Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Pharmaceutical and Biomedical Analysis 37 (2005) 1149–1154
JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS
www.elsevier.com/locate/jpba

Short communication

Antioxidant and electrochemical properties of calcium and lithium ascorbates

O.A. Avramchik[a], E.I. Korotkova[a,*], E.V. Plotnikov[b], A.N. Lukina[a], Y.A. Karbainov[a]

[a] *Department of Physical and Analytical Chemistry, Tomsk Polytechnic University, Lenin 30, 634050 Tomsk, Russia*
[b] *Siberian State Medical University, Moscow Tract 2, Tomsk, Russia*

Received 22 May 2004; received in revised form 9 November 2004; accepted 9 November 2004
Available online 25 December 2004

Abstract

The calcium and lithium pharmaceutical products have been widely used in medicine, especially at diseases of the mind. Bioactivity and toxically of novel complex ascorbates of calcium and lithium were considered in this work. Study of antioxidant properties of new forms of the compounds was carried out by differential pulse voltammetry. Cyclic voltammetry was used for investigation of their electrochemical properties in order to obtain information about electron-transfer reactions. The influence of these substances on the electrochemical oxygen reduction and its kinetic was also studied. As a result, the kinetic parameters interaction between reactive oxygen species and ascorbates of calcium and lithium were evaluated.

Keywords: Antioxidant; Calcium ascorbate; Lithium ascorbate; Voltammetry

1. Introduction

Over the last few years the calcium and lithium pharmaceutical products, such as a chloride of calcium, a chloride of lithium, a carbonate of lithium and other, have been widely used in medicine [1]. Calcium plays a major role in several physiological processes of living organisms [1,2]. It is known that calcium ions are useful for realization of process of nervous pulse transfer and activity of some enzymes. Lithium influences on neurochemical processes proceeding in a brain [3]. It is established, that lithium ions are able to stop acute maniac excitation, and it may be used as adjuvant therapy in schizophrenic patients [4–6]. Lithium is still the first drug of choice for treatment of affective disorders [7,8]. Nowadays a large number of the preparations of calcium and lithium have been known. Unfortunately, most of them have been found to be toxic [9]. Lithium intoxication may be a life-threatening complication of chronic lithium therapy for manic-depressive disorders [10–12]. Consequently synthesis of new forms of compounds on the basis of salts of calcium and lithium and study of their properties are very actual.

Bioactivity and toxicity of novel complex compounds of calcium and lithium, which contain ascorbic acid (AA) as bioactive ligand, are considered in this work (Fig. 1). It is known that these investigated samples have psychotropic action. The study of antioxidant properties of calcium ascorbate (CA) and lithium ascorbate (LA) could be an interesting subject for investigation. Influence of CA and LA on the electroreduction of oxygen (ER O_2) and the mechanisms of its interaction with reactive oxygen species (ROS) at the surface of an electrode have been also considered.

Search of novel analytical methods to evaluate the antioxidant capacity of the various pharmaceutical products have increased considerable in during last years. There are many methods of total antioxidant activity (TAA) determination [13]. They are generally based on the inhibition model reactions by the presence of antioxidants. The most widely used

* Corresponding author. Tel.: +7 3822 563832; fax: +7 3822 563435.
E-mail address: eikor@mail.ru (E.I. Korotkova).

0731-7085/$ – see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.jpba.2004.11.016

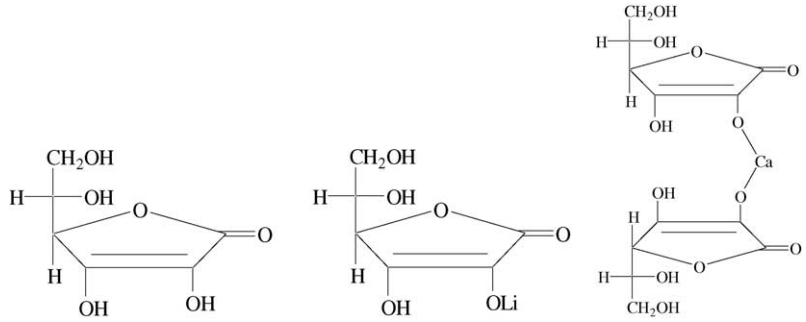

Fig. 1. Scheme of ascorbic acid, calcium ascorbate and lithium ascorbate structures.

methods are those that involve the generation of radical compounds. In the present of antioxidants the methods determine the disappearance of these radicals. Strategies for measuring the TAA are widely discussed [14,15].

In our opinion the model reaction for the TAA determination play a major role in different instrumental approaches. If we consider the use of antioxidants in medicine and pharmaceutical industry, these reactions have to be similar to the reactions in tissues of organism. As it was established before, voltammetry is the suitable method for similar investigations [16,17].

In this work we have applied an effective and convenient approach for the determination of the antioxidant activity of the investigated substances by recording the current of the electrochemical oxygen reduction (ER O_2) at a mercury film electrode (MFE). The latter process has been treated as a 'model' reaction because of similar processes of ER O_2 and the oxygen reduction in tissues. It proceeds at the cathode in several stages with formation of the ROS, such as $O_2^{\bullet}$ and $HO_2^{\bullet}$, which are results from the univalent reduction of oxygen:

$$O_2 + e^- \xrightarrow{k_0} O_2^{\bullet -} \quad (1)$$

$$O_2^{\bullet -} + H^+ \rightleftarrows HO_2^{\bullet} \quad (2)$$

$$HO_2^{\bullet} + H^+ + e^- \rightleftarrows H_2O_2 \quad (3)$$

ROS are highly reactive and toxic. They are involved in the pathogenesis of a number of human diseases. An antioxidant reacting with $O_2^{\bullet}$ and $HO_2^{\bullet}$ decrease their concentration at the electrode under otherwise equal conditions. However the current of ER O_2 also decreases.

This approach allows evaluating the interaction between the antioxidant and ROS. We have suggested the following mechanism of this interaction:

$$O_2^{\bullet -} + R{-}OH \overset{k_1^*}{\rightleftarrows} HO_2^{\bullet} + R{=}O \quad (4)$$

$$HO_2^{\bullet} + R{-}OH \rightleftarrows H_2O_2 + R{=}O \quad (5)$$

where R–OH is the reduced form of the antioxidant and R=O is the oxidized form of one.

Applying the above approach, we have studied the influence of CA and LA on the ER O_2 and its kinetics. A comparative analysis of the antioxidant activity of CA, LA and some standard antioxidants has been also carried out.

2. Theoretical

As is known, ER O_2 at the MFE is a quasi-reversible process. It depends on diffusion as well as on the rate of the kinetic interconversion. It proceeds at the cathode in several stages with formation of ROS. The step (1) is limiting and controls the kinetic of the whole process. Surface reactions between the antioxidant and ROS at the working electrode surface on kinetic and potential of the ER O_2. The shift of the ER O_2 potential toward positive values could be attributed to following chemical reaction after electrode stage of the ER O_2 process (6):

$$O_2 + e^- \xrightarrow{k_0} O_2^{\bullet -} + R{-}OH \overset{k_1^*}{\rightleftarrows} HO_2^{\bullet} + R{=}O \quad (6)$$

$$E_{O_2/O_2^{\bullet -}} = E^0 + \frac{RT}{zF} \ln \frac{a_{O_2}}{a_{O_2^{\bullet -}}} \quad (7)$$

By according to Nernst Eq. (7) the decrease of $a_{O_2^{\bullet -}}$ scheme (6) leads to the increase of $E_{O_2/O_2^{\bullet -}}$.

In the limiting case of semi-infinite diffusion the boundary problem for the ER O_2 at the MFE (scheme (6)) can be described by

$$\frac{\partial C_{O_2}(x,t)}{\partial t} = D_{O_2} \frac{\partial^2 C_{O_2}(x,t)}{\partial x^2}, \quad 0 \le x \le \infty \quad (8)$$

$$\frac{\partial C_{O_2^{\bullet -}}(x,t)}{\partial t} = D_{O_2^{\bullet -}} \frac{\partial^2 C_{O_2^{\bullet -}}(x,t)}{\partial x^2}, \quad 0 \le x \le \infty \quad (9)$$

The boundary conditions can be estimated by

$$t = 0, \quad x \ge 0, \quad C_{O_2}(x,0) = C_{O_2}^0; \qquad C_{O_2^{\bullet -}}(x,0) = 0 \quad (10)$$

$$t > 0, \quad x \to \infty, \quad C_{O_2}(\infty,t) = C_{O_2}^0 \quad (11)$$

$$D_{O_2} \left.\frac{\partial C_{O_2}(x,t)}{\partial x}\right|_{x=l} = k_0 C_{O_2}^s(x,t) \quad (12)$$

$$D_{O_2}\left.\frac{\partial C_{O_2}(x,t)}{\partial x}\right|_{x=l} = -D_{O_2^{\bullet-}}\left.\frac{\partial C_{O_2^{\bullet-}}(x,t)}{\partial x}\right|_{x=l} \quad (13)$$

Taking into account the decrease of oxygen concentration because of reacting with antioxidant the equation for the ER O_2 current on the MFE can be given by

$$I = zFSD_{O_2}\left.\frac{\partial C^*_{O_2}(x,t)}{\partial x}\right|_{x=l} = zFS(k_0 C_{O_2}(l,t) - k_1^* C_{O_2^{\bullet-}}(l,t)) \quad (14)$$

$$C_{O_2}(l,t) = C^0_{O_2}\xi\left(\frac{k_0\sqrt{t}}{\sqrt{D}_{O_2}}\right) \quad (15)$$

$$C_{O_2^{\bullet-}}(l,t) = C^0_{E_2}\sqrt{\frac{D_{O_2^{\bullet-}}}{D_{O_2}}}\left[1 - \xi\left(\frac{k_0\sqrt{t}}{\sqrt{D}_{O_2}}\right)\right] \quad (16)$$

where z is the number of electrons involved in the limiting stage of the process, F the Faraday constant, S the area of the electrode surface in cm^2, D the diffusion coefficient of the corresponding species, $C^*_{O_2}$ the oxygen concentration at the electrode in presence antioxidant in $mol\,l^{-1}$, $C^0_{O_2}$ the oxygen concentration at the electrode in absence antioxidant in $mol\,l^{-1}$, t the time of the interaction between ROS and antioxidant in s, k_0 and k_1^* are rate constants at process (6) in $cm\,c^{-1}$.

$$k_1^* = k_1 C^0_{ROH} \quad (17)$$

where C^0_{ROH} is the antioxidant concentration.

Thus, after corresponding transformation, in the limiting case of semi-infinite diffusion the ER O_2 current on the MFE can be deduced as the following equations without Eq. (18) and with Eq. (19) antioxidant in solution, respectively

$$I_0 = zFSk_0 C^0_{O_2}\xi\left(\frac{k_0\sqrt{t}}{\sqrt{D}_{O_2}}\right) \quad (18)$$

$$I = zFSC^0_{O_2}\xi\left(\frac{k_0\sqrt{t}}{\sqrt{D}_{O_2}}\right) \times \left[k_0 + k_1^*\sqrt{\frac{D_{O_2^{\bullet-}}}{D_{O_2}}} - k_1^*\sqrt{\frac{D_{O_2^{\bullet-}}}{D_{O_2}}}\frac{1}{\xi\left(\frac{k_0\sqrt{t}}{\sqrt{D}_{O_2}}\right)}\right] \quad (19)$$

Taking in to account, that in limiting case when $t \to 0$ then $\xi\left(\frac{k_0\sqrt{t}}{\sqrt{D}_{O_2}}\right) \to 1$, the Eq. (18) with error $\sigma < 5\%$ can be given by

$$I_0 = zFSk_0 C^0_{O_2} \quad (20)$$

It should be noted that I_0 does not depend on the diffusion coefficient in the abovementioned limiting case [18].

It is known [19,20], that with growth t the function $\xi\left(\frac{k_0\sqrt{t}}{\sqrt{D}_{O_2}}\right)$ decreases and when $\left(\frac{k_0\sqrt{t}}{\sqrt{D}_{O_2}}\right) > 3.16$ this function with error $\sigma < 5\%$ can be given by

$$\xi\left(\frac{k_0\sqrt{t}}{\sqrt{D}_{O_2}}\right) = \frac{\sqrt{D}_{O_2}}{k_0\sqrt{t}\sqrt{\pi}} \quad (21)$$

Thus, if $\sqrt{\frac{D_{O_2^{\bullet-}}}{D_{O_2}}} \approx 1$ in Eq. (19), the expression (22) had been obtained, from which the value of the rate constant of following chemical reaction between antioxidant and ROS (k_1^*) can be defined.

$$R = \frac{I}{I_0} = 1 - \frac{k_1^*\sqrt{\pi}\sqrt{t}}{\sqrt{D_{O_2}}} \quad (22)$$

Applying the above approach, we have K as TAA coefficient of substances, which reflects the ROS reacting with antioxidant at $\mu mol\,l^{-1}\,min^{-1}$

$$K = \left(1 - \frac{I}{I_0}\right)\frac{C^0}{t} \quad (23)$$

where C^0 is the oxygen concentration at the electrode in absence antioxidant in $\mu mol\,l^{-1}$, I the ER O_2 current with the investigated substance addition in A, I_0 the limiting ER O_2 current without substance in the solution in A, and t the time of interaction between ROS and antioxidant at the MFE in minutes.

3. Experimental

3.1. Chemicals and reagents

We used in this work follow chemicals: ascorbic acid, calcium ascorbate and lithium ascorbate. All chemicals were of analytical grade and were used without further purification. As a supporting electrolyte, phosphate buffer $0.025\,mol\,l^{-1}$ (equimolar mixtures of Na_2HPO_4 and KH_2PO_4, pH 7.3) were used. Nanopure water was used for making solutions.

3.2. Instrumentation

A voltammetric analyzer model TA-2 (Tomsk production) in connection with PC and polarographic analyzer model PU-1 in conjunction with *X–Y* recorder were used in this work. The electrochemical cell with three-electrode configuration was connected to the analyzer. A working mercury film electrode, a silver–silver chloride reference electrode with KCl-saturated (Ag–AgCl–KCl_{sat}) and a glassy carbon counter electrode were used. An open-type cell was used in this investigation. The reference and indicator electrodes were held in the electrochemical cell. The thermostatic cell was maintained at $25.0 \pm 0.5\,^{\circ}C$. The solution was stirred by a magnetic stirrer Model 305. The rate and time of stir-

ring should be monitored to minimize the experimental error. The pH was measured using digital pH-meter Model M64. Electrolytic cell with second platinum electrode was used for preparation of working electrode. A working glassy carbon electrode was used for cyclic voltammetry, with length 0.5 cm and diameter 0.3 cm. The oxygen concentration in the solutions was monitored with an oxygen analyzer Model P5972 (Poland).

3.3. Preparation of the working electrode

The working electrode was placed as cathode in the electrolytic cell with saturated $Hg_2(NO_3)_2$. A platinum wire was used as anode. Mercury film was formed on the surface of the silver electrode by electrolysis under the constant current (1 A). The thickness of the mercury film was controlled by time of the electrolysis. For length of the silver wire of the indicator electrode 0.7 cm, diameter 0.09 cm, time of electrolysis 20 s and the thickness of mercury film 2.5×10^{-3} cm. It was constant for all measurements. In order to remove residual adsorbed impurities, the indicator electrode was subjected to 20 voltammetric cycles between 0.0 and −2.0 V at $0.1\ V\ s^{-1}$.

3.4. Procedures

A volume of 5 ml of phosphate buffer was placed in the electrochemical cell. The measurement involved the recording of voltammograms of the cathodic reduction of oxygen by differential pulse voltammetry without and with the investigated substances under the following conditions: potential rate scan, $0.05\ V\ s^{-1}$; potential range, $E = 0$ to −0.6 V; amplitude, 10 mV. After substance addition, the solution was stirred with a magnetic stirrer about 20 s. After stirring is stopped, the potential was scanned negatively, causing oxygen reduction, giving a current first wave ER O_2. Its value was proportional to the amount of oxygen in the bulk of the solution. Oxygen concentration was monitored by oxygen analyzer. Based on the ammetric measurements the concentration of oxygen in phosphate buffer at $25.0 \pm 0.5\ ^\circ C$ was $2.56 \pm 0.05 \times 10^{-4}\ mol\ l^{-1}$.

Cyclic voltammetry was performed in the electrochemical cell containing phosphate buffer and the investigated substances in concentrations 0.1–1 $mmol\ l^{-1}$. The potential range was from 0.0 to +1.0 V. The potential scan rate was $0.05\ V\ s^{-1}$. The working electrode was cleaned before each measurement by first dipping it in ethanol for 10 min, and then polishing it with a cleaning paste. The solution being analyzed was de-oxygenated by passing nitrogen for 10 min prior measurements.

4. Results and discussion

Toxicity CA and LA was investigated on mice of a line BALB/c at intraperitoneal introduction of a compounds (0.1, 0.5 and 1 g/kg) and supervision within a month. It is known, that LD_{50} of a calcium chloride and a lithium carbonate is varied in range (0.36–0.6 g/kg). Therefore an intraperitoneal introduction of preparation consists of 0.1, 0.5 and 1 g/kg, respectively. The ascorbates of the investigated metals in this spectrum of doses showed absence of toxic action for experimental animals. Decrease of toxicity is supposed to concern with presence antioxidant activity at calcium and lithium ascorbates.

In order to investigate the antioxidant activity, voltammograms of ER O_2 current were recorded as a function of potential of the working electrode in supporting electrolyte containing the substances under investigation at the MFE (Fig. 2).

As a result the curves of the relative change of the ER O_2 current density $(1 - I/I_0)$ against time of the interaction between ROS and antioxidant at the MFE in supporting electrolyte at effective concentration of antioxidant were plotted

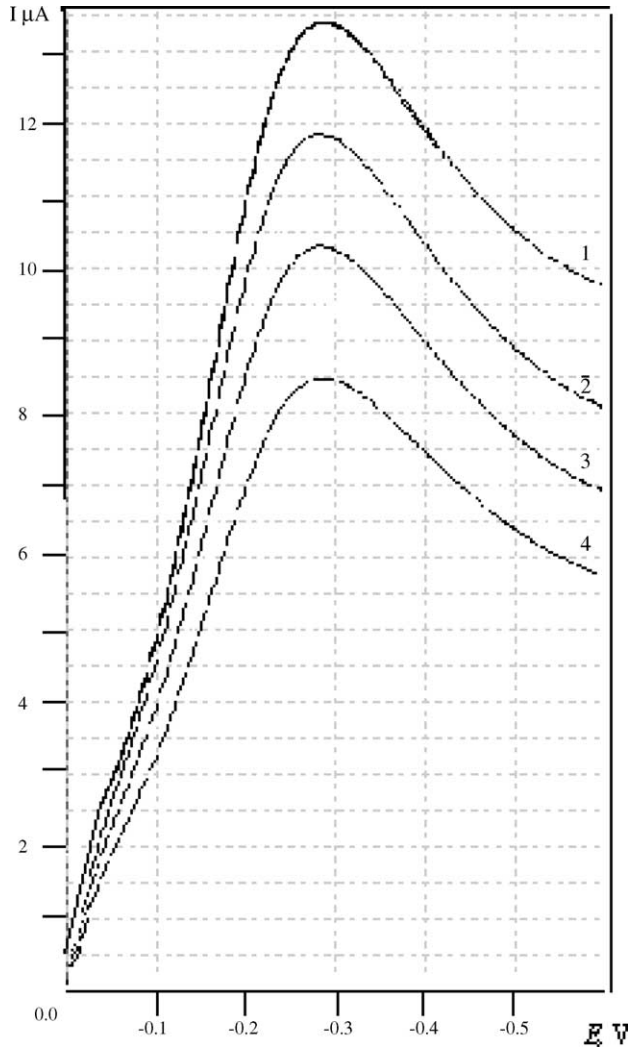

Fig. 2. Voltammograms of the ER O_2 current in phosphate buffer (0.025 M, pH 7.3) on the MFE without (1) and with 0.27 $mmol\ l^{-1}$ of ascorbic acid at $t = 10$ min (2), $t = 20$ min (3), and $t = 30$ min (4). Scan rate $0.05\ V\ s^{-1}$. For other conditions see Section 3.4.

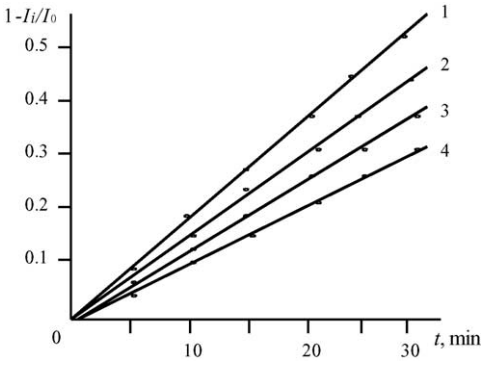

Fig. 3. Dependence of the relative change of the ER O_2 current against time of the interaction between ROS and antioxidant at the MFE in phosphate buffer (0.025 M, pH = 7.3) for 0.27 mmol l^{-1} lithium ascorbate (1), ascorbic acid (2), calcium ascorbate (3) and glucose (4).

(Fig. 3). All the curves represent straightforward lines in the range of relatively low antioxidant concentrations. The slope angle tangent of these lines is suggested to be a coefficient of the antioxidant activity K given by Eq. (23).

The hypothesis of linearity of the described curves by regression analysis was verified. The results were compared using the Fisher criterion and they do not exceed the corresponding standard value. The estimated experimental errors (σ, %) do not exceed 10%.

Data on K and experimental errors (Sr) are shown for CA and LA (Table 1). For comparison, coefficients of antioxidant activity of some standard antioxidants, which have been determined under the same conditions, are also shown. Study of decrease of the ER O_2 current at MFE in the present of CA and LA demonstrated excellent TAA. It is observed, LA shows excellent antioxidant activity, higher then AA (Table 1).

CA and LA as well as AA have carbonyl and enol groups in its structure, which could be reduced and oxidized at the electrode. Investigation of their reduction and oxidation potentials is very important to obtain information about its electron-transfer reactions. Experiment was carried out using cyclic voltammetry in a deoxygenated (by N_2) aqueous solution containing 0.025 mol L^{-1} phosphate buffer in the −0.2 to +1.0 V potential range. The others conditions were the same as described in Section 3.

Table 1
Total antioxidant activity coefficients of investigating antioxidants

Substance name	K (μmol l^{-1} min^{-1})	Sr
Lithium ascorbate	1.25	0.09
Calcium ascorbate	0.57	0.05
Ascorbic acid	1.15	0.07
Glucose	0.29	0.06
Catechol	0.23	0.08
Resorcinol	0.14	0.03

Cyclic voltammograms of AA was obtained (Fig. 4A), similar [21,22]. One anodic wave of AA was obtained at $E = 0.28 \pm 0.02$ V at the glassy carbon electrode, which is related to enol groups undergoing oxidation during the cycle. Moreover the anodic current height proportionally increased with AA concentration in solution. The increasing concentrations of calcium ascorbate produced a series of anodic waves characterized by the same $E = 0.32 \pm 0.02$ V, with anodic current height, which increased proportionally (Fig. 4B). Likewise, the increasing concentrations of lithium ascorbate gave an increase of anodic wave at similar potential $E = 0.30 \pm 0.02$ V (Fig. 4C).

Thus, anodic waves of these ascorbates are supposed to represent the oxidation of enol group, and they cannot be ruled out by other groups. In a reverse scan of cyclic voltammetry no reduction waves were observed at this potential range.

Theoretical investigation for evaluation of kinetic parameters of the ER O_2 at present antioxidants was carried out in detail in this work, according to Eqs. (8)–(22).

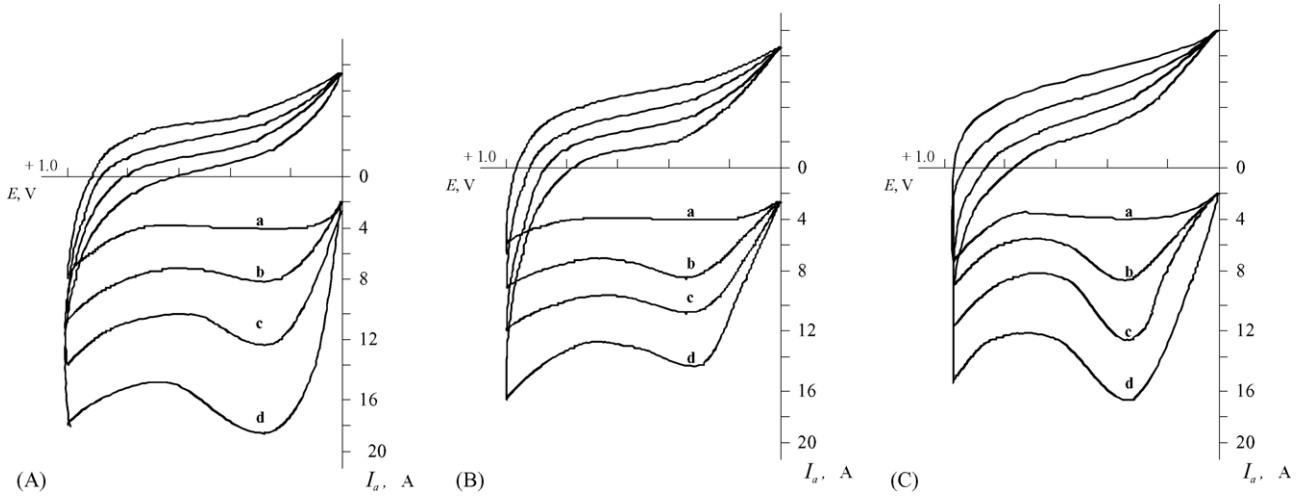

Fig. 4. Cyclic voltammograms increasing concentrations of (A) ascorbic acid ($a = 0$, $b = 0.1$, $c = 0.27$, $d = 1$ mM), (B) calcium ascorbate ($a = 0$, $b = 0.1$, $c = 0.27$, $d = 1$ mM), and (C) lithium ascorbate ($a = 0$, $b = 0.1$, $c = 0.27$, $d = 1$ mM) in phosphate buffer (0.025 M, pH 7.3). Scan rate 0.05 V s^{-1}. For other conditions, see Section 3.4.

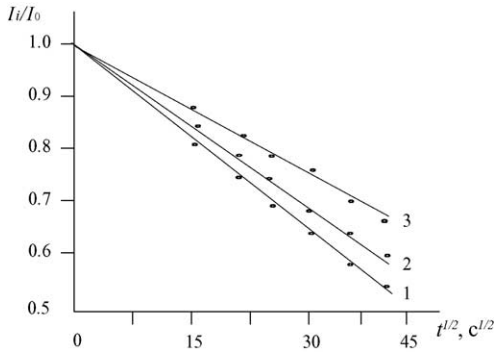

Fig. 5. Dependence of the relative change of the ER O_2 current against time of the interaction between ROS and antioxidant at the MFE in phosphate buffer (0.025 M, pH = 7.3) for 0.27 mmol l^{-1} lithium ascorbate (1), ascorbic acid (2), calcium ascorbate (3) and glucose (4).

The voltammogram of the oxygen reduction was scanned in the supporting electrolyte without substances to obtain the original limiting value of the oxygen current (I_0), which corresponds to oxygen solubility in this electrolyte $2.56 \pm 0.05 \times 10^{-4}$ mol l^{-1}. Then the supporting electrolyte was bubbled for 10 s during 5 min with nitrogen under pressure through the gas tube to remove oxygen from the electrolyte. The voltammograms of the supporting electrolyte without oxygen were scanned to obtain the residual current value (I_{res}). Degree of these changes in dependence on the oxygen concentration in the solution has afforded to determine the rate constant of the ER O_2 process (k_0) by Eq. (20) which corresponds to $(1.33 \pm 0.02) \times 10^{-3}$ cm c^{-1} [19].

Then the solution of antioxidant with a known concentration was added to the renewed portion of the supporting electrolyte; under the same conditions, the proportional decrease of the ER O_2 current at the corresponding time of interaction between ROS and antioxidant was observed. The voltammograms of the oxygen reduction current in supporting electrolyte containing the investigating antioxidant at the MFE were recorded (Fig. 3). Curves of the relative change of the oxygen current (I/I_0) against the time of the interaction between ROS and antioxidant in the supporting electrolyte were plotted in this work (Fig. 5).

As a result, the values of the rate constant of following chemical reaction between AO and ROS (k_1^*) have been determined according to Eq. (22) (Table 2). This rate constant has biochemical mind. For LA k_1^* was higher than AA and CA.

Table 2
The kinetic patameters of ER O_2 with antioxidants

Substance name	C^0_{ROH} (mM)	k_1^* (c^{-1})	k_1 ($c^{-1}\,\mu^{-1}$)
Lithium ascorbate	0.27	$(1.72 \pm 0.05) \times 10^{-5}$	$(0.64 \pm 0.05) \times 10^{-1}$
Calcium ascorbate	0.27	$(0.76 \pm 0.03) \times 10^{-5}$	$(0.28 \pm 0.03) \times 10^{-1}$
Ascorbic acid	0.27	$(1.38 \pm 0.04) \times 10^{-5}$	$(0.51 \pm 0.04) \times 10^{-1}$

5. Conclusion

Thus, the abovedescribed investigation of the antioxidant activity of ascorbates of calcium and lithium by differential pulse voltammetry allowed to compare the activity of this substance and some standard antioxidants. Also these ascorbates in investigating (0.1, 0.5 and 1 g/kg) spectrum of doses did not show toxic action for mice. Investigations of redox–oxidative abilities of AA, CA and LA in wide potential range were carried out. The anodic waves of AA, CA and LA were obtained at $E = 0.28 \pm 0.02$, 0.32 ± 0.02, 0.30 ± 0.02 V versus Ag–AgCl–KCl_{sat} electrode, respectively, which are related to the oxidation of enol group.

Moreover the kinetic parameters of ER O_2 with antioxidant were evaluated.

References

[1] M.D. Mashkovsky, The Medicinal Preparations, 14th ed., Medicine, Moscow, 2000.
[2] L. Rasmussen, S.E. Husted, S.P. Johnsen, Acta Anaesthesiol. Scand. 47 (2003) 1038–1040.
[3] F. Angelucci, L. Aloe, P.J. Vasquez, A.A. Mather, Int. J. Neuropsychopharmacol. 6 (2003) 225–231.
[4] L. Johnson, A. El-Khoury, A. Wistedt, R. Malmgren, A.A. Mathé, Int. J. Neuropsychopharmacol. 4 (2001) 329–336.
[5] W. Coryell, G. Winokur, D. Solomon, T. Shea, A. Leon, M. Keller, Psychol. Med. 27 (1997) 281–289.
[6] M. Canal, E. Legangneux, J. van Lier, A. van Vliet, C. Coulouvrat, Int. J. Neuropsychopharmacol. 6 (2003) 103–109.
[7] A. Serretti, R. Lilli, C. Lorenzi, L. Franchini, E. Smeraldi, Int. J. Neuropsychopharmacol. 1 (1998) 125–129.
[8] T. Kato, T. Inubushi, N. Kato, Int. J. Neuropsychopharmacol. 3 (2000) 83–85.
[9] V.A. Filov, The Inorganic Compounds of Elements of I–IV Group, Khimiya, Leningrad, 1988.
[10] J. Guddant, R.S.J. Frackowisk, C.D. Pusey, Brit. Med. J. 302 (1991) 1267–1269.
[11] B. Stemper, N. Thurauf, B. Neundorfer, J.G. Heckmann, Eur. J. Neurol. 10 (2003) 743–744.
[12] S. Nogue, M. Torra, D. Soy, P. Nadal, J. Nicolas, P. Munne, Toxicol. Lett. 88 (1996) 48–49.
[13] M. Antolovich, P.D. Prenzler, E. Patsalides, S. McDonal, K. Robards, Analyst 127 (2002) 183–198.
[14] M.B. Arnao, A. Cano, M. Acosta, Free Rad. Res. 31 (1999) 89–96.
[15] K. Honer, R. Cervellati, C. Neddens, Eur. Food Res. Technol. 214 (2002) 356–360.
[16] E.I. Korotkova, Y.A. Karbainov, A.V. Shevchuk, J. Electroanal. Chem. 518 (2002) 56–60.
[17] E.I. Korotkova, Y.A. Karbainov, O.A. Avramchik, Anal. Bioanal. Chem. 375 (2003) 465–468.
[18] Y.A. Karbainov, E.I. Kovedyaeva, Rus. J. Anal. Chem. 46 (1991) 328–329.
[19] A.V. Lykov, The Theory of Transcalency, Higher School, Moscow, 1967.
[20] B.B. Damaskin, O.A. Petry, The Introduction in Electrochemical Kinetics, Higher School, Moscow, 1975.
[21] E.A. Ivanovskaya, R.S. Krasnov, Rus. J. Anal. Chem. 52 (1997) 773–774.
[22] S. Chevion, E.M. Berry, N. Kitrossky, R. Kohen, Free Radic. Biol. Med. 22 (1997) 411–421.