr6+ and Ni2+ from aqueous solution using bagasse and fly ash, Waste Manag. 22 (2002) 821–830.
- [39] H. Häkkinen, The gold–sulfur interface at the nanoscale, Nat. Chem. 4 (2012) 443.
 [40] R. Patiño-Herrera, R. Catarino-Centeno, A.G. Goicochea, M. Robles-Martínez,
- [40] R. Pathio-Herrera, R. Catarino-Centeno, A.G. Golcochea, M. Robles-Martínez, R.R. Martínez, E. Pérez, Friction coefficient between a hydrophobic soft solid surface and a fluid: determined by QCM-D, Chem. Phys. 513 (2018) 41–49.
- [41] Y. Yuan, T.R. Lee, Contact angle and wetting properties, in: G. Bracco, B. Holst (Eds.), Surface Science Techniques, Springer Berlin Heidelberg, Berlin, Heidelberg, 2013, pp. 3–34.
- [42] F. Cramer, Emil fischer's lock-and-key hypothesis after 100 years—towards a supracellular chemistry, in: J.P. Behr (Ed.), Perspectives in Supramolecular Chemistry, John Wiley & Sons, 1994, pp. 1–23.
- [43] F.N. Memon, S. Memon, Sorption and desorption of basic dyes from industrial wastewater using calix[4]arene based impregnated material, Separ. Sci. Technol. 50 (2015) 1135–1146.
- [44] L. Mutihac, J.H. Lee, J.S. Kim, J. Vicens, Recognition of amino acids by functionalized calixarenes, Chem. Soc. Rev. 40 (2011) 2777–2796.
- [45] C. Xu, S.C. Ng, H.S.O. Chan, Self-Assembly of perfunctionalized β-cyclodextrins on a quartz crystal microbalance for real-time chiral recognition, Langmuir 24 (2008) 9118–9124.
- [46] W. Chen, F. Deng, M. Xu, J. Wang, Z. Wei, Y. Wang, GO/Cu2O nanocomposite based QCM gas sensor for trimethylamine detection under low concentrations, Sens. Actuators B Chem. 273 (2018) 498–504.
- [47] V.K. Gupta, M.L. Yola, T. Eren, N. Atar, Selective QCM sensor based on atrazine imprinted polymer: its application to wastewater sample, Sens. Actuators B Chem. 218 (2015) 215–221.
- [48] B. Kaur, T. Pandiyan, B. Satpati, R. Srivastava, Simultaneous and sensitive determination of ascorbic acid, dopamine, uric acid, and tryptophan with silver nanoparticles-decorated reduced graphene oxide modified electrode, Colloids Surfaces B Biointerfaces 111 (2013) 97–106.
- [49] A. Safavi, N. Maleki, O. Moradlou, F. Tajabadi, Simultaneous determination of dopamine, ascorbic acid, and uric acid using carbon ionic liquid electrode, Anal. Biochem. 359 (2006) 224–229.
- [50] H. Bi, A.C. Fernandes, S. Cardoso, P. Freitas, Interference-blind microfluidic sensor for ascorbic acid determination by UV/vis spectroscopy, Sens. Actuators B Chem. 224 (2016) 668–675.
- [51] N. Li, Y. Li, Y. Han, W. Pan, T. Zhang, B. Tang, A highly selective and instantaneous nanoprobe for detection and imaging of ascorbic acid in living cells and in vivo, Anal. Chem. 86 (2014) 3924–3930.
- [52] D. Wu, N. Hu, J. Liu, G. Fan, X. Li, J. Sun, C. Dai, Y. Suo, G. Li, Y. Wu, Ultrasensitive colorimetric sensing strategy based on ascorbic acid triggered remarkable photoactive-nanoperoxidase for signal amplification and its application to α-glucosidase activity detection, Talanta 190 (2018) 103–109.
- [53] S.R. Dash, S.S. Bag, A.K. Golder, Synergized AgNPs formation using microwave in a bio-mediated route: studies on particle aggregation and electrocatalytic sensing of ascorbic acid from biological entities, J. Electroanal. Chem. 827 (2018) 181–192.
- [54] C.S.T. Araújo, I.L.S. Almeida, H.C. Rezende, S.M.L.O. Marcionilio, J.J.L. Léon, T.N. de Matos, Elucidation of mechanism involved in adsorption of Pb(II) onto lobeira fruit (Solanum lycocarpum) using Langmuir, Freundlich and Temkin isotherms, Microchem. J. 137 (2018) 348–354.
- [55] M. Monier, A.L. Shafik, D.A. Abdel-Latif, Surface molecularly imprinted aminofunctionalized alginate microspheres for enantio-selective extraction of l-ascorbic acid, Carbohydr. Polym. 195 (2018) 652–661.
- [56] M. Anbia, Z. Parvin, M. Sepehrian, Application of modified nanoporous materials in ascorbic acid adsorption, Part. Sci. Technol. (2018) 1–7.
- [57] S. Kamran, M. Asadi, G. Absalan, Adsorption of folic acid, riboflavin, and ascorbic acid from aqueous samples by Fe3O4 magnetic nanoparticles using ionic liquid as modifier, Anal. Methods 6 (2014) 798–806.
- [58] A. Dehmolaei, M. Vadi, Comparative study of adsorption isotherms of vitamin C on multi wall and single wall carbon nanotube, Orient. J. Chem. 30 (2014) 233–236.