J.Serb.Chem.Soc. 65(8)595-601(2000)
JSCS-2782

UDC 546.23:543.062:535.243
Original scientific paper

Kinetic determination of Se(IV) in pharmaceutical samples

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(Received 9 December 1999, revised 1 April 2000)

A kinetic method is described for the determination of Se(IV) based on its inhibiting effect on the Fe(III) catalysis of the oxidation of C_6H_5COONa with hydrogen peroxide. The detection limit is 0.06 μg cm^{-3}. The relative error ranges between 2.1 and 9.5 % for the concentration interval 0.26 to 2.6 μg cm^{-3}. Kinetic equations are proposed for the investigated process. The effects of certain foreign ions upon the reaction rate were determined in order to assess the selectivity of the method. The method was applied for the determination of Se(IV) in pharmaceutical samples.

Keywords: kinetic method, Se(IV), pharmaceutical samples.

INTRODUCTION

Selenium is an essential microelement. Investigations have been performed to determine supplementation with a moderate amount of selenium in the form of Se enriched yeast has an effect on lipid peroxidation in the tissues of rats after oxidative stress experimentally induced by ionising radiation. The results showed that even 150 days after exposure to radiation stress Se intake had a positive effect in decreasing lipid peroxidation as the malonilaldehyde (MDA) concentration in rat tissues, especially in the front and hear brain. Se supplementation was also shown to decrease the natural elevation of MDA that appears in the brain with ageing.[1,2]

The average dietary intake of Se with diet by young healthy population of Serbia during the 1996–1997 period confirmed that average daily intake of Se is low (26 μg).[3]

Micro amounts of selenium in hyman hair were satisfactorily determined by using a spectrophotometric method based on the catalytic effect of Se(IV) on the oxidation of Neutral Red with KIO_4. The sensitivity of the method is 8 ng/cm^3.[4]

The method for the determination of Se(IV) in mineral water is based on the action of Se(IV) upon the oxidation of Nile Blue A by hydrogen peroxide in the

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presence of phosphate buffer (pH 10.8) in ethanolic solution. The sensitivity of the method is 0.95×10^{-2} ng/cm^3.[5]

Micro amounts of selenium in health care products were determined by monitoring photometrically the decolorization of Methyl Orange at 525 nm, in the oxidation of hydrazine with $KBrO_3$. The sensitivity of the method is 0.5 μg/cm^3.[6]

A new kinetic method for the determination of Se(IV), with a sensitivity of 0.26 μg cm^{-3}, is described in this paper. The oxidation of C_6H_5COONa with hydrogen peroxide in an acetic acid solution gives a colored product. The reaction is catalysed by traces of Fe(III). We have observed that small amounts of Se(IV) strongly inhibit the catalysis of this reaction by Fe(III). 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 ultramicro amounts of Se(IV).

EXPERIMENTAL

Apparatus

A spectrophotometric method was used for following the investigated reaction rate. The dependence of the absorbance (A) on time (t) was measured using a Perkin-Elmer Lamda 15 spectrophotometer, connected to a thermocirculaing bath. The pH was measured by means of a radiometer PHM 29b pH meter and a combined glass-calomel electrode, GK 2311C. The solutions were thermostated at 25±0.1 °C before the beginning of the reaction.

Reagents

The stock $FeCl_3$ solution (1×10^{-3} mol dm^{-3}) was prepared by dissolving $FeCl_3$ in water. The C_6H_5COONa solution (1×10^{-3} mol dm^{-3}) was prepared by dissolving C_6H_5COONa in water. The acetic acid solution (1 mol dm^{-3}) was prepared from 99.0 % glacial acetic acid. The hydrogen peroxide solution (1 mol dm^{-3}) was prepared from the 34 % reagent. The $SeCl_4$ (1×10^{-3} mol dm^{-3}) was prepared by dissolving $SeCl_4$ in water.

All chemicals were of analytical reagent grade and were supplied by Merck unless indicated otherwise. The solutions were made using deionized water. All the stock solutions were stored in polyethylene containers. The working solutions of Fe(III) and H_2O_2 were prepared immediately before use.

All the polyethylene containers and the glassware used were cleaned in aqueous HCl (1:1) and then thoroughly rinsed with deionised water.

Procedure

A measured amount of hydrogen peroxide was stored in one compartment of a special vessel, the Fe(III) solution was placed in the second compartment, C_6H_5COONa in the third compartment and acetic acid (acetic acid and Se(IV)) and water (up to a total volume of 15 cm^3) in the fourth compartment. The spectrophotometer cell was rinsed well and filled with the solution. The absorbance at 540 nm was measured every 30 s over a period of 5–8 min after the addition of hydrogen peroxide. The measurement were made at 25±0.1 °C.

RESULTS AND DISCUSSION

Kinetic studies

A differential variant of the tangent method was used for processing the kinetic data, because a linear correlation exists between the absorbance and time dur-

ing the first 5 to 8 min after the addition of hydrogen peroxide. The reaction rate was followed by the change in the values of the tangent of the angle (tan α) of the slope of the linear part of the kinetic curve to the abscissa in the co-ordinates A–t,[6] because tan $\alpha = dA/dt$.

In order to determine the lowest possible determinable concentration of Se(IV), the conditions needed to be optimised. Therefore, the dependencies of the rates of both the catalytic and the inhibited reactions on the concentration of each of the reactants were determined.

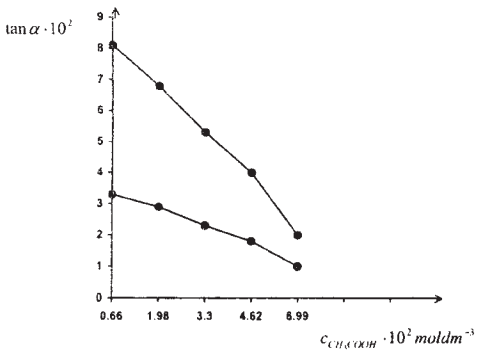

Fig. 1. Dependence of the rate of the catalysed 1) and inhibited 2) reaction on the acetic acid concentration. Initial concentrations: $c_{C_6H_5COONa} = 2\times10^{-4}$ mol dm^{-3}, $c_{H_2O_2} = 0.266$ mol dm^{-3}, $c_{Fe(III)} = 2\times10^{-4}$ mol dm^{-3}, $c_{Se(IV)} = 5.2$ μg cm^{-3}, $T = 295.5$ K.

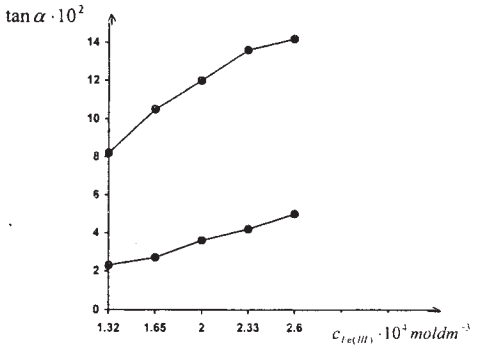

Fig. 2. Dependence of the rate of the catalysed 1) and inhibited 2) reaction on the C_6H_5CONa concentration. Initial concentrations: $c_{Fe(III)} = 2\times10^{-4}$ mol cm^{-3}, $c_{CH_3COOH} = 2\times10^{-2}$ mol dm^{-3}, $c_{H_2O_2} = 0.266$ mol dm^{-3}, $c_{Se(IV)} = 5.2$ μg cm^{-3}, $T = 295.5$ K.

Figure 1 shows the influence of pH on the rate of both reactions. It can be seen that the greatest difference between the reaction rates occurs at $c_{CH_3COOH} = 6.67\times10^{-3}$ mol dm^{-3}, when Se(IV) maximally decreases the catalytic reaction rate. For further work an acetic acid concentration of 2×10^{-2} mol dm^{-3} was selected.

The dependence of tan α on the C_6H_5COONa concentration is shown in Fig. 2, which shows that the difference in the rates of the inhibited and catalytic reactions increases with increasing C_6H_5COONa concentration. For further work a C_6H_5COONa concentration of 3.33×10^{-4} mol dm^{-3} was selected.

The correlation between tan α and the Fe(III) concentration is shown in Fig. 3. Both reactions are first order with respect to the Fe(III) concentration. A Fe(III) concentration of 2×10^{-4} mol dm^{-3} was selected, for furher work, because at higher concentrations the linear part of the kinetic curve (A–t) is rather short.

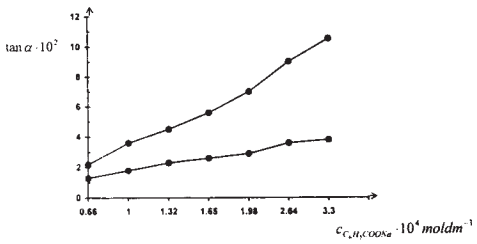

Fig. 3. Dependence of the rate of the catalysed 1) and ihibited 2) reaction on the Fe(III) concentration. Initial concentrations: $c_{CH_3COOH} = 2\times10^{-2}$ mol dm^{-3}, $c_{H_2O_2} = 0.266$ mol dm^{-3}, $c_{C_6H_5COONa} = 3.3\times10^{-4}$ mol dm^{-3}, $c_{Se(IV)} = 5.2$ μg cm^{-3}, $T = 295.5$ K.

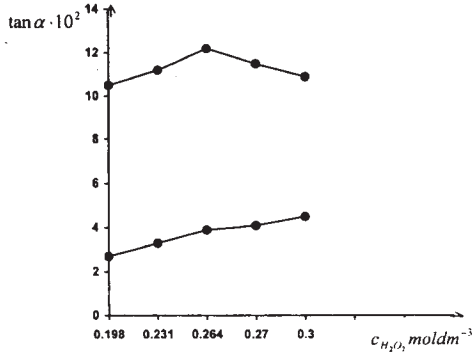

Fig. 4. Dependence of the rate of the catalysed 1) and inhibited 2) reaction on the H_2O_2 concentration. Initial concentrations: $c_{CH_3COOH} = 2\times10^{-2}$ mol dm^{-3}, $c_{Fe(III)} = 2\times10^{-4}$ mol dm^{-3}, $c_{C_6H_5COONa} = 3.3\times10^{-4}$ mol dm^{-3}, $c_{Se(IV)} = 5.2$ μg cm^{-3}, $T = 295.5$ K.

The dependence of the reaction rates on the concentration of H_2O_2 is shown in Fig. 4, in which it can be seen that the inhibited reaction is first order with respect to the H_2O_2 concentration, whereas the catalytic reaction is only first order with respect to the

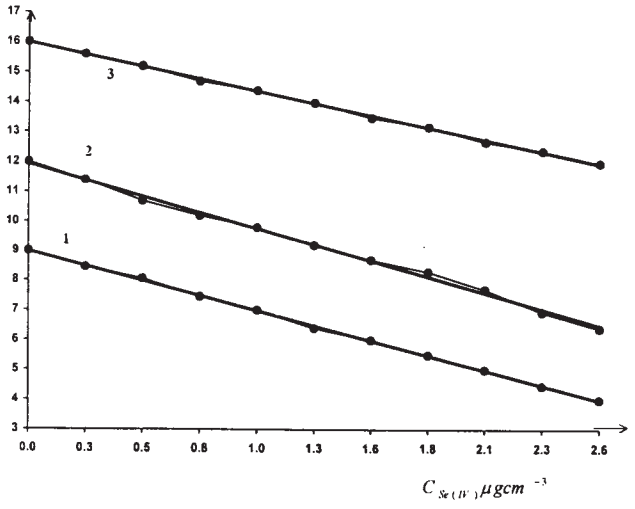

Fig. 5. Dependence of the rate of the catalysed 1) and inhibited 2) reaction on the Se(IV) concentration. Initial concentrations: $c_{CH_3COOH} = 2\times10^{-2}$ mol dm^{-3}, $c_{Fe(III)} = 2\times10^{-4}$ mol dm^{-3}, $c_{C_6H_5COONa} = 3.3\times10^{-4}$ mol dm^{-3}, $c_{H_2O_2} = 0.266$ mol dm^{-3}. 1) $T = 295.5$ K; 2) $T = 298.0$ K; 3) $T = 300.5$ K.

H_2O_2 concentration up to 0.266 mol cm^{-3} and negative first order at higher concentrations. A H_2O_2 concentration of 0.266 mol dm^{-3} was selected for further work.

Under the optimal reaction conditions ($c_{H2O2} = 0.266$ mol dm^{-3}, $c_{C6H5COONa} = 3.33\times10^{-4}$ mol dm^{-3}, $c_{Fe(III)} = 2\times10^{-4}$ mol dm^{-3}, $c_{CH3COOH} = 2\times10^{-2}$ mol cm^{-3}) the Se(IV) concentration was varied from 0.26 to 2.6 μg cm^{-3}.

Three calibration lines, obtained at different temperatures, are shown in Fig. 5, which can be used for the determination of the Se(IV) concentration in the interval mentioned.

The following kinetic equations for the investigated process were deduced on the basis of the graphic correlations obtained.

For the catalysed reaction:

$$\frac{dc}{dt} = k_1 \times c^{-1}_{CH3COOH} \times c_{C6H5COONa} \times c_{Fe(III)} \times c_{H2O2}$$

were k_1 is a constant proportional to the rate constant of the catalysed reaction.

For the inhibited reaction:

$$-\frac{dc}{dt} = k_2 \times c^{-1}_{CH3COOH} \times c_{C6H5COONa} \times c_{Fe(III)} \times c_{H2O2} \times c^{-1}_{Se(IV)}$$

were k_2 is constant proportional to the rate constant of the inhibited reaction.

On the basis of these equations, the rate constants for the inhibited and catalysed reactions were calculated.

A linear relationship between the logarithm of the rate constant and the reciprocal of the absolute temperature was found for the inhibited as well as for the catalysed reaction. The activation energies were found to be 15.8 kJ mol^{-1} for the inhibited reaction and 10.0 kJ mol^{-1} for catalysed reaction.

The minimum concentration of Se(IV) which can be determined by this method may be calculated by the method given by Perez-Bendito and Silva.[8] The detection limit was found to be 0.06 μg cm^{-3}.

TABLE I. Accuracy and precision of the Se(IV) determinations

Taken×10^7 g cm^{-3}	Found($\bar{x}$)×10^7 g cm^{-3}	n	S×10^8 g cm^{-3}	G/%	($\bar{x}$–μ)×100/μ %
2.6	2.66	5	2.06	9.5	+2.3
13.0	12.7	5	4.18	4.08	–2.3
26.0	26.2	5	4.47	2.11	+0.76

x - Mean value; μ - true value; n - number of determinations; S - standard deviation; G - relative error (= 100 $t\,s/\bar{x}\,\sqrt{n}$, where $n = 5$ and t is Student's t for 95 % confidence)

The accuracy and precision of the measurements are presented in Table I. The relative error ranges from 2.1 to 9.5 % for Se(IV) concentrations from 0.26 to 2.6 μg cm^{-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) concentra-

tion of 1.3 μg cm^{-3} (Table II). It may be seen that SCN^- and $C_2O_4^{2-}$ in a 1:1 ratio with Se(IV) interfere with the reaction. The other investigated ions have practically no influence on the determination of Se(IV) by this method.

TABLE II. Tolerance levels of interferents in the kinetic determination of 1.3 μg cm^{-3} Se(IV) using the optimum conditions

Tolerance level $c_{ION}/c_{Se(IV)}$	Ion added
10^2	Na^+, K^+, Ca(II), Mg(II), Cl^-
10	NO_3^-, SO_4^{2-}, Sr(II),
1	CO_3^{2-}, HCO_3^-, PO_4^{3-}, ClO^-, Se(IV)
	Zn(II), Cd(II), Co(II), Pb(II)
	SCN^-, $C_2O_4^{2-}$-inhibited

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) and b) "Coenzyme-Q" tablets.

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

TABLE III. Determination of Se(IV)/(mg/tablet) in pharmaceutical preparations

Sample	Kinetic method	Rel. st. dev.	AAS method	Specified on the by manufactures
Oligogal–Se	0.098[a]	0.62[b]	0.975	0.1
Coenzyme-Q	0.972	0.64	0.987	0.1

[a]Mean for $n = 5$; [b]Standard deviation

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

И З В О Д

КИНЕТИЧКО ОДРЕЂИВАЊЕ Sc(IV) У ФАРМАЦЕУТСКИМ УЗОРЦИМА

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Предложена је кинетичка метода за одређивање Se(IV) на бази инхибиторног дејства у реакцији оксидације натријумбензоата водоник-пероксидом која је катализована са гвожђем(III). Граница детекције методе је 0,06 μg cm^{-3}. Релативна грешка се креће од 2,11 до 9,5 % за интервал коцентрација 0,26 до 2,6 μg cm^{-3}. Предложене су кинетичке једначине за проучавани процес. Ради оцене селективности методе испитан је утицај извесног броја страних јона на брзину реакције. Метода је примењена за одређивање трагова Se(IV) у фармацеутским препаратима.

(Примљено 9. децембра 1999, ревидирано 1. априла 2000)

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