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A KINETIC METHOD FOR THE DETERMINATION OF SELENIUM(IV) IN PHARMACEUTICAL PREPARATION

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A kinetic method is described for the determination of Se(IV) based on its inhibiting effect on the phosphate catalysis of the oxidation of pirogallol by dissolved oxygen. The detection limit of this method is 35 $ng \cdot cm^{-3}$. The relative error ranges between 1.7–5.7% for the concentration interval 0.4–2.37 $\mu g \cdot cm^{-3}$. Kinetic equations are proposed for the investigation process. The interference effect of several species was also investigated, and it was found that the most common cations and anions do not interfere with the determination. The method was applied for the determination Se(IV) in pharmaceutical samples.

INTRODUCTION

Selenium is a ubiquitous trace element that is essential to life at sub-per-million (ppm) levels.[1,2]

Many analytical methods have been developed for the determination of selenium (IV), but the majority of them suffers of poor selectivity through having high sensitivity. Spectrophotometric, fluorometric, voltammetric, and X-ray fluorescence analysis methods have been also successfully employed to determine selenium levels in blood, tissue, and human hair. Of these, fluorometric methods are the most commonly used. The reaction of selenium(VI) with 2,3-diaminonaphthalene (DAN) or with 3,3-diaminobenzidine (DAB) to form a fluorescent Se-DAN or Se-DAB heterocyclic compound is the basis of the fluorometric method of selenium determination. The piazselenol formed with DAN as reagent has a greater fluorescence sensitivity than the piazselenol formed with DAB as reagent and is also extractable into organic solvents from acid solution.[3,4] Fluorometric techniques require sample digestion to destroy organic matter and sample reduction to convert the selenium to the selenium(IV) oxidation state. Hydride-generation AAS is the most sensitive AAS technique for Se and has been extensively applied to biological materials, although some metals can interfere with formation of H_2S gas.[5] Anodic stripping voltammetry[6] and high performance liquid chromatography[7] have been also used for the determination of selenium(IV) with high sensitivity and selectivity, but are more or less time consuming procedures requiring expensive and complicated instrumentation.

In order to overcome these problems a successful attempt was made at developing and validating a rapid, sensitive and selective kinetic method for the determination of selenium(IV) in pharmaceutical samples.

A new kinetic method for the determination of Se(IV), with detection limit of 35 $ngcm^{-3}$, is described in this paper. The oxidation of pirogallol by dissolved oxygen in a perchloric acid solution gives a colored product.[8] The reaction is catalyzed by traces of phosphate. We have observed that small amounts of Se(IV) strongly inhibit the catalysis of this reaction by phosphate. The rate of the reaction is inversely proportional to the Se(IV) concentration. This fact was used as the basis of a kinetic method for the determination of micro amounts of Se(IV).

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EXPERIMENTAL

Apparatus

A spectrophotometric method was used to follow the investigated reaction rate. The dependence of the absorbance (A) on the time (t) was measured using a Perkin-Elmer Lambda 15 Spectrophotometer, connected to a thermocirculating bath. The pH was measured by means of a Radiometer pHm 29b pH meter and a combined glass-calomel electrode, G K 2311 C. The solution were thermostatted at 25 ±∈0,1°C before beginning of the reaction.

The tangent method was also applied to determine Se(IV) in the two pharmaceutical preparations specified above. The reproducibility was very good. The results obtained by the proposed method also agreed well with the values claimed on the labels.

Reagents

All chemicals were of analytical reagent grade and were provided by Merck unless indicated otherwise. Solutions were prepared in doubly distilled water.

Pirogallol solution ($1\cdot10^{-2}$ moldm^{-3}) was prepared by dissolving pyrogallol in about 2 cm^3 of 0.01 moldm^{-3} $HClO_4$, and the solution obtained was diluted to 100 cm^3 with doubly distilled water. A stock solution of doubly distilled water perchloric acid solution (0,12 moldm^{-3}) was prepared from 70% reagent. The solution of Se(IV) was prepared by dissolving sodium selenite anhydrous in water.

All the stock solution were stored in polyethylene containers. Working solutions of phosphate and pyrogallol were prepared immediately before use.

All the polyethylene containers and glass wake used were cleaned with aqueous HCl(1:1) and then thoroughly rinsed with doubly distilled water.

Procedure

Selected volumes of the reactants first pyrogallol then perchloric acid, $NaClO_4$, inhibitor were put into a 10 cm^3 standard flask. Water was added to the predetermination volume. The flask was first thermostatted for 10 min, and then the vessel was filled up to the mark with phosphate solution and vigorously shaken. The cell on the spectrophotometer was rinsed well and filled with solution. Absorbance (A) was measured every 30 s for 5–6 min, as zero time the moment of phosphate solution addition was checked. The measurements were made at 25±0,1°C.

The pharmaceutical samples for analysis were prepared by the following procedure. To the mass of five capsules add 5 cm^3 of a mixture (2:1) conc. HNO_3 and $HClO_4$. The mixture was heated until the evaluation of nitrogen oxides ceases and white smoke of $HClO_4$, developed. The procedure was repeated by another addition of a further 2 cm^3 of acidic mixture to the sample. Add 2 cm^3 of the mixture to previous mixture and repeat the proceeding. The obtained solution must be colorless after complete dissolution of the tablets. A long heating time was required because Se(IV) can be oxidized to Se(VI) which is inactive. The adjusted pH was between 5.5–6.0. The obtained solution was diluted with distilled water to the 50 cm^3.[9]

RESULTS AND DISCUSSION

Pirogallol solution in the presence of perchloric acid is very slowly oxidized in air at room temperature by atmospheric oxygen. However the oxidation of pirogallol by dissolved oxygen in the presence of phosphate acid medium is characterized by the occurrence of a slight absorption maximum at 300 nm, which significantly increases with time. Therefore it can be concluded that phosphate acts as a catalyst in the oxidation of pirogallol by dissolved oxygen. The presence of small amounts of Se(IV) strongly inhibits the catalysis of this reaction by phosphate.

The reaction rate was estimated from the changes of the tangent of angle (tanα) between the slope of the linear part of the kinetic curve and the abscissa of the coordinate system A-t.[10] The optimum reaction concentrations were determined by estimating the concentration effects of the reactants in the mixture where concentration of one of reactants was varied and concentrations of the others were kept constant. Therefore, the dependencies of the rates of both the catalytic and inhibited reactions of the concentration of each reactant are given in Table 1.

Under the optimal reaction conditions:

$c_{HClO_4} = 1.8\cdot10^{-5}$ mol·dm^{-3}, $c_{Phosphate} = 3.0\cdot10^{-5}$ mol·dm^{-3}, $c_{Pg} = 1.0\cdot10^{-3}$ mol·dm^{-3}, $c_{NaClO_4} = 0.1$ mol·dm^{-3},

the selenium concentration was varied from 0.4–2.37 μgcm^{-3}. (Fig. 1)

Table 1

Summary of the kinetic data for the oxidation of pirogallol by dissolved oxygen in the presence of phosphate in acid medium catalyzed by Se(IV)

Variable and concentration range	Partial order for catalyzed reaction	Partial order for catalyzed reaction
$1.2 \cdot 10^{-5}\,\text{mol} \cdot \text{dm}^3 < c_{\text{HClO}_4} < 3.6 \cdot 10^{-5}\,\text{mol} \cdot \text{dm}^{-3}$	–0.25	–0.5
$0.66 \cdot 10^{-5}\,\text{mol} \cdot \text{dm}^3 < c_{\text{Pg}} < 1.66 \cdot 10^{-5}\,\text{mol} \cdot \text{dm}^3$	+1	+1
$0.166 \cdot 10^{-5}\,\text{mol} \cdot \text{dm}^3 < c_{\text{Pg}} < 2.66 \cdot 10^{-5}\,\text{mol} \cdot \text{dm}^3$	0	0
$1 \cdot 10^{-5}\,\text{mol} \cdot \text{dm}^3 < c_{\text{phosphate}} < 6 \cdot 10^{-5}\,\text{mol} \cdot \text{dm}^3$	+1	+1

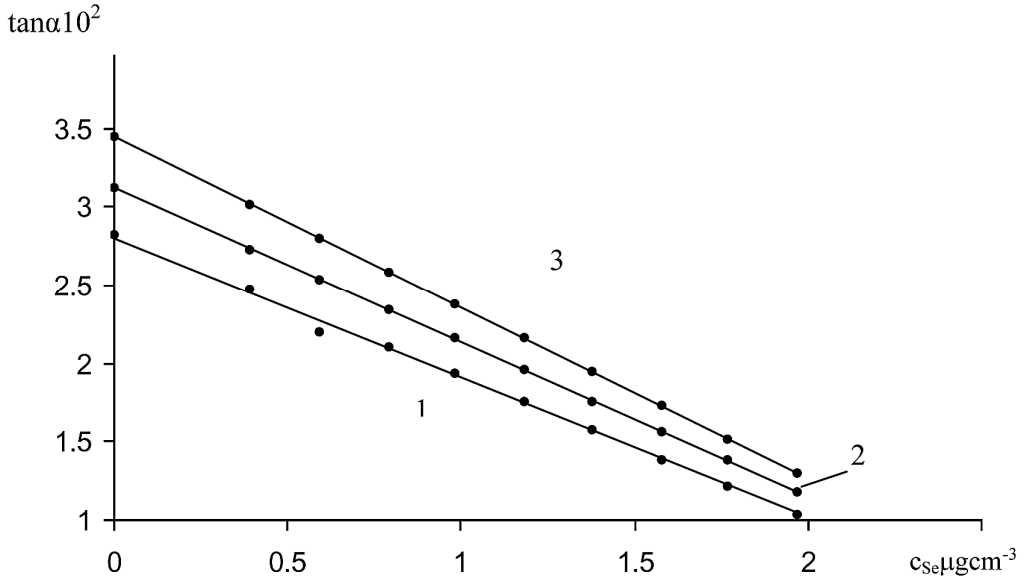

Fig. 1 – Dependence of the rate of the Se(IV) concentration. Initial concentrations: $c_{\text{HClO}_4} = 1.8 \cdot 10^{-5}$ mol·dm^{-3}, $c_{\text{phosphate}} = 3.0 \cdot 10^{-5}$ mol·dm^{-3}, $c_{\text{Pg}} = 1.0 \cdot 10^{-3}$ mol·dm^{-3}, $c_{\text{NaClO}_4} = 0.1$ mol·dm^{-3}, curve 1 at $t = 25 \pm 0.1$°C, curve 2 at $t = 28 \pm 0.1$°C, curve 3 at $t = 31 \pm 0.1$°C.

The equations of line and recovery (r) for the determination of selenium(IV) in the interval mentioned were calculated at the three temperatures

$$\tan \alpha = -9.0 \cdot 10^{-3} \cdot C_{\text{Se}} + 0.0282, \quad r = 0.996 \text{ at } 25 \pm 0.1\text{°C} \tag{1}$$

$$\tan \alpha = -9.8 \cdot 10^{-3} \cdot C_{\text{Se}} + 0.0312, \quad r = 0.998 \text{ at } 28 \pm 0.1\text{°C} \tag{2}$$

$$\tan \alpha = -10.9 \cdot 10^{-3} \cdot C_{\text{Se}} + 0.0345, \quad r = 0.995 \text{ at } 31 \pm 0.1\text{°C} \tag{3}$$

The following kinetic equations[11] for the investigated process were deduced on the basis of the graphic correlations. For the catalytic reaction:

$$\frac{\text{d}c}{\text{d}t} = k_1 \cdot c_{\text{HClO}_4}{}^{-0.25} \cdot c_{\text{Pg}} \cdot c_{\text{phosph.}}, \quad \text{for} \quad c_{\text{Pg}} < 1.66 \cdot 10^{-5}\ \text{mol} \cdot \text{dm}^{-3}, \tag{4}$$

where k_1 is a constant proportional to the rate constant of the catalyzed reaction.

$$\frac{\text{d}c}{\text{d}t} = k_2 \cdot c_{\text{HClO}_4}{}^{-0.50} \cdot c_{\text{Pg}} \cdot c_{\text{phosph.}} \cdot c_{\text{se}}{}^{-1}, \quad c_{\text{Pg}} < 1.66 \cdot 10^{-5}\,\text{mol} \cdot \text{dm}^{-3} \tag{5}$$

where k_2 is a constant proportional to the rate constant of the inhibited reaction.

From the results obtained the kinetic equation is proposed for pirogallol concentration lower than $1.8 \cdot 10^{-5}$ mol·dm^{-3}, the conditional rate constants were calculated for three different temperatures.

Table 2

Conditional rate constants for catalyzed and inhibited reactions at the three temperatures

T(K)	$k_1 \cdot 10^4$ (mol$^{-0.75}$ dm$^{2.25}$ min^{-1})	$k_2 \cdot 10^{-2}$ (mol$^{0.50}$ dm$^{-1.50}$ min^{-1})
298	5.87	1.76
301	6.43	1.97
304	7.06	2.19

The linear relationship between the logarithm of the relative rate constant and the reciprocal of the absolute temperature were found for the catalytic as well as the inhibited reaction. The activation energies were found to be 21.05 kJ·mol^{-1} for the catalytic and 27.75 kJ·mol^{-1} for the inhibited reaction.

The minimum concentration of Se(IV) that could be determined by this method may be calculated by the method given by Yatsimirskii.[12]

$$c_{\min} \geq 0.1 \cdot \frac{k_2 \cdot c_{\mathrm{HClO_4}}^{-0,5}}{k_1 \cdot c_{\mathrm{HClO_4}}^{-0.25}}, \quad (6)$$

By entering these values in the previous equation we find that $c_{\min} \geq 0.44 \cdot 10^{-5}$ mol·dm^{-3} or 35 ng·cm^{-3}.

The precision of the proposed method was evaluated using an ordinary statistical study, under 95% probability level and expressed by the confidence interval of each sample.[12] The relative error ranges from 1.7–5.7% in the Se(IV) concentration range 0.4–2.37 μgcm^{-3}.

To assess the selectivity of the method, the influence of several foreign ions on the rate of the inhibited reaction rates was studied at a constant Se(IV) concentration of 1.58 μg·cm^{-3}. It may be seen that Ba(II), Sr(II), Ca(II), Mg(II), tartarate, acetate, in a 100:1 ratio with Se(IV) and Ni(II), Zn(II), Mn(II),Cu(II), Fe(III), Al(III), Br^-, J^-, F^-, MoO_4^- in a 10:1 ratio with Se(IV) interfere with the reaction. As^{3+}, HCO_3^- and $C_2O_4^{2-}$ in a 1:1 ratio with Se(IV) interfere with the reaction.

Determination of Se(IV) in pharmaceutical preparations

The developed method was directly applied to the determination of Se(IV) in the following pharmaceutical preparations:

a) OLIGOGAL-Se----tablets ICN-Galenika

b) Coenzyme Q--------tablets Life Production Inc.Farmington, Conecticut 06032, SAD

A comparison of the proposed procedure with other procedures is given in Table 3.

Table 3

A comparison of the proposed method with other methods for the determination of Se(IV)

Type of sample	Analytical method	Sample detection limit	Reference
plant	gravimetric[13]	$2 \cdot 10^{-6}$ g/g	AOAC 1984, method 3.101
plant	fluorimetric[14]	$4 \cdot 10^{-6}$ g/g	AOAC 1984, method 3.102-3.107
marine samples	HGAAS[15]	$2 \cdot 10^{-7}$ g/g	Wang 1986
eggs and liver	GFAAS[16]	$4 \cdot 10^{-7}$ g/g	Dedina 1987
organic waste	cathodic stripping[17]	$5 \cdot 10^{-7}$ g/g	
biological samples	HPLC/fluorescence determination[18]	$5 \cdot 10^{-10}$ g/g	Hawkes,1996

(continues)

Table 3 (continued)

Type of sample	Analytical method	Sample detection limit	Reference
help care product	kinetic method toluidine blue+Na_2S[19]	$1.5 \cdot 10^{-6}$ g/mL	Afchami A., Safavi A., 1992
help care product	kinetic method Hydrazine+$KBrO_3$[20]	$5 \cdot 10^{-7}$ g/mL	Parham H, Shamsipur, 1991
help care product	kinetic method sodium benzoate-Fe(III)-H_2O_2[21]	$6 \cdot 10^{-8}$ g/mL	S. S. Mitić *et al.*, 1999
help care product	kinetic method	$3.5 \cdot 10^{-8}$ g/mL	present paper

HGAAS-hydride generation atomic apsorption spectroscopy,
GFAAS-graphite furnance atomic apsorption spectroscopy.

CONCLUSIONS

Anodic stripping voltammetry and high performance liquid chromatography have been also used for the determination of selenium(IV) with high sensitivity and selectivity, but are more or less time consuming procedures requiring expensive and complicated instrumentation. Some kinetic methods for determination of trace levels have been also published using various types of indicator reactions. Most of these kinetic methods have a narrow dynamic range of determination and are applicable only to microgram amounts. In this respect the present novel procedure shows that the pirogallol-phosphate-H_2O_2 system can be successfully used for the quantitative determination of trace amounts of selenium(IV) in real samples at normal temperature with a minimum time analysis and without using activators or surfactants. The novel method is quite sensitive, precise, rapid and selective, and can be used to determine Se(IV) at concentrations as low as 0.4 $\mu g \cdot cm^{-3}$.

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REFERENCES

1. H. M. Ohlendorf, *Selenium in Agriculture and the Environment*, **1989**, *23*, 133–137.
2. J. A. Pererson and A. V. Nabeker, *Arh.Environ.Contam.Toxicol*, **1992**, *23* , 154–162.
3. K.Heydoron and B. Griepink, *Fresenius Z. Anal. Chem*., **1990**, *338*, 287–292.
4. S. J. Hill., L. Pitts and P. Worsfold, *J. Anal. Atomic Spec*, **1986**, *325*, 32.
5. B. Kubota and K. Okutani, *Anal. Chim. Acta*, **1997**, *351*, 319.
6. S. H.Ta and and S. P. Kounaves, Electroanalysis, **1998**, *10*, 364.
7. W. C. Hawkes and M. A. Kutnink, *Anal. Biochem.*, **1996**, *241*, 206.
8. S. S. Mitić, M. V. Obradović , D. S. Veselinović and G. Ž. Miletić , *Latvias Kimias Žurnals*, **1997**, *125*, 31.
9. I. I. Nazarenko, I. V. Kislova, T. M. Guejnov and A. M. Kislov, *Zh. Anal. Khim.*, **1975**, *4*, 733.
10. D. Perez Bendito and S. Silva, *Kinetic Methods in Analytical Chemistry*, *Ellis Harwood*, **1988**, *256*.
11. K. B. Jatcimirskii, *Kinetic methods of Analysis*, *Pergamon*, Oxford U.K., **1996**.
12. D. A. Skoog, D. M. West and F. J. Holer., *Fundamentals of Analytical Chemistry*, *Saunders College publishing*, *Philadelphia.*, **1996**.
13. AOAC, Official Methods of Analysis, Asociation of Official Analytical Chemist, Arlington, V.A., 1984, method 3.101.
14. AOAC , Official Methods of Analysis, Asociation of Official Analytical Chemist, Arlington, V.A., 1984, method 3.102–3.107.
15. X. Wang and Z. Fang, *Fenxi Huaxue*, **1986**, *14*, 738.
16. J. Dedina,W. Frech, I. Linderberg, E. Linderberg and A. Cedergren, *J. Anal. At. Spectrom*., **1987**, *2*, 287.
17. B. Lange and F. Scholz, *Frenesius J. Anal. Chem*., **1997**, *358*, 736.
18. W. C. Hawkes and M. A. Kutnink, *Analytical Biochemistry*, **1996**, *241*, 206.
19. A. Safavi, A. Afkhami and A Massoumi, *Talanta*, **1992**, *39*, 993.
20. H. Parham and M. Ghamsipur, *Bull. Chem. Soc. Japan*, **1991**, *64*, 3067.
21. S. S. Mitić, S. M. Miletić, J. I. Vučetić and D. A. Kostić, *J. Serb. Chem. Soc.*, **2000**, *65*, 595.