

## Determination of Penicillamine by Batch and Flow-injection Potentiometry with AgI-based Sensor

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Potentiometric determination of penicillamine (pen) is described based on a batch experiment and flow-injection analysis (FIA) using a chemical sensor with AgI-based membrane. The membrane was prepared by pressing silver salts (AgI, Ag<sub>2</sub>S) and powdered Teflon. This membrane was incorporated in a multipurpose electrode body for batch measurements, and in a tubular flow-through sensor body for FIA measurements. For batch measurements, the equilibrium potentials recorded with continuous addition of standard penicillamine solution were considered in relation to  $\lg(c_{\text{pen}}/\text{mol L}^{-1})$ . Linear response with slope of 60 mV was obtained in the concentration range from  $2.5 \times 10^{-5} \text{ mol L}^{-1}$  to  $1.8 \times 10^{-2} \text{ mol L}^{-1}$ . In using the tubular sensor with a membrane of the same composition for FIA measurements, the linear response with slope of 59 mV was recorded in the concentration range from  $1 \times 10^{-4} \text{ mol L}^{-1}$  to  $1 \times 10^{-1} \text{ mol L}^{-1}$ . The response of the applied chemical sensor to penicillamine (designated also as RSH) is explained by the formation of sparingly soluble RSAg in the reaction solution and/or on the exposed surface of the sensor. The solubility product  $K_s(\text{RSAg})$  was determined using experimental values recorded both by batch measurements and by the continuous-flow experiment. The mean value obtained by different measurements and using a membrane of the same composition is  $K_s(\text{RSAg}) = (1.4 \pm 0.1) \times 10^{-20} \text{ mol}^2 \text{ L}^{-2}$ .

*Key words:* batch potentiometry, flow-injection analysis, membrane electrode, tubular sensors, penicillamine.

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## INTRODUCTION

Thiol-containing compounds are often used as therapeutic substances. The most frequently used compounds are penicillamine and thiopronine. Penicillamine is applied in the treatment of Wilson's disease (accumulation of copper in organism),<sup>1</sup> and as antirheumatic drug.<sup>2</sup> Both compounds are efficient antidotes used against specific cases of heavy metal poisoning. As chelating agents, they turn heavy metal into complexes, thus enabling their excretion in urine.

Different methods dealing with penicillamine determination are found in literature. The various chromatographic techniques mostly involve application of chemiluminescence detection,<sup>3</sup> UV-spectrometry,<sup>4,5</sup> electrochemistry.<sup>6,7</sup> Some of the methods are based on classical potentiometry.<sup>8-10</sup> A relatively small number of works deal with determination of penicillamine by flow-injection analysis (FIA).<sup>11-14</sup> The cited FIA methods use spectrometric detectors<sup>11,12</sup> or detectors based on chemiluminescence.<sup>13,14</sup>

A survey of literature shows a lack of works that use potentiometric detectors in determination of penicillamine by FIA. The aim of this work was to develop a simple and inexpensive method of determining penicillamine by flow-injection potentiometry. Previous experience from our laboratory in determining compounds with sulphur by the classical potentiometric method (batch procedure)<sup>15</sup> and FIA analysis,<sup>16,17</sup> suggested the possibility of penicillamine determination by FIA and batch procedures using a detector based on the laboratory prepared potentiometric chemical sensor.<sup>18</sup>

## EXPERIMENTAL

### *Apparatus*

Schematic representation of the multi-purpose FIA system with tubular flow-through or cascade detector is shown in Figure 1. The sensor in tubular or cascade design combined with the reference electrode was incorporated in the flow-through system containing: a) the injection valve V-100, Tecator, Sweden; b) chemifold type II, Tecator, Sweden; c) peristaltic pump Minipols 2, Gilson, France; d) mV-meter MA 5740, Iskra, Slovenia; e) recorder, and f) personal computer which ensured continuous recording, storing and processing of data. The reference electrode used was Orion 90-02 double junction reference electrode (RE). All parts of the flow-through injection system were interconnected by inactive silicone tubing of 1.5 mm diameter.

Preparation of the tubular sensor with AgI-based membrane was described previously.<sup>17</sup> A 2.0 mm-diameter channel was drilled through the electrode center. The channel diameter and length determined the active sensor volume of approximately 4  $\mu$ L. The sensor was prepared using membranes of heterogeneous composition: a) AgI 25%, Ag<sub>2</sub>S 25% and PTFE 50%; b) AgI 22.7%, Ag<sub>2</sub>S 22.7%, PTFE 45.5% and Ag 0.9%

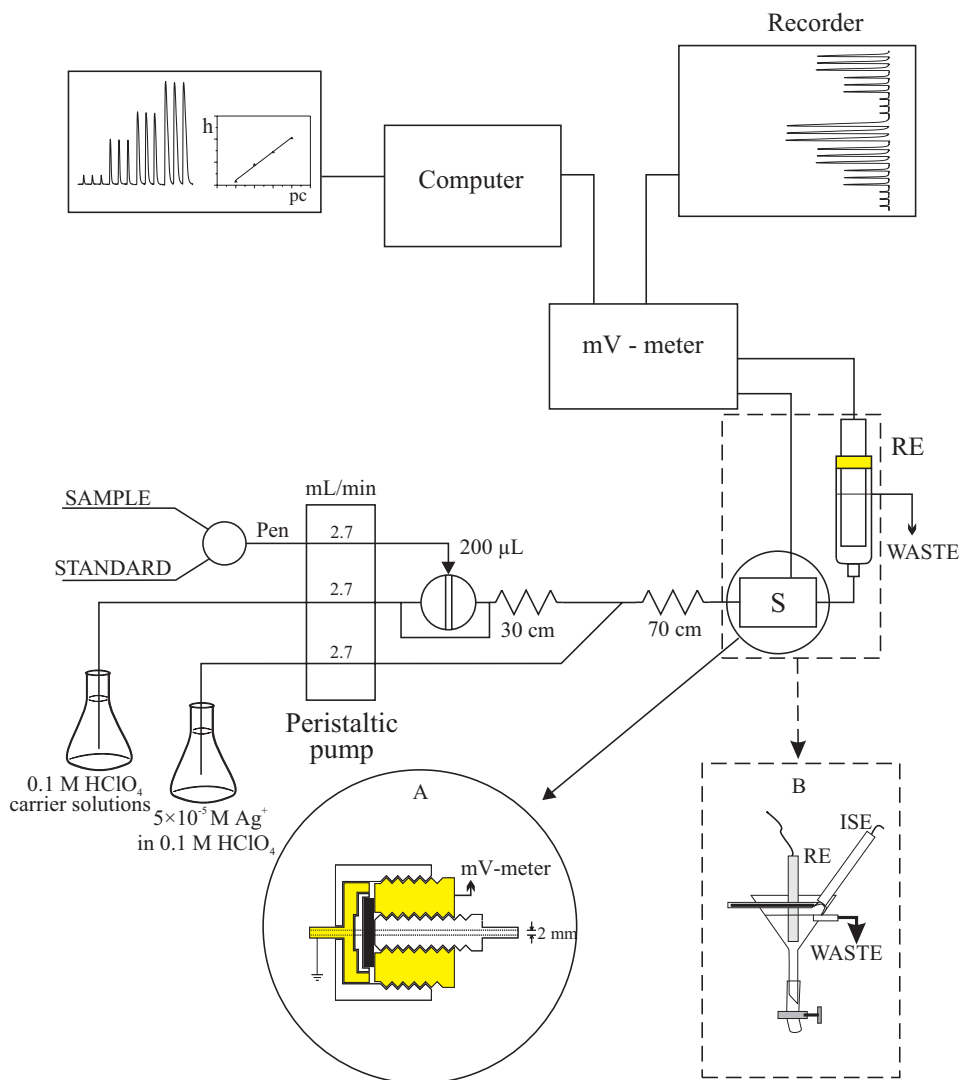


Figure 1. Manifold and flow diagram of the FIA system. S, sensor; RE, Orion 90-02 double-junction reference electrode; ISE, ion-selective electrode. A) The flow-through tubular sensor with AgI-based membrane hydrophobized by PTFE. B) The cascade flow cell with iodide-ion selective electrode (commercial or laboratory prepared) and a reference electrode.

(mass fractions,  $w$ ). The preparation procedure and the characteristics of membrane (a) were described earlier.<sup>18</sup> The same procedure was applied in preparing membrane (b) except that, in order to increase the conductivity, before pressing a certain percentage of powdered silver, Alfa, Division, Donvers, MA, USA was added into the

electrode material. In batch experiments, the prepared membranes were incorporated into the multi-purpose electrode body of laboratory design.<sup>18</sup> A double-walled thermostated reaction vessel, maintained at 298 K, was used for batch measurements.

### *Reagents*

All chemicals were of analytical-reagent grade and were used without further purification. All solutions were prepared with water that was doubly distilled in glass.

#### *Penicillamine Solutions*

The solutions of penicillamine (pen) were prepared by dissolving the necessary amount of penicillamine in perchloric acid,  $c(\text{HClO}_4) = 0.100 \text{ mol L}^{-1}$ . Stock solution of penicillamine,  $c(\text{pen}) = 0.100 \text{ mol L}^{-1}$ , was prepared by dissolving an appropriate amount of pen in  $0.100 \text{ mol L}^{-1}$  perchloric acid. Solutions with lower concentrations were obtained by diluting the stock pen solution with perchloric acid to the necessary concentration, while keeping the concentration of acid constant,  $c(\text{HClO}_4) = 0.100 \text{ mol L}^{-1}$ . The tested concentration range of penicillamine was from  $2 \times 10^{-5} \text{ mol L}^{-1}$  to  $1 \times 10^{-1} \text{ mol L}^{-1}$ .

#### *Silver Nitrate Solutions*

The standard silver nitrate solution was  $0.100 \text{ mol L}^{-1}$ . The solution of silver nitrate was prepared by dissolving an appropriate amount of silver nitrate in  $0.100 \text{ mol L}^{-1}$  perchloric acid. Solutions with lower concentrations of silver ion, including reagent solution in the FIA experiment, were obtained by diluting the stock silver solution with  $0.100 \text{ mol L}^{-1}$  perchloric acid.

#### *Buffer Solutions*

The applied basic buffer solution  $\text{pH} = 2.0$  was prepared by mixing acetic, boric and phosphoric acids of final concentrations  $4 \times 10^{-2} \text{ mol L}^{-1}$ . Buffer solutions with higher  $\text{pH}$  values were prepared by mixing the basic buffer solution with sodium hydroxide solution,  $c(\text{NaOH}) = 2.0 \text{ mol L}^{-1}$ .

### *Procedure*

#### *Batch Procedure*

The response of the electrochemical cell with different electrodes (membranes) to  $\text{Ag}^+$  ions was tested by the method of continuous decrease in the concentration of silver ions in the reaction vessel. Serial dilution  $0.100 \text{ mol L}^{-1}$  of the standard silver nitrate solution was performed using  $0.100 \text{ mol L}^{-1}$  perchloric acid. After decreasing the  $\text{Ag}^+$  ions concentration up to the concentration  $6.3 \times 10^{-6} \text{ mol L}^{-1}$  different volumes of standard penicillamine solution were added into the same perchloric acid solution of silver ions. This procedure was used in testing the response of the electrochemical cell to the increase of penicillamine concentration. All measurements were performed under constant mixing and at a temperature of 298 K.

#### *FIA Procedure*

The physical and chemical characteristics were optimized:  $2.7 \text{ mL min}^{-1}$  flow-rate, 200 L injection volume, 3-min injection frequency, injection time 30 s, carrier

solution  $0.100 \text{ mol L}^{-1}$  perchloric acid and reagent solution was  $5 \times 10^{-5} \text{ mol L}^{-1}$   $\text{AgNO}_3$ . In part of the experiment, designated as single-line FIA system, the reagent solution was omitted, and solution  $5 \times 10^{-5} \text{ mol L}^{-1}$   $\text{AgNO}_3$  was used as the carrier solution. Since both the sample and reagent solutions were prepared in  $0.100 \text{ mol L}^{-1}$  perchloric acid, the pH value remained constant. Besides testing the flow-through, the volume of injection, and the reactor length, we also examined different positions of the sensor in the FIA system. Both the tubular sensor (Figure 1-A) and the cascade flow sensor (Figure 1-B) were examined. The characteristics of the detector with the tubular sensor were described in a previous work.<sup>17</sup> With the cascade detector, the solution passes over the sensor surface area, thus creating continuous electrolytic contact with the solution in which the reference electrode is immersed.

## RESULTS AND DISCUSSION

### *Batch Measurements*

In this experiment, any of the electrodes used in combination with the reference electrode responds primarily to the activity of  $\text{Ag}^+$  ions in the solution or on the phase boundary surface membrane/solution, according to Nernst equation.<sup>16</sup>

$$E_1 = E'' + S \log c_{\text{Ag}^+} \quad (1)$$

As it has been discussed previously,<sup>16,17</sup> when a sample of penicillamine (designated also as RSH) is injected into the reaction solution in a sufficiently high concentration to cause precipitation of  $\text{RSAg}$ , the concentration of  $\text{Ag}^+$  ions will decrease, and the potential of the electrochemical cell will be determined by the analytical concentration of penicillamine in solution.

The response of the electrochemical cell with different indicator electrodes to the concentration of silver ions and the concentration of penicillamine is shown in Figure 2.

In the batch experiment, the response of all tested electrodes to penicillamine was linear in the concentration range of penicillamine  $2.5 \times 10^{-5} \text{ mol L}^{-1}$  to  $1.8 \times 10^{-2} \text{ mol L}^{-1}$ . The obtained experimental slopes of 60 mV, Figure 2-A, 57 mV, Fig. 2-B, 62 mV, Fig. 2-C, and 60 mV, Fig. 2-D, were in good agreement with the theoretical values.

### *Determination of Solubility Product of RSH*

Based on the experimental values of the potential, the constants of the solubility product,  $K_s(\text{RSH})$ , under chosen experimental conditions, were calculated by using the appropriate relation.<sup>16</sup> Quantities  $E''$  and  $S$  in the used equation were determined for each electrode used in the first part of

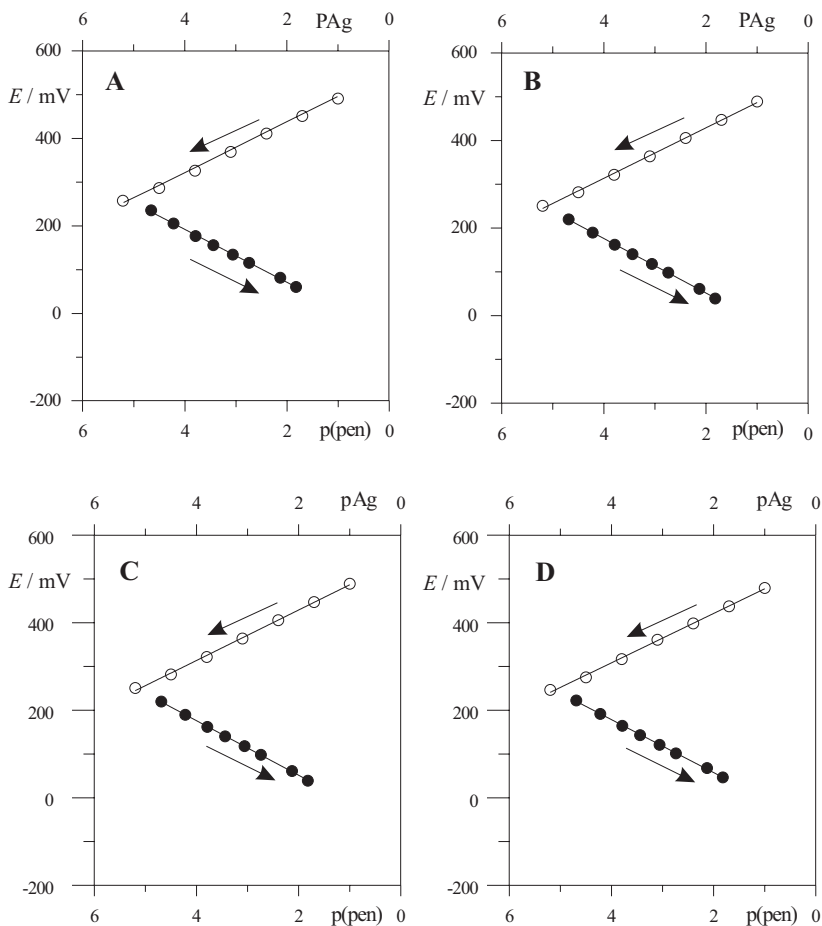


Figure 2. Response of the electrochemical cell with different indicator electrodes to silver ion (—○—) and penicillamine (—●—). A) Iodide electrode with heterogeneous membrane: AgI 25%, Ag<sub>2</sub>S 25% and PTFE 50% (mass fractions, *w*). B) Electrode with Ag-plate membrane. C) Commercial iodide electrode D) Commercial silver/sulphide electrode.

the experiment in which the concentration of Ag<sup>+</sup> ions was continuously diluted. Table I gives the constants of the solubility product obtained from experimental data recorded using a number of electrodes with heterogeneous membrane compositions.

#### Potential pH Response

The formation of RAg on the sensing part of the electrode and its effect on the electrode response to RSH in the contact solution were postulated and also discussed previously.<sup>16</sup>

TABLE I

Constants of the solubility product,  $K_s(\text{RSAg})$ , obtained by the use of different electrodes

Electrode used	$K_s(\text{RSAg})$
Laboratory prepared electrode with heterogeneous membrane composition (mass fractions, $w$ ): AgI 25%, Ag <sub>2</sub> S 25%, PTFE 50%	$1.3 \times 10^{-20} \text{ mol}^2 \text{ L}^{-2}$
Laboratory prepared electrode with Ag-plate membrane	$5.6 \times 10^{-20} \text{ mol}^2 \text{ L}^{-2}$
Commercial iodide electrode	$1.1 \times 10^{-20} \text{ mol}^2 \text{ L}^{-2}$
Commercial silver/sulphide electrode	$6.5 \times 10^{-21} \text{ mol}^2 \text{ L}^{-2}$

The theoretical potentials given in Figure 3, by curve  $E_1$ , were calculated using equation (1). Constant  $E''$  obtained from experimental values of the potential with continuous dilution of  $\text{Ag}^+$  ions (Figure 2-A) and the theoretical value of the change in potential with decade decrease (increase) of  $\text{Ag}^+$  ions concentration, 59 mV ( $\text{pAg}$ )<sup>-1</sup>, were taken into the account.

It is evident from the previous paper that the potential of the electrochemical cell in penicillamine solution of appropriate concentration will depend on the concentration of  $\text{H}^+$  ions in accordance with the following simplified expression:

$$E_2 = \text{constant} + 59 \text{ mV} \log \{K(\text{RSH}) + [\text{H}^+]\} \quad (2)$$

where the constant contains:  $E''$ ,  $K_s(\text{RSAg})$ ,  $c(\text{RSH})$ .

Using  $E''$  from previous calculations, the experimentally established constant of solubility product,  $K_s(\text{RSAg}) = 1.3 \times 10^{-20}$ , the dissociation constant of penicillamine<sup>2</sup>  $K(\text{RSH}) = 3.16 \times 10^{-11}$ , and applying equation (2) accordingly, the theoretical potentials for different pH values were calculated, and are given by curves  $E_2$  in Figure 3.

The calculated potential values shown in Figure 3 can be applied in estimating the detection limit of penicillamine by batch and FIA procedures. It is also evident that, at a constant concentration of penicillamine, the potential is changed by 59 mV per one pH unit change in acidity.

The influence of pH on the potential of the electrode with silver iodide-based membrane hydrophobized by PTFE was investigated experimentally for different concentrations of penicillamine. The pH was changed from 2 to 12 by mixing  $4 \times 10^{-2} \text{ mol L}^{-1}$  of acetic, boric and phosphoric acids with the necessary volume of 2 mol L<sup>-1</sup> sodium hydroxide.

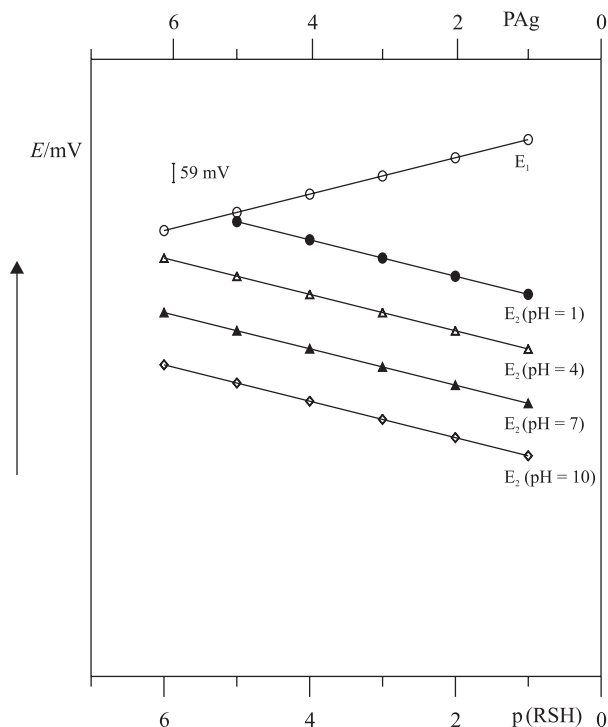


Figure 3. The calculated response of the electrode with a AgI-based membrane hydrophobized by PTFE to silver ion and penicillamine at different pH values.  $E_1$ , theoretical response to silver ion.  $E_2$ , theoretical response to penicillamine.

The pH response of the utilized electrode, for different concentrations of penicillamine, is shown in Figure 4. According to experimental data, the assumed response mechanism based on the formation of sparingly soluble RSAg was confirmed in a wide pH range up to  $\text{pH} \approx 7$ . Above this pH value, other reactions may possibly occur in the solution and/or on the sensing part of the membrane, which disturb the assumed response mechanism. Application of the utilized electrode enables determination of penicillamine in a wide pH range, but the pH of reaction solutions should be kept constant.

### FIA Experiment

#### Optimization of the Flow Injection Analysis System

Parameters of the FIA system were varied in order to maximize the dynamic range, the precision and the sampling rate. The flow rate and the sampling volume were varied as shown in Figure 5. The response of the detector with potentiometric sensor in FIA can be greatly affected by the de-



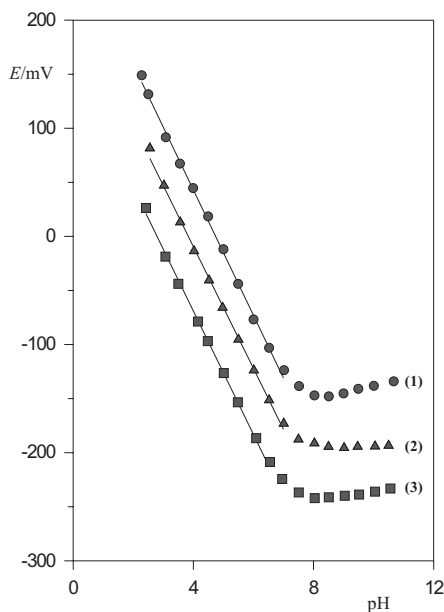


Figure 4. Potential–pH response of the electrochemical cell with a AgI-based membrane hydrophobized by PTFE in solution with penicillamine. The concentrations of penicillamine are (1)  $1 \times 10^{-4}$ ; (2)  $1 \times 10^{-3}$ ; (3)  $1 \times 10^{-2}$  mol L<sup>-1</sup>.

sign, contact surface and active volume of the constructed unit. The tubular electrode with an internal diameter of 2.0 mm and the sensing area length 1.2 mm gave better results than the cascade detector with selective electrode (Figures 1-A and B). Also, the FIA system with carrier solution (0.1 M HClO<sub>4</sub>) and reagent solution ( $5 \times 10^{-5}$  M Ag<sup>+</sup> in 0.1 M HClO<sub>4</sub>) gave better results than the single-line FIA system where reagent solution serves as carrier solution. Reagent concentration of  $5 \times 10^{-5}$  mol L<sup>-1</sup> silver nitrate was chosen as the compromise between the sampling rate, linear dynamic range and lower detection limit. For all FIA measurements, the sensor with AgI-based membrane hydrophobized by PTFE {AgI 25%, Ag<sub>2</sub>S 25% and PTFE 50% (mass fractions, *w*)} was used.

#### *Linear Response Range*

For the determination of penicillamine, we used a two-channel FIA system. The reagent stream contains silver ions in 0.1 mol L<sup>-1</sup> perchloric acid, while the carrier stream is 0.1 mol L<sup>-1</sup> perchloric acid into which the sample containing penicillamine is injected. The tubular electrode and the reference electrode are located downstream after mixing the two channels.

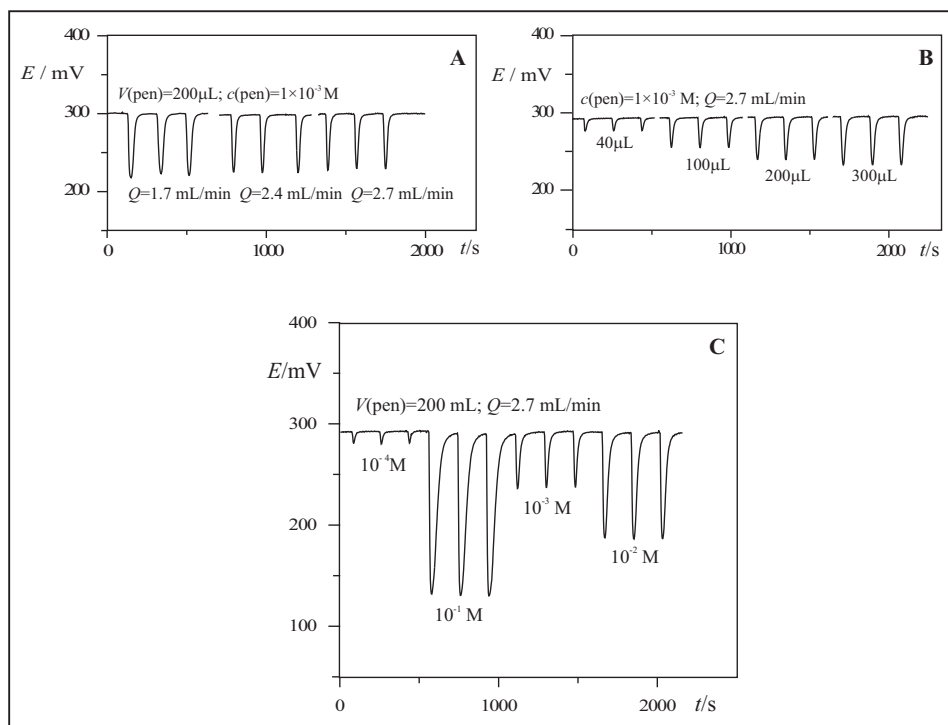


Figure 5. Response of the tubular sensor with AgI-based membrane to penicillamine. A) Constant sample volume and concentration but different flow rate ( $Q$ ). B) Constant sample concentration and flow rate but different sample volume. C) Constant sample volume and flow rate but different sample concentration.

As discussed previously,<sup>16</sup> if dilution of reagent solution ( $m$ ), dilution and dispersion of the sample ( $d$ ), pH of solutions and concentration of reagent solution are kept constant, we can expect a linear dependence between the peak height and the logarithm of penicillamine concentration in the injected sample. The peak height is determined by the following simple relation

$$h = S \{K + c(\text{pen})\} \quad (3)$$

where  $K$  denotes the constant depending on the solubility product of the formed silver salt (RSAg), the dissociation constant of penicillamine,  $\{K(\text{RSH})\}$ , and on experimental quantities:  $m$ ,  $d$ , pH.

The data given in Figures 5-C and 6 show the typical response of the tubular sensor with a AgI-based membrane to penicillamine. It is evident

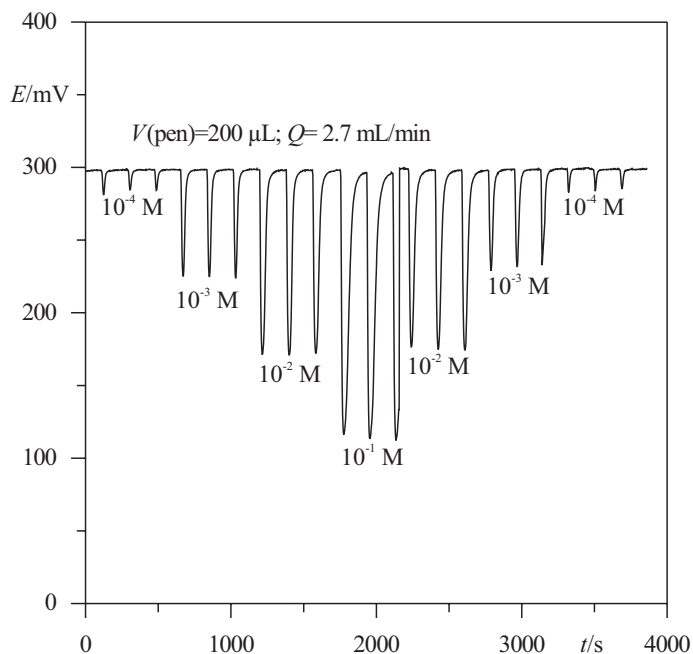


Figure 6. Recording of peaks obtained for injection of penicillamine into a carrier stream. Two-line FIA system was applied. Experimental conditions are as follows: flow rate,  $2.7 \text{ mL min}^{-1}$ ; injection volume,  $200 \text{ }\mu\text{L}$ ; carrier stream,  $0.100 \text{ mol L}^{-1} \text{ HClO}_4$ ; reagent,  $5 \times 10^{-5} \text{ mol L}^{-1} \text{ Ag}^+$ ; carrier/reagent ratio, 1/1.

from the figures that a change in potential of the flow-injection system with the tubular potentiometric detector, under optimized conditions, follows the change of penicillamine concentration in the injected sample. The obtained peaks are sharp and reproducible. The signal return to the base line is achieved within three minutes even with the highest concentrations of penicillamine, while with the lower sample concentrations this time is even shorter.

When the recorded signal heights in mV are plotted to the negative logarithms of penicillamine concentration in the injected sample (Figure 6), we obtain the value of  $58.9 \text{ mV}$  for the injected rising series of penicillamine concentrations or a slightly lower value of  $55.6 \text{ mV}$  for the injected falling series of penicillamine concentrations. The recorded changes in potential are in good agreement with the theoretical value of  $59 \text{ mV}$  for monovalent active ions, which supports the assumed mechanism of signal formation.

In one part of the experiment of constructing the tubular sensor, we used the membrane prepared by adding powdered silver before pressing (membrane composition is designated with »b« in the experimental part).

Applying this membrane in FIA measurements gave no evidence of any differences in the signal.

In using the single-line FIA system, where the sample is injected into the carrier solution containing  $\text{Ag}^+$  ions, the sparingly soluble RSAg is formed by diffusion in the zone of the injected sample and/or at the surface of the sensing part of the membrane. In these experimental conditions, the dynamic characteristics of the sensor response depend not only on the constant of the solubility product of silver salt RSAg but also on the share of the processes of diffusion, adsorption and desorption taking place at the membrane surface, as well as on the kinetics of RSAg formation. Furthermore, the dynamics of the response curve also depends on the reactor length, *i.e.* on the length of the tubing from the point of injection to the detector. In optimizing the measuring system, it is necessary to optimize not only the length of the path but also the flow rate, *i.e.* the tubing diameter, in order to achieve good mixing and the time required for the formation of sparingly soluble RSAg.

In the experimental application of the single-line FIA system (Figure 7-A), the peaks are sharp and reproducible but the signal returning to the base line is slightly slower than in the two-line FIA system.

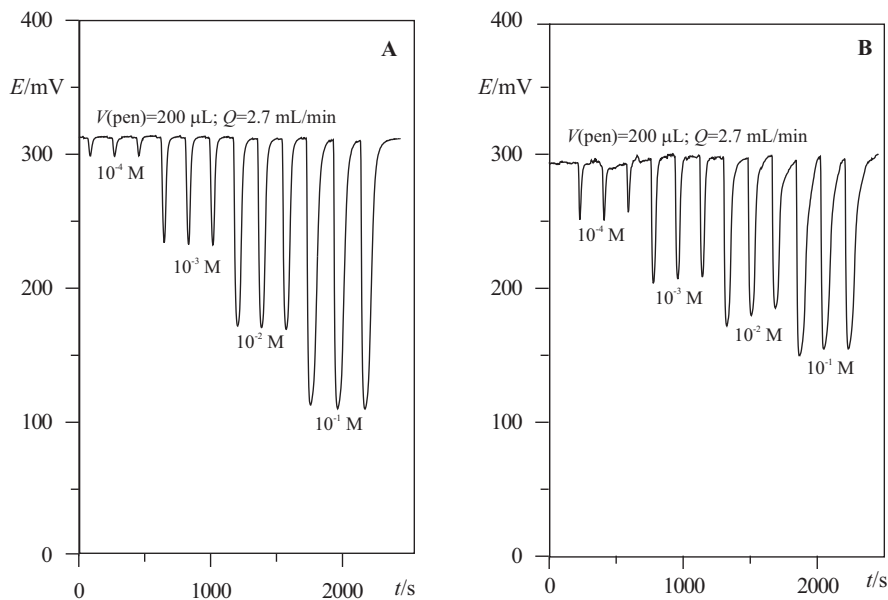


Figure 7. Recording of peaks obtained for injection of penicillamine into a carrier stream. A) Single-line FIA system with the tubular sensor with  $\text{AgI}$ -based membrane was applied. B) Two-line FIA system with the cascade flow cell with iodide-selective electrode was applied.

In the two-line FIA system, when applying the cascade flow cell design with commercial iodide-selective electrode instead of the detector with tubular sensor, the peaks are irreproducible and the signal return to the base line is slow (Figure 7-B).

According to the measurement results, the described two-line FIA system with potentiometric tubular sensor with AgI-based membrane enables determination of penicillamine in a wide pH range. Linear dependence between the recorded signal and the concentration is established, at pH = 1, in the concentration range of penicillamine from  $1 \times 10^{-4}$  mol L<sup>-1</sup> to  $1 \times 10^{-1}$  mol L<sup>-1</sup>.

Since penicillamine contains a sulfhydryl group which is readily oxidized in basic and moderately acidic media, the strong acid solution ( $1 \times 10^{-1}$  mol L<sup>-1</sup> HClO<sub>4</sub>) was chosen as the carrier solution for penicillamine determination.

According to theoretical considerations (Figure 3) and to experimental testing (Figure 4), it is important to emphasize the parallel reaction of penicillamine with H<sup>+</sup> ions in the determining penicillamine and in defining the limit of detection. The results of calculations and measurements lead to the conclusion that, with higher pH values, the detection limit of penicillamine by using FIA method can be moved below the value of  $10^{-4}$  mol L<sup>-1</sup> concentration.

Keeping the analytical concentration of Ag<sup>+</sup> ions, in order to maintain the stability of the base line, at the level applied in this experiment ( $5 \times 10^{-5}$  mol L<sup>-1</sup>), the shift to determination of lower concentrations of penicillamine should be looked for in transforming Ag<sup>+</sup> ions into an appropriate complex, in the FIA system before mixing with the carrier solution or with the injected sample. Our further investigations are aimed at finding the experimental conditions for extending the linear dynamic range of the tubular sensor detector toward lower concentrations of penicillamine.

#### *Determination of the Solubility Product of RSAg*

When applying in the experiment a continuous flow of standard penicillamine solution instead of the flow-injection technique, the dispersion of the penicillamine sample can be neglected and the potential of the signal will reach a stable value  $h'$  after an appropriate flow time. Based on an experimental value and with a fixed known concentration of H<sup>+</sup>, it is possible to calculate  $K_s(\text{RSAg})$  using the following expression:

$$\begin{aligned} \log K_s(\text{RSAg}) = \\ = \log c(\text{Ag}^+) + \log c(\text{RSH}) - \log \left( \frac{K(\text{RSH}) + [\text{H}^+]}{K(\text{RSH})} \right) + 2 \log m - \frac{h'}{S} \end{aligned} \quad (4)$$

Constant  $m$  depends on the flow rate in the channels before and after mixing, and can be calculated referring to our previous work.<sup>19</sup> Since in this work the flow rates before mixing were the same ( $2.7 \text{ mL min}^{-1}$ ), the calculated constant  $m$  is 0.5.

The  $h'$  values were determined on the basis of experimental results obtained with four different concentrations of penicillamine. The solubility constant  $\text{RSAg}$  is calculated using equation (4).

The calculated mean value of  $K_s(\text{RSAg}) = 1.5 \times 10^{-20} \text{ mol}^2 \text{ L}^{-2}$  is in good agreement with the value obtained by batch measurements, using a membrane of the same composition (see Table I).

In conclusion, the proposed FIA method is a simple and rapid way for determining penicillamine in the concentration range from  $1 \times 10^{-4} \text{ mol L}^{-1}$  to  $1 \times 10^{-1} \text{ mol L}^{-1}$ . In batch experiments, the response of all tested electrodes to penicillamine was linear in the concentration range from  $2.5 \times 10^{-5} \text{ mol L}^{-1}$  to  $1.8 \times 10^{-2} \text{ mol L}^{-1}$ . The described two-line FIA system with the potentiometric tubular sensor with AgI-based membrane gave better results than the single-line system, where reagent solution serves as carrier solution. Also, this configuration enables determination of penicillamine with good accuracy and reproducibility, but the described method was less sensitive than the FIA methods, cited in this paper, with spectrometric detectors or detectors based on chemiluminescence.

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## SAŽETAK

### Određivanje penicilamina primjenom klasične i protočno-injekcijske potenciometrije

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Opisano je potenciometrijsko određivanje penicilamina (pen) primjenom klasične potenciometrije i protočno-injekcijske analize (FIA) uporabom kemijskog senzora s membranom na osnovi AgI. Membrana, pripravljena prešanjem soli srebra (AgI, Ag<sub>2</sub>S) i Teflona u prahu, ugrađena je u višenamjensko tijelo elektrode za klasična potenciometrijska mjerenja, odnosno u tijelo protočnoga cjevastog detektora za FIA. Ravnotežni potencijali, zabilježeni pri uzastopnim dodatcima standardne otopine penicilamina kod klasične potenciometrije, stavljeni su u odnos prema  $\lg(c_{\text{pen}} / \text{mol L}^{-1})$ . Linearni odziv s nagibom od 60 mV dobiven je u koncentracijskom području od  $2,5 \times 10^{-5} \text{ mol L}^{-1}$  do  $1,8 \times 10^{-2} \text{ mol L}^{-1}$ . Pri uporabi cjevastog senzora s membranom istog sastava kod FIA-mjerenja zabilježen je linearni odziv s nagibom 59 mV u koncentracijskom području od  $1 \times 10^{-4} \text{ mol L}^{-1}$  do  $1 \times 10^{-1} \text{ mol L}^{-1}$ . Odziv korištenog kemijskog senzora prema penicilaminu (označen i kao RSH) protumačen je nastajanjem teško topljivog RSAg u reakcijskoj otopini ili/i na izloženoj površini senzora. Na temelju eksperimentalnih vrijednosti zabilježenih pri mjerenjima primjenom klasične potenciometrije i eksperimenta s kontinuiranim protokom kroz cjevasti senzor određen je produkt topljivosti  $K_s(\text{RSAg})$ .

Dobivena srednja vrijednost različitih mjerenja s membranom istog sastava jest:  $K_s(\text{RSAg}) = (1,4 \pm 0,1) \times 10^{-20} \text{ mol}^2 \text{ L}^{-2}$ .