Development of a sol–gel optical sensor for analysis of zinc in pharmaceuticals

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Abstract

A Zn(II) optical sensor was developed by incorporating 4-(2-pyridylazo)resorcinol (PAR) in a sol–gel thin film. Acid- and base-catalyzed methods to prepare the sol–gel layers have been studied, as well as different types of precursors and different PAR concentrations. Sensors based on co-polymerization of tetraethoxysilane (TEOS) with 3-amino-1-propyltriethoxysilane (3-APTES), basic catalysis, water:alkoxide ratio of 4 and PAR concentration of 1.0 g l$^{-1}$ showed optimum performance in the proposed working conditions. The sensor was coupled to a multicommutated flow system and applied to the direct determination of Zn(II) in injectable insulins. Optical transduction was based on the use of a blue LED and a photodiode. The sensor showed optimum response at pH 5.5 with maximum absorbance at 500 nm. Its regeneration was accomplished with a solution of KSCN acidified to pH 3.0 with HCl. Linear response was obtained for Zn(II) concentration range of 5.0–25.0 /Hg$^{-1}$, with detection limit of 2.0 /Hg$^{-1}$ and sampling frequency of 16 samples h$^{-1}$. Interference from foreign ions was studied at 10:1 (w/w) ratio added ion:Zn. The results obtained on real samples analyzed were in good agreement with those obtained by a standard method, with relative deviation errors inferior to 1.2%.

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Keywords: Zn(II) optical sensor; Sol–gel films; 4-(2-Pyridylazo)resorcinol; Multicommutated flow analysis; Dual-wavelength; Pharmaceuticals

1. Introduction

Organic indicator dyes currently used in the spectrophotometric determination of various metal ions play a fundamental role in the design of chemical optical sensors [1]. Several classical indicators have been used in the development of optodes which were successfully applied to metal ions sensing, namely dithizone [2], xylene orange [3], 5,10,15,20-tetra(p-sulfonatophenyl)porphyrin [4], PAN and other azo-derivatives [5–7]. There is a growing interest in developing new sensing schemes and immobilization methods to obtain optodes with improved characteristics. 4-(2-Pyridylazo)resorcinol (PAR) has become very popular as an unselective chelating agent since it forms very stable, water-soluble and highly colored complexes with the vast majority of transition metals [8–13]. In acetate medium (pH 3.0–6.0) PAR forms a red-orange 1:2 (metal:ligand) complex with zinc which can be monitored spectrophotometrically [8,14,15]. The molar absorptivity reported for the PAR–Zn(II) complex (ε = 7.7 × 10$^4$ 1mol$^{-1}$ cm$^{-1}$ [16]) is considerably greater than for other reagents, which makes PAR a superior chelating agent for zinc analysis [17]. PAR has been immobilized for metals sensing purposes in polymeric materials like XAD-4, XAD-7 and Dowex ion-exchange resins [5], and chitosane membrane [18].

When choosing the polymeric support for chemical sensors development, the sol–gel technology is a very promising and extensively investigated strategy [19–23], since it provides a low-temperature process to obtain porous silicate glass matrices in which organic reagents and molecular receptors may be easily entrapped. The structures obtained possess excellent properties, such as chemical and thermal stability, chemical inertness, high purity and homogeneity and very high transparency in a broad wavelength range from ultraviolet to infrared. One of the unique features of the sol–gel process is that the properties of the final network structure, such as hydrophobicity, thickness, porosity, flexibility, reactivity and stability, can be easily tailored by controlling the process conditions, the type and size of precursors and catalysts [19,20,23,24]. In addition, glass materials of various shapes can be easily prepared. Sol–gel thin films have proved to be excellent hosts for organic dyes [25].

This paper describes the incorporation of PAR in sol–gel thin films in order to obtain Zn(II) optical sensors, which
were coupled to a multicommutated flow system and applied to the determination of zinc in pharmaceuticals.

Zinc compounds are found as active ingredients in pharmaceutical preparations such as ointments and creams for external use, collyria and ophthalmic ointments, mineral–vitamin supplements and mouthwashes [26]. Zinc is also an integral part of the injectable form of slow-action insulin. Thus, determination of zinc in pharmaceutical preparations is an important analytical task. A flow-through optode has already been developed and used for this purpose by Albero et al. [7], based on the immobilization of PAN in a plasticized PVC membrane. Albeit its simplified preparation procedure, it presented serious interference of several ions and short useful lifetime. The new sensor proposed in the present work intends to associate the advantages of the sol–gel technology with the high sensitivity of PAR. In addition, by coupling the sensor to a continuous flow technique, simpler manipulation of solutions, simplified manifold, reagent economy and a cleaner determination of PAR. In addition, by coupling the sensor to a continuous flow technique, simpler manipulation of solutions, simplified manifold, reagent economy and a cleaner determination procedure may be achieved, with additional increase in sensitivity, stability and selectivity [27].

2. Experimental

2.1. Reagents and solutions

Analytical grade chemicals were used without further purification, unless stated otherwise. Milli-Q (Millipore) de-ionized water with resistivity above 18 MΩ cm was used to prepare all solutions.

Tetraethoxysilane (TEOS, ref. 86578) methyltriethoxysilane (MTES, product no. 69435), 4-(2-pyridylazo)resorcinol (product no. 82970) and nitric acid (product no. 84385) were from Fluka. Tetramethylylammonium hydroxide, 25 wt.% solution in water (TMAOH; product no. 33,163–5) was from Sigma. Ethanol and potassium thiocyanate were from Merck. KSCN solution was purified from traces of metals with non-ionic polymeric adsorbent Amberlite XAD-2 (Sigma, product no. 21,646–1).

A stock standard solution containing 1.0 g l⁻¹ Zn(II) was prepared by dissolving 100.0 mg of metallic zinc (product no. 8756, Merck) in a mixture of 2.0 ml of concentrated chloridric acid (Merck) and 1.0 ml of water and then diluting to 100.0 ml with distilled water. Working zinc solutions were obtained by dilution of this stock standard with water. Citrate, acetate, borate and phosphate buffer solutions with pH ranging from 3.0 to 8.0 were prepared with analytical grade reagents from Merck, and purified from traces of metals by shaking with portions of dithizone solution in CHCl₃.

Four injectable insulins available in the Portuguese market (Humulin Ultralente®, Humulin Lente®, Ultratard® and Monotard®) were used as samples. The contents of five ampoules of each insulin injection were blended and an accurately measured volume, corresponding to ca. 5.0 µg of Zn(II), was transferred into a 100 ml volumetric flask, diluted with water and mixed in a vortex.

2.2. Instrumentation

Conventional absorbance measurements for sensors characterization were performed in a Lambda 45 UV–Vis spectrophotometer (Perkin-Elmer, Shelton, CT). Surface area, total volume of pores and average pore volume were estimated from N₂ adsorption/desorption analysis, performed on a Micromeretics ASAP 2000 apparatus (Mönchengladbach, Germany). Microstructure of the sensors was investigated using a scanning electron microscope (SEM) JEOL JSM-6360 (Peabody, MA), with an acceleration voltage of 20kV, and an atomic force microscope (AFM) TopoMetrix Discover TMX2010 (Santa Clara, CA).

The flow manifold was assembled with four NRResearch 161 T031 three-way solenoid valves (Stow, MA) and a Gilson Minipuls 3 peristaltic pump (Villiers-le-Bel, France) equipped with isoversinic pump tube of the same brand. Flow lines were made of PTFE-0.8 mm i.d. tubing. For absorbance measurements in the flow system plastic optical fibers (ref. FOP1-ST) connected to a digital color wheel source (ref. FOCWDIG), a silicon photodiode detector (ref. VI5D) and a photodetector amplifier (ref. PDA1) from WPI (World Precision Instruments, Florida) were used. The control of the commutation devices and signal acquisition were accomplished through VisiDAQ 3.1 Software program using a computer equipped with a PCL–818 L Advantech interface card.

2.3. Preparation of the sensors

Different types of multicomponent sols were prepared by combining TEOS with MTEOS or 3-APTES in increasing ratios. Water:alkoxyde ratio and catalysis were also studied. The compositions of the most representative sols produced are summarized in Table 1. PAR was added to the sols previously dissolved in ethanol. For each type of film several increasing concentrations of PAR were tested, in order to study the effect of the immobilized reagent concentration. All the sol–gel solutions were allowed to gelate at room temperature and mechanically stirred continuously prior to coating. All the films were obtained by spin-coating (3000 rpm, 15 s).

Table 1

<table>
<thead>
<tr>
<th>Composition of sols for preparation of sensor thin films (all values in ml)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEOS</td>
<td>4.0</td>
<td>3.6</td>
<td>3.0</td>
<td>3.0</td>
</tr>
<tr>
<td>MTEOS</td>
<td>–</td>
<td>0.4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3-APTES</td>
<td>–</td>
<td>4.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ethanol</td>
<td>16.0</td>
<td>16.0</td>
<td>16.0</td>
<td>16.0</td>
</tr>
<tr>
<td>HNO₃ (10⁻¹ M)</td>
<td>2.0</td>
<td>2.0</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>TMAOH</td>
<td>–</td>
<td>–</td>
<td>2.18</td>
<td>2.18</td>
</tr>
</tbody>
</table>
100 μl on glass slides 18 mm × 18 mm, previously treated with concentrated nitric acid, ethanol and rinsed with distilled water, followed by drying at 100 °C, in order to activate the silanol groups on the surface of the glass. After coating, all films were dried at room temperature for at least 5 days.

2.4. Characterization of the sensors

The different sensor films obtained were characterized in terms of spectral characteristics, porosity, surface area and extension of dye leaching.

To enable spectroscopic characterization and simultaneously study the effect of pH on the formation of immobilized PAR−Zn(II) complex, the sensors were immersed in Zn(II) solutions of two different concentrations (10.0 and 100.0 mg l$^{-1}$) prepared with buffers of pH ranging from 3.0 to 8.0. The correspondent spectra, as well as the ones referent to the sensor immersed on each buffer solution without zinc, were recorded in the wavelength range between 400 and 650 nm. The same study was carried out with 10.0 mg l$^{-1}$ solutions of other ions capable of forming complexes with PAR.

Area and porosity of the films were estimated by recording the nitrogen adsorption/desorption isotherms at 77 K on the full range (0.1) of relative pressure $P/P_0$. Surface area and total volume of pores were calculated directly based on the mass of adsorbent after adsorption versus pressure. Average pore diameter was calculated as (4 × volume/BET area). Scanning electron microscopy was used to examine the surface morphology of the sensors. Differences between the acid and base catalyzed films were confirmed by atomic force microscopy.

The extent of leaching was evaluated by immersing the sol−gel film doped with PAR repeatedly for 2 min intervals in 2.0 ml of buffer solution (pH 5.5). After each interval, the sensor was withdrawn and the absorbance of the solution registered at the wavelength of 410 nm (wavelength of maximum absorbance for PAR).

2.5. Flow system

The response time of the sensor films and their analytical performance were evaluated at the wavelength of 500 nm under flow conditions by incorporating two sensor layers in a home-made flow through cell with an internal volume of 240 μl (Fig. 1A) and by coupling it to a multicommutated flow system whose components were arranged as illustrated in Fig. 1B. Three-way solenoid valves $V_1$, $V_2$, $V_3$ and $V_4$ enabled the access of sample, carrier or regeneration solution by a programmed activation cycle (Fig. 1C). The sample flow through the mixing coil L placed before the detector was ensured by simultaneous activation of valves $V_1$ and $V_2$ during 100 s. In this time period, cycles ON/OFF lasting 4 s each were applied to each valve. In this way, a binary sampling of sample and carrier (acetate buffer solution, pH 5.5) allowed the insertion of small plugs of each solution, which after mixing in coil L were inserted in the flow cell containing the sensor layers for Zn(II) sensing. By selecting different ON/OFF time ratios, different sample/carrier dilutions...
could be produced. This procedure was used for calibration purposes resorting to one only zinc calibrating solution. Afterwards, valve V1 was activated continuously during 120 s for insertion of the regeneration solution (1 mol l$^{-1}$ KSCN, pH 3.0). Valve V4 enabled sample change by simultaneous activation with valve V1 for 10 s. Flow rate was fixed at 0.8 ml min$^{-1}$. The absorbance of the Zn(II)-immobilized PAR was recorded at the wavelength of 500 nm using a dual-color (green/red) LED and a photodiode.

The effect of foreign ions in the determination of Zn(II) using the system described above was studied by adding the potentially interfering ions to samples containing...
10.0 μg^{-1} Zn(II) in a ratio 1:10 (w/w) zinc:foreign ion. The degree of interference was recorded by recording the analytical signal in the presence and in the absence of the interfering ion.

3. Results and discussion

3.1. Evaluation of the sensors

The sol–gel process involves the hydrolysis of an alkoxide precursor under acidic or basic conditions, followed by polycondensation of the hydroxylated monomers to form a porous gel network. Afterwards, gel aging and drying can be conducted in order to obtain densified solid matrices. The rate, extent and even the mechanism of the reaction are profoundly affected and may be controlled by many factors such as pH, water:alkoxyde ratio (R), type of catalyst, solvent and precursor [19,20].

The effect of the type of catalyst on the matrix structure is very strong. Acid catalysis is the most frequently used method in the production of sol–gel optical sensors because it typically produces structures with higher durability, regular surface and less prone to leaching [28]. Under acid catalysis, gels composed of entangled linear chains and low pore volume matrices are formed [19,20,29] and so it was the first strategy adopted for the preparation of the sensor. Films F1, based on polymerization of tetraethoxysilane with nitric acid, presented good optical quality, with regular and homogeneous structure (Fig. 2A) and extremely low porosity (Table 2). Simultaneously, films F2 were produced with the same catalyst but by mixing TEOS with methyltriethoxysilane, in order to influence porosity and obtain a more stable structure in a short time. Taking in account that the sol–gel matrix undergoes structural changes, namely pore size reduction, long after gelation as occurred [19], the addition of a more hydrophobic precursor reduces the number of free silanol groups on pore walls, preventing further polymerization and shrinkage [30]. The spectroscopic characterization of these two types of acid-catalyzed films (F1 and F2) showed no reaction with zinc on any of the pH values tested. The same was observed even when other ratios of MTES:TEOS were tried. This fact may be attributed to two factors: (i) the low pore volume which may be insufficient for the Zn(II)–PAR complex establishment; (ii) the ionization of the para-OH group in the PAR molecule, which occurs in acidic medium and is not favorable for the metal chelates forming mechanism [13].

Table 2: Pore structure characterization of films F1 (acid-catalyzed) and F4 (base-catalyzed).

<table>
<thead>
<tr>
<th>Sensor</th>
<th>Surface area (m² g⁻¹)</th>
<th>Total volume of pores (cm³ g⁻¹)</th>
<th>Average pore diameter (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.0852</td>
<td>0.01759</td>
<td>9.48</td>
</tr>
<tr>
<td>F4</td>
<td>1.3299</td>
<td>0.02224</td>
<td>32.21</td>
</tr>
</tbody>
</table>

In order to increase porosity maintaining good optical quality, and at the same time enable the reaction between immobilized PAR and zinc, the co-polymerisation of 3-aminopropyltriethoxysilane and TEOS associated with a base-catalyzed sol–gel method was tested (films F3 and F4). By a basic mechanism, a highly porous matrix with a more open structure is produced [19] and a basic medium also seems to be positive to the complexation mechanism of PAR [13]. 3-APTES is one of the most frequently used organo-silane coupling agents for sensors, because it has excellent affinity for glass silanols and it also provides a means of bonding between organic indicators and inorganic substrates, improving the uptake of the dye into the sol–gel matrix [31]. It contributes to stabilize the film in a similar way to that intended by the use of MTES in film F2, since it possesses a hydrophobic amino-group that is not involved in the sol–gel reactions. More, addition of 3-APTES to the sol inherently decreases the network connectivity and a more open framework is formed, with easier diffusion of the analyte into the film [32]. However, acid catalysts lead to protonation of the amino-group and immediate precipitation of 3-APTES, resulting in cloudy and double-phased gels, unsuitable for optical applications. A basic catalyst, like TMAOH, allows optically transparent gels even with high concentrations of 3-APTES, and reduces long gelation times usually associated with the use of this precursor [33]. Therefore, the approach adopted in films F3 and F4 seemed to offer multiple and mutual advantages in the preparation of this particular sensor. The films obtained presented good optical transparency, similar to the acid-catalyzed sensors F1 and F2. However, the SEM and AFM results (Fig. 2) evidence the morphological differences between acid- and base-catalyzed mechanisms, demonstrating that the surfaces of films prepared with a basic catalyst and a mixture of two alkoxide precursors were rougher and more heterogeneous than those prepared with an acid.

Films F3, produced with 3-APTES as single precursor, as well as other films produced with 3-APTES:TEOS ratios higher than 1.3 (v/v), had good optical quality but poor mechanical resistance and presented extremely high leaching of PAR. They became immediately disrupted when immersed in buffer solution containing the analyte, even when leaching trials were performed after 1 month of film drying, which made impossible their spectroscopic characterization and analytical application. For films F4, with a 3-APTES:TEOS ratio of 1.3 (v/v), no significant leaching was registered even after long immersion times in buffer solution (Fig. 3), and so they were adopted for further studies.

Besides the type of catalyst and precursor, the amount of water has a strong influence on surface area and porosity, and it was also evaluated in this study. Theoretically, since water is one of the final products of the condensation reaction, a water:alkoxyde ratio (R) of 2 would be sufficient for complete hydrolysis and condensation. However, due to the formation of intermediate species, an excess amount of water is required [19]. An increase of R produces a decrease in
thickness, shrinkage and pore volume [34–36]. Films produced with \( R = 2 \) showed visible leaching when dipped in aqueous solution. So, \( R \) was adjusted to 4 in order to balance the high porosity typical of basic catalysis and polymerization of 3-APTES, and thus provide proper entrapment of PAR with minimal leaching.

The effect of the immobilized reagent amount was studied by using different initial concentrations of PAR, in the range 0.25–1.50 mg ml\(^{-1}\). The higher the reagent concentration, the higher was the absorbance signal obtained, but concentrations of PAR above 1.0 mg ml\(^{-1}\) disturbed the optical quality of the films and the homogeneous distribution of the dye. Therefore, the concentration of 1.0 mg ml\(^{-1}\) of PAR was adopted.

After establishing the composition of the sensor, the optimum response features were evaluated. As shown in Fig. 4, the absorbance spectrum of the film was similar to the one characteristic of PAR in bulk solution [11], with maximum absorbance around 410 nm, which evidences that the immobilization procedure did not affect significantly the chemical structure of the dye. It can also be seen that the formation of a complex with zinc causes a decrease of absorbance at 410 nm and the appearance of a new absorption band with a maximum at 500 nm, which was the wavelength adopted for analytical measurements. At the same wavelength the appearance of a band for copper and a small absorption due to Fe(II) and Fe(III) were observed.

The complex formation between metal ions and PAR is highly dependent on the pH of the solution, because it involves protonation and deprotonation of the ligand [13]. For films F4, the optimum pH value for complex formation between immobilized PAR and zinc was 5.5 (Fig. 5). At pH 7.0, higher response with 10.0 mg l\(^{-1}\) Zn(II) was observed, but extensive leaching occurred after the first utilization of the sensor, leading to large loss of sensitivity and reduction of the sensor’s lifetime. Moreover, much more intense absorption was registered due to formation of PAR–Cu(II) complex.

Regeneration of the sensor was accomplished with KSCN, which forms complexes with metals in acidic medium [8]. Short regeneration times with stable base line and no deterioration of the sensor’s lifetime were obtained using a
concentration of 1.0 mol l$^{-1}$ in KSCN with pH adjusted to 3.0 by addition of HCl to the solution.

Hence, sensors F4, based on co-polymerisation of TEOS with 3-APTES, basic catalysis, water:alkoxyde ratio ($R_o$) of 4 and PAR concentration of 1.0 mg ml$^{-1}$, were found to be the most suitable to be used as Zn(II) sensors in the proposed working conditions and were adopted for further studies in flow conditions and for real samples analysis.

3.2. Optimization of the flow manifold

In order to study the developed sensors in flow conditions, two slides of sensor F4 were placed inside a home-made flow-cell (Fig. 1A) and coupled to a multicommutated flow system (Fig. 1B). Calibration curves were enabled after alternate activation of valves $V_1$ and $V_2$ during 2 s each, thus allowing, respectively, the injection of zinc calibrating standards and buffer solution (pH 5.5). Prior to detection both solutions were mixed in the coil L both by convective transport and by molecular diffusion. By fixing the flow rate at 0.8 ml min$^{-1}$, it was observed that it was necessary to apply at least 25 ON/OFF cycles to each valve in order to assure maximum intensity signals. These corresponded to the differences between the absorbance of the PAR–Zn(II) complex monitored at its maximum absorbance wavelength, 500 nm, and the apparent absorption observed at a reference wavelength of 650 nm, due only to Schlieren noise [37]. Between measurements, the sensor was regenerated by flowing through the system 0.1 mol l$^{-1}$ KSCN solution when $V_3$ solenoid valve was activated. By assaying increasing time periods of valve activation it was concluded that for a 100 s period a complete regeneration of the sensor was accomplished. This time was much shorter than the corresponding period for other PAR-based sensors reported in the literature [18].

Typical analytical profile of the sensor’s response to Zn(II) in the proposed working conditions is presented in Fig. 6 and it shows that a linear response is obtained for concentrations of Zn(II) between 5.0 and 25.0 µg l$^{-1}$. The general regression equation \(A = 0.001 (\pm 1 \times 10^{-5}) \times [Zn(II)] + 0.0005 (\pm 2 \times 10^{-5})\) was obtained for five successive injections of five calibrating solutions, with a correlation coefficient of...
The described system was applied to the determination of zinc in injections of insulin available in the Portuguese market (Humulin Ultralenta®, Humulin Lenta®, Ultratard® and Monotard®). The results obtained for the samples examined (Table 3) with five replicate injections are in good agreement with the labeled information provided by the manufacturer and with the results obtained by AAS standard method, presenting deviation errors of results better than 1.2%.

4. Conclusions

The immobilization of PAR using a base-catalyzed sol–gel process in the presence of amino-groups proved to be advantageous over the acid-catalyzed method, providing a Zn(II) optical sensor with very high sensitivity, as well as good teaching characteristics and fast response. In addition, its insertion in a continuous flow system enabled very low detection limit, reagent economy, manifold simplicity and no need of complicated procedures before determination of the analyte. Moreover, the results obtained in the interfering ions study evidence the possible application of these sensors to the multi-determination of metals applied to environmental analysis.

Acknowledgements

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References


Table 3

Determination of zinc in injections of insulin

<table>
<thead>
<tr>
<th>Sample</th>
<th>Labeled Zn(II) amount (µg/ml)</th>
<th>Zn(II) found (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Proposed method</td>
<td>Standard AAS method</td>
</tr>
<tr>
<td>Humulin Ultralenta®</td>
<td>150</td>
<td>146.0 ± 1.9</td>
</tr>
<tr>
<td>Humulin Lenta®</td>
<td>150</td>
<td>148.9 ± 1.9</td>
</tr>
<tr>
<td>Ultratard®</td>
<td>149</td>
<td>145.1 ± 1.9</td>
</tr>
<tr>
<td>Monotard®</td>
<td>149</td>
<td>145.1 ± 1.9</td>
</tr>
</tbody>
</table>

0.9998. The apparent molar absorptivity was estimated as 3.4 × 10^3 1 mmol^-1 cm^-1, which is considerably higher than the one reported for the reaction in bulk solution [16] and for optrode schemes based on the immobilization of PAR in other polymeric supports [5]. This improvement in sensitivity was due to the extent of PAR amount that was possible to immobilize in a very short path length. The detection limit of 2.0 µg l^-1 was calculated from the standard deviation of the signals obtained by injection of a blank without analyte (3σ) [38]. A maximum sampling frequency of 16 samples h^-1 was achieved.

The useful lifetime of the sensor was estimated by consecutive injections of a solution containing 15.0 µg l^-1 Zn(II). After 120 determinations, the sensitivity of the sensor showed a reduction of 10%, and of 20% after 170 determinations. The long-term stability of the sensors was evaluated by testing them in flow conditions periodically. After 1 year of preparation, the films, stored at room temperature, maintained their analytical performance, which may be due to the stabilizing effect of 3-APTES.

Potential interference of Mg(II), Cd(II), Ni(II), Fe(II), Fe(III), Cu(II), Co(II) and Pb(II) was studied for the determination of 10.0 µg l^-1 Zn(II) using a ratio of foreign ion:Zn(II) of 10:1 (w/w). As expected, since PAR is a non-selective dye used for the analysis of several metals, some degree of interference was observed for these ions which resulted in the increase of the analytical signal registered, except for Fe(III) (+3.7%), Ni(II) (+7.4%) and Cd(II) (-3.7%). The most significant interference (above 25%) was from Pb(II), Fe(II) and Cu(II). However, these results did not impair the analytical application intended for these sensors in the proposed work (analysis of zinc in injectable insulins) and no masking procedures were necessary.

3.3. Analytical application

The system was applied to the determination of zinc in injections of insulin available in the Portuguese market (Humulin Ultralenta®, Humulin Lenta®, Ultratard® and Monotard®). The results obtained for the samples examined (Table 3) with five replicate injections are in good agreement with the labeled information provided by the manufacturer and with the results obtained by AAS standard method, presenting deviation errors of results better than 1.2%.


Biographies

Paula C.A. Jerónimo received her diploma in Pharmaceutical Sciences from the University of Porto, Portugal, Faculty of Pharmacy, in 2000. Currently, she is a PhD student in the Department of Physical-Chemistry of the Faculty of Pharmacy (UP). Her work is related to the development of optical chemical sensors and biosensors based on the sol–gel technology and their application to pharmaceutical and environmental analysis coupled to automated flow systems.

Alberto N. Araújo is currently an associated professor at the Department of Physical Chemistry of the Faculty of Pharmacy, University of Porto, Portugal. He obtained his PhD in pharmaceutical chemistry in 1994 at University of Porto, Faculty of Pharmacy, and he has been a lecturer in Instrumental Methods of Analysis at this school since 1991. His present research interests are on automation and development of sensors.

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