

Full Research Paper

Potentiometric Responses of Ion-Selective Electrodes Doped with Diureidocalix[4]arene towards Un-dissociated Benzoic Acid

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Abstract: Diureidocalix[4]arene have been applied as new ionophore in liquid membrane electrode (ISE) sensitive towards un-dissociated benzoic acid. The electrode demonstrated response towards benzoic acid with the detection limit 2.0×10^{-4} M which is sufficient for the determination of benzoic acid added to beverages as preservative in milimolar concentration. The selectivity coefficients measured by the matched potential method (MPM) showed its good selectivity against common anions present in drink samples. All measurements were made in presence of 1.0×10^{-2} M NaHSO₄ pH 3.0 in order to reduce the influence of OH⁻. The applicability of diureidocalix[4]arene incorporated ISE has been checked by recovery test of benzoic acid in the presence of artificial drink matrix and by standard addition method.

Keywords: Diureidocalix[4]arene, Liquid membrane electrodes, Benzoic acid, Drink analysis.

1. Introduction

Calixarenes are macrocyclic compounds widely used in supramolecular chemistry for charged and neutral compounds recognition [1, 2]. These macrocycles, belonging to the class of compounds named

cavitands, possess 'cup' like shape characterized by wide upper and narrow lower rims and central annulus. They have hydrophobic cavities which can complex small molecules or ions. It was shown that simple unfunctionalized calix[4]arene, like *p*-tert-butylcalix[4]arene, can interact with amines [3]. Calix[4]arenes and calix[6]arenes possess cavities suitable for Na⁺ and Cs⁺ complexation, respectively [4]. It has been reported that in the pores of silica calix[n]arenes (n = 4, 6, 8) form supramolecular complexes with C₆₀ [1]. Calix[4]arene possesses wide derivatisation possibilities and consequently, its upper and lower rims can be easily modified to yield various versatile receptors [5]. The introduction of amide, urea and thiourea moieties into the upper rim of calixarene and preorganisation in the cone conformation form receptors enabling the binding of anions by hydrogen bonds [6, 7].

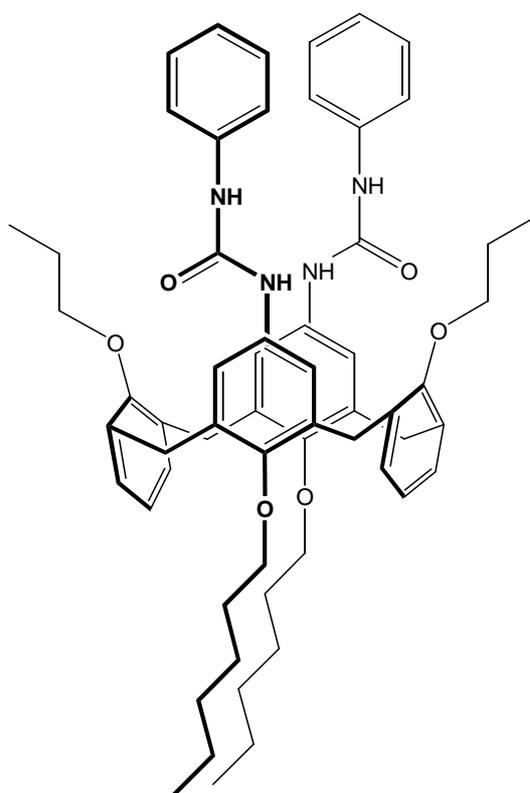


Figure 1. The structure of diureidocalix[4]arene.

Biscalix[4]arenes in which the upper rim of one calixarene moiety is covalently linked via amide bonds to the lower rim of another can bind F⁻ [8]. The 1,3 alternate conformers can possess two independent ionophoric sites on either side of the cavity, but it has been proved that diureido derivatives of calix[4]arenes in 1,3-alternate conformer, such as investigated in this work, represents ionophores with one possible binding site and exhibit binding affinity towards selected anions. Similar calixarene with two ureido moieties were used to measure the complexation ability in organic solution by standard ¹H NMR titration experiments using constant concentration of receptor and increasing concentrations of the appropriate anions. These investigations showed strong interaction with benzoate anions (probably because of additional interactions between aromatic parts of receptor and analyte), while the complexation constants towards chloride, acetate and phosphate are much lower [9]. Thus, such a type of receptors might be suitable for sensing benzoic acid.

This acid and its sodium salt are used as food preservatives. It is the most suitable for fruit juices and soft drinks which possess acidic pH [10].

Analytical methods used for determination of benzoic acid include spectroscopic technique [11, 12], gas chromatography (GC) [13, 14], high performance liquid chromatography (HPLC) [15, 16] or capillary electrophoresis [17]. All of them involve extensive extraction procedures which are time-consuming and expensive.

In this paper we propose a potentiometric sensor based on a ISE incorporating diureidocalix[4]arene (1,3-alternate conformer, which possesses only one binding site), for the direct and rapid determination of un-dissociated benzoic acid in drink samples.

2. Materials and Methods

2.1. Reagents

The diureidocalix[4]arene used as ionophore was synthesised according to procedure already published [5] and the experimental details will be published elsewhere.

High molecular weight poly(vinyl chloride) (PVC) used as polymer matrix was purchased from Wako Pure Chemical (Japan). Dioctyl phthalate (DOP) used as membrane solvent and tri(dodecyl)methylammonium chloride (TDDMACl) were obtained from Aldrich Chemie, Germany. Potassium tetrakis(4-chlorophenyl)borate (K-TpCIPB) was obtained from Dojindo Laboratories (Kumamoto, Japan), benzoic acid from Serva (Germany), sulfuric acid, sodium sulfate, glucose, sodium chloride, sodium bromide, acetic acid, ascorbic acid, citric acid, phosphate monosodium salt were purchased from POCh (Gliwice, Poland). Tetrahydrofuran (THF) was purchased from POCh (Gliwice, Poland) and used freshly distilled from solid NaOH.

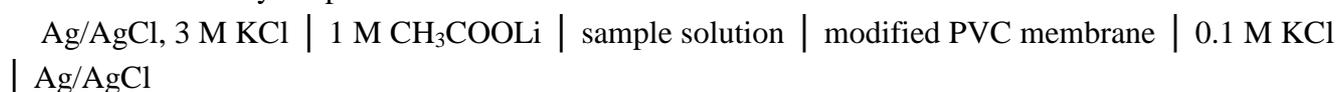
Aqueous solutions were prepared with deionized water (18.2 M Ω resistivity) obtained with a Simplicity[®] 185 Water System (Millipore, Molsheim, France).

2.2. Membranes and Electrodes Preparation

Polymeric liquid membranes were prepared according to the standard procedure. The membranes consist of: ca. 1 wt% receptor, 66 wt% DOP and 33 wt% PVC. Some membranes were additionally incorporated with 50 mol% (versus receptor) of lipophilic salt TDDMACl or K-TpCIPB.

All components were dissolved in about 2 ml of THF and resulting solution was transferred to the glass ring (diameter 30 mm) and left for 48 h to evaporate the solvent. The membrane circles (diameter 6 mm) were then cut out and placed in the liquid membrane-type Philips ISE body (Glasbläserei Möller, Zürich). Electrodes were conditioned for 24 h in an aqueous solution of 1.0×10^{-2} M NaHSO₄.

The cell assembly for potentiometric measurements was as follows:



2.3. EMF Measurements

Potentiometric measurements were made using a multi-channel station Donau-Lab (Warsaw, Poland) at room temperature. The reference electrode was a double junction Ag/AgCl, 3 M KCl | 1 M CH₃COOLi electrode obtained from Philips. The pH values were monitored using glass electrode HI 1139 obtained from Hanna Instruments. The effect of the pH changes from 2.5 to 9.5 on the membrane potential was measured by addition of 1.0 x 10⁻¹ M NaOH solution containing 1.0 x 10⁻² M Na₂SO₄ to a solution of 1.0 x 10⁻² M H₂SO₄. The effect of pH changes from 9.5 to 2.5 was measured by addition of 1.0 x 10⁻¹ M H₂SO₄ solution containing 1.0 x 10⁻² M NaHSO₄ to a solution of 1.0 x 10⁻² M NaOH.

Calibration curves were constructed by plotting the observed changes in potential vs the logarithm of benzoic acid concentration at constant pH. The selectivity coefficients ($\log K_{Benz,j}^{MPM}$) were determined by the matched potential method (MPM) in mixed solutions [18-20].

The recovery test was done using juice matrix with the following typical composition: 1.0 x 10⁻² M citric acid and 2.5 g glucose/L [21].

The contents of benzoic acid were analysed in lemon soft drink Hoop (produced by HOOP S.A) to which this compound was added as preservative. The composition of measured beverage declared by producer included sugar, glucose-fructose syrup, CO₂, citric acid and sodium citrate as acidity regulators, aroma, ascorbic acid, sodium benzoate. The beverage was degassed in an ultrasonic bath for 20 min before use. The determination of benzoic acid was carried out using the standard addition method, which involved the addition of 1 ml aliquots of a 1.0 x 10⁻² M benzoic acid stock solution to a 100 ml of aqueous solution of 1.0 x 10⁻² M Na₂SO₄ containing 10 vol% of beverage. The membrane potential was recorded after each addition [22, 23].

3. Results and Discussion

3.1. Potential Response of ISEs Incorporating Diureidocalix[4]arene towards pH Changes.

The responses of ISEs towards pH changes in aqueous solution are very important parameters, which allow to optimized the measuring conditions of selected analytes and explored the mechanism of the potentiometric responses.

The membrane modified only with diureidocalix[4]arene showed potentiometric response in relation to pH change of aqueous solution in range from 2.5 to 9.5 pH unit. This phenomenon was completely reversible. The pH changes from 9.5 to 2.5 caused the same potential response.

In order to elucidate the nature of the response of diureidocalix[4]arene-ISE towards pH changes, membranes were additionally incorporated with anionic and cationic lipophilic salts. The presence of anionic sites in membrane caused a lack of its response towards pH (Figure 2). Large lipophilic anion TpCIPB⁻ hindered the ionophore-OH⁻ complex formation probably because of electrostatic repulsion. On the other hand, cationic salt additive improved the pH response of diureidocalix[4]arene-ISE. The presence of large lipophilic cation TDDMA⁺ facilitated formation of ionophore-OH⁻ complex. Diureidocalix[4]arene is neutral ionophore and addition of cationic sites, with the charge sign opposite to that of OH⁻ anion, to the membrane composition is effective in improving the electrodes response towards this anion [24-27].

Thus, it might be concluded that the potentiometric responses of diureidocalix[4]arene-ISE towards pH changes of aqueous solution occurred due to complexation of OH^- by receptor molecules at the organic/aqueous interface.

The similar phenomenon was observed for ISE incorporating calix[4]pyrroles [28].

Figure 2 shows the potential changes of ISEs studied vs. pH changes in aqueous solution.

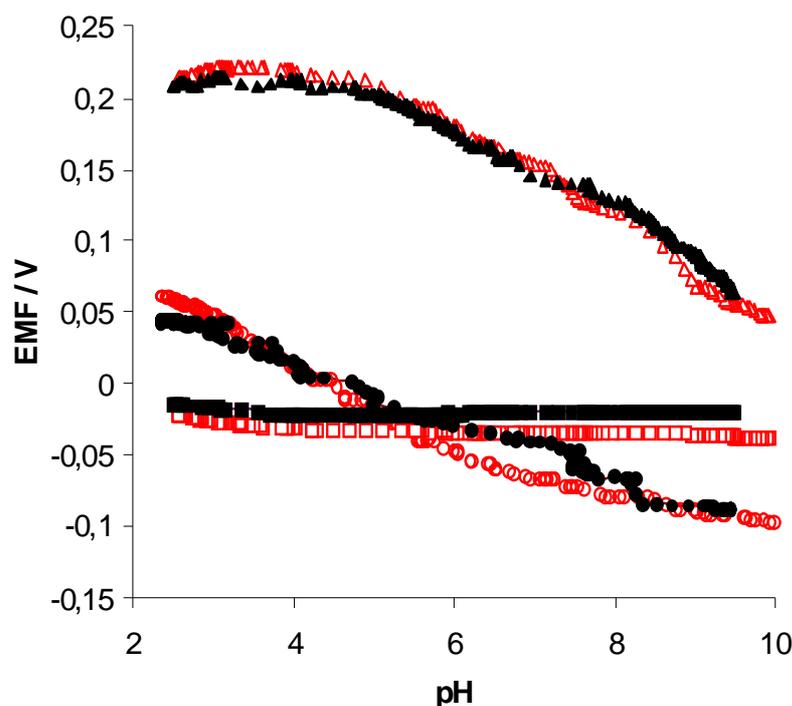


Figure 2. Potential vs pH curves obtained by electrodes containing: (○) ligand; (△) ligand + 50% TDDMACl; (□) ligand + 50% K-TpCIPB (pH was changed from 9.5 to 2.5); (●) ligand; (▲) ligand + 50% TDDMACl; (■) ligand + 50% K-TpCIPB (pH was changed from 2.5 to 9.5). Measuring conditions – see part 2.3.

3.2. Potentiometric Responses of Diureidocalixarene-containing ISE towards Benzoic Acid

Diureido derivatives of calix[4]arenes in 1,3-alternate conformer represents ionophores with one anionic binding site (Figure 1). It has been already reported that similar calixarene with two ureido moiety showed strongest interaction in one organic phase with benzoate ions [9]. In the work presented, diureidocalixarene has been studied as the ionophore of ISE destined for determination of benzoic acid in its undissociated form.

The measurements were performed in solution of 1.0×10^{-2} M NaHSO_4 . The interaction between investigated ionophore and sulfate anions have been studied. The electrodes showed no response towards sulfate anions in concentration range from 1.0×10^{-6} M to 5.0×10^{-3} M in the solution of 1.0×10^{-2} M citric buffer, pH = 3.0. On the basis of this results we used this salt in background solution.

The measurements were carried out at pH = 3.0 in which electrodes showed best potentiometric response (Figure 3). Under these conditions benzoic acid is present in 85% as neutral compound ($\text{pK}_a = 4.21$). Also, acidic solution diminished the competition caused by OH^- complexation. The pH 6.2,

where benzoic acid exists in dissociated form, was unsuitable for potentiometric measurements with using diureidocalixarene –ISE, mainly because of strong competition with OH⁻ (results are not shown).

The research presented concerned the interaction between neutral carrier - diureidocalix[4]arene and neutral analyte - benzoic acid. In such a case the optimalization of membrane composition is rather puzzling problem.

The addition of 50 mol % vs ionophore of lipophilic cationic sites TDDMA⁺ increased the membrane response towards benzoic acid (Figure 3). On the other hand, the addition of 50 mol % vs ionophore of lipophilic anionic sites TCIPB⁻ caused lack of responses towards benzoic acid (results are not showed).

It might be concluded that the membranes which showed the highest responses towards pH changes (Figure 2), displayed the strongest responses towards benzoic acid (Figure 3). The similar phenomenon was observed in the case of calix[4]pyrrole- ISE derivatives used for potentiometric determination of nitrophenol isomers existing in the neutral forms [28].

The presence of lipophilic cationic sites TDDMA⁺ in the membrane doped with diureidocalix[[4]arene, decreased its resistance, but also might facilitated the interaction with benzoic acid.

The research on the elucidation of the role of TDDMA⁺ in the potentiometric responses of diureidocalix[[4]arene –ISE will be carried on in our laboratory.

The macrocyclic hexamine-ISE [29] and diureidocalixarene–ISE showed comparable detection limits (in the range of 10⁻⁴ M of benzoic acid). The optimum pH values of benzoic acid solutions to be measured with macrocyclic hexamine-ISE and diureidocalix[4]arene–ISE were 5.0 and 3.0, respectively. The major of soft drinks have rather low pH. Therefore, the pH adjustment could be avoided for the determinations of benzoic acid contents in soft drinks using diureidocalix[4]arene–ISE.

Based on the results obtained, diureidocalixarene can be added to the group of receptors, which are able to recognize the neutral molecules potentiometrically.

Generation of potentiometric signals of ISEs in the presence of neutral forms of phenol derivatives, have been already reported. This phenomenon was observed for electrodes incorporated with macrocyclic polyamine [30], calix[4]pyrrole [28, 32, 33] and corrole [34].

For these electrodes two steps mechanism of potentiometric response generation was proposed [35]. First step concerns formation of supramolecular host-guest complex between ionophore and analyte by hydrogen bonding. In the consequence, proton from OH of phenolic group involved in hydrogen bonding become more acidic and dissociate at the organic membrane / aqueous interface (second step).

The same mechanism might be proposed for the phenomenon investigated in this work. Diureidocalix[4]arene creates at the membrane / aqueous interface supramolecular complex with undissociated benzoic acid. Hydrogen bonds might be formed between hydrogen atoms from ureido groups of ionophore and oxygen atoms from carboxylic group of benzoic acid. π - π interaction between phenyl rings of analyte and ionophore also can play some role. The creation of complex based on hydrogen bonds formation cause increase of acidity of proton from benzoic acid molecule. Therefore this proton can dissociate at pH 3.0 and can be shifted from the surface of the membrane towards water

solution surface. As a consequence, the charge separation at the organic / aqueous interfaces is created and anionic potentiometric signal is generated.

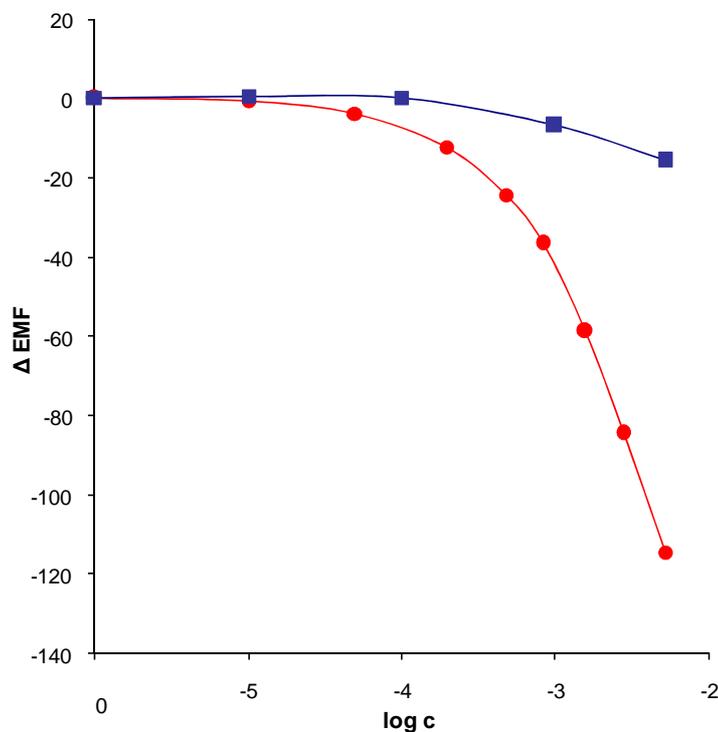


Figure 3. Potential changes vs. concentration curves obtained for ISEs doped with ligand (■) and ligand + 50% TDDMACl (●). Measurements were taken in 1.0×10^{-2} M NaHSO_4 pH 3.0 ($n = 4$; $0,31 < \text{SD} < 15,46$).

3.3. Time of Response of Diureidocalix[4]arene ISE towards Benzoic Acid

A response time is important parameter which characterize ISEs. Figure 4 illustrates a representative plot of the potential changes vs time for electrode with diureidocalix[4]arene and lipophilic salt TDDMACl after additions aliquots of 1.0×10^{-2} M aqueous stock solution of benzoic acid. The electrode responses towards changes in concentration of benzoic acid were relatively fast (ca. 100 s) within the whole concentration range, when we assume response mechanism including more than one step, which are necessary in the case of uncharged analytes.

3.4. Potentiometric Selectivity of Electrode Incorporating Diureidocalix[4]arene

Potentiometric selectivity coefficient defines the ability of the ISE to differentiate a particular (primary) ion from others (interfering ions) [18-20]. Matched potential method (MPM) was used to determine of these parametrs. In this method the selectivity coefficient is defined as the activity (concentration) ratio of the primary ion and interfering ion which give the same potential change in a reference solution.

This method can be used in case of differences in charge number between primary and interfering ions and don't require Nernstain responses to the activity (concentration) of primary or interfering ions.

This is only one method suitable for determination of selectivity coefficients concerning the neutral compounds.

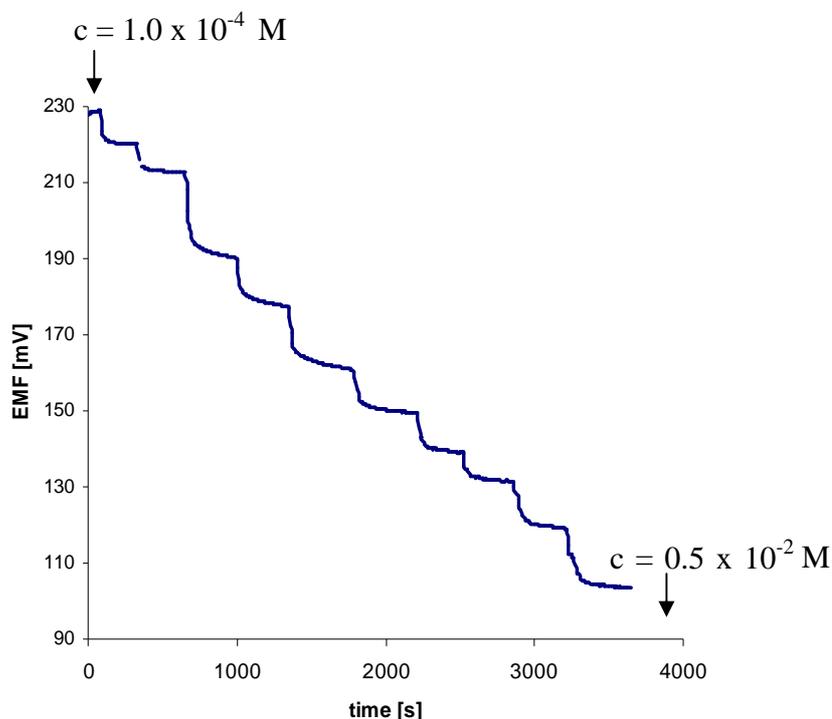


Figure 4. Response time towards benzoic acid addition. Aliquot of the stock solution 1.0×10^{-2} M analyte was added to 100.0 ml 0.01 M Na_2SO_4 , pH 3.0 to increase acid concentration from 1.0×10^{-4} M to 0.5×10^{-2} M.

Solution 1.0×10^{-3} M of benzoic acid and 1.0×10^{-2} M NaHSO_4 was used as background. For the calculation of selectivity coefficients, $\Delta\text{EMF} = -2.0$ mV was used. The calculated values of selectivity coefficients are summarized in Table 1. These results showed that electrodes studied are selective towards benzoic acid in the presence of several interferents commonly occurring in beverages. According to the selectivity coefficient values the interfering substances could be ordered as follows:

chloride > phosphate >> ascorbate \approx acetate \approx citrate \approx glucose

The several potentiometric sensors destined for benzoic acid and/or benzoate determination have been already reported, macrocyclic polyamine –ISE [30], Pt | Hg | $\text{Hg}_2(\text{benzoate})_2$ | graphite) [36], just to name a few.

ISEs doped with diureidocalix[4]arene and macrocyclic polyamine showed similar selectivity. The major interferents (citrate and acetate ions) present in the soft drinks possess only very small effect on the benzoic acid determination (Table 1). On the other hand, the Pt | Hg | $\text{Hg}_2(\text{benzoate})_2$ | graphite electrode can not be used for the direct determination of benzoic acid because of serious interference caused by chloride anions [36].

Table 1. Potentiometric selectivity coefficients of ISEs determined by matched potential method.

Interferent, <i>j</i>	$\log K_{Benz.,j}^{MPM}$ $\Delta EMF = -2 \text{ mV}$
Chloride	-0,42
Ascorbate	<<0
Phosphate	-1,22
Acetate	<<0
Citrate	<<0
Glucose	<<0

The log K values were determined in the background solution consists of 1.0×10^{-2} M NaHSO₄ and 1.0×10^{-3} M benzoic acid pH 3.0 as background and calculated for the $\Delta EMF = 2$ mV. Standard deviations: $0.02 < SD < 0.28$.

3.5. Determination of Benzoic Acid in Beverage.

In order to display the potential applicability of diureidocalix[4]arene ISEs they were used for the direct determination of benzoic acid content in investigated lemon soft drink. The determination was done using the standard addition method.

The selectivity coefficients describing above showed no interferences from other compounds presented in this beverage. Nevertheless the standard addition method was used to minimize the matrix effect. For this purpose beverage was initially degassed and diluted 10-fold with 1.0×10^{-2} M Na₂SO₄.

The results were obtain from 3 electrodes and 3 repetitions. The determined concentration of benzoic acid was $1.6 \pm 0.1 \times 10^{-4}$ M in diluted sample which gives $1.6 \pm 0.1 \times 10^{-3}$ M of benzoic acid in beverage. This concentration is equal 0.20 ± 0.01 g/L of this preservative. This amount corresponds with benzoate contents determined in lemon soda drink (Sprite) by HPLC – 237.4 ± 3.1 ppm [36] and to contents define by the Regulation of the Minister of Health in Poland – 0.15 g/L maximum [37].

3.6. Recovery Test

The recovery test was successfully performed by determination of milimolar amounts of benzoic acid in artificial juice matrix (for composition see Material and Methods).

The results are showed in Table 2 and demonstrate that the components of artificial juice matrix do not interfere significantly with the benzoic acid determination. The recovery values of 100.8 – 107.7 % were obtained for determination of: 0.479, 0.741, 1.000 and 1.380 mM of benzoic acid.

Table 2. Recovery test of benzoic acid added to the artificial juice matrix (n = 8).

Concentration known (mM)	Concentration found (mM)	Recovery (%)
0.479	0.516 ± 0.042	107.7 ± 8.7
0.741	0.760 ± 0.031	102.6 ± 4.1
1.000	1.016 ± 0.033	101.6 ± 3.3
1.380	1.391 ± 0.028	100.8 ± 2.1

3.7. Conclusions

The liquid membrane electrode doped with diureidocalix[4]arene and additionally with 50 mol % vs ionophore of lipophilic cationic salt, tridodecylmethylammonium chloride, can be used for the direct determination of un-dissociated benzoic acid in beverages. The proposed ISE was effective regarding the following parameters: the sufficient detection limit 2.0×10^{-4} M, good selectivity towards substances commonly occurred in drink samples, reversibility and short response time.

Therefore, the diureidocalix[4]arene-ISE might be recommended for the direct potentiometric determination of un-dissociated benzoic acid in beverages.

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