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Mathematical Modelling and Numerical Simulation of the Processes in Noninvasive Potentiometric Method of Evaluating Antioxidant/Oxidant State of Skin

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Abstract The article proposes theoretical and experimental justification for using potentiometry as a new noninvasive method of evaluating antioxidant/oxidant state (oxidative stress) of a skin. Since the inductor of oxidative stress is an overall deficit of electrons accessible to cells, electrochemical methods of evaluating this parameter are naturally considered as fully corresponding with the nature of the phenomenon. A mathematical model is proposed that describes the processes determining analytical signals in the 'skin-gel-electrode' system. The signal occurs as a result of interaction between antioxidants/oxidants diffusing from the epidermis of the skin into the gel and the mediator system oxidised or reduced component introduced into the gel. The information source with regard to AOA/OA (antioxidant/oxidant activity) is the electrode potential shift. It occurs when the gel comes into contact with the skin. The series of potential determining substance-time dependences was obtained as a result of numerical simulation and experiment. Typical relationships between different parameters (chemical reaction rate, gel layer thickness, time) and concentration equal to antioxidant or oxidant activity, (AOA or OA) were found. An agreement between the calculated and experimental data was obtained. Findings analysis enables to forecast features of the experimental relations and provided an opportunity to choose experimental conditions ensuring the most reliable results.

Keywords Potentiometry, Noninvasive Method, Skin, Antioxidant, Oxidant, Oxidative Stress

1. Introduction

The study of causes and development of oxidative stress (OS) in the human skin, its association with skin diseases and other types of diseases has been conducted by scientists in different fields: medicine, chemistry, biology[1–3]. Oxidative stress contributes (or appears) significantly to the development of some nervous, lung, eye, and blood diseases as well as aging, coronary deficiency, strokes; take part in progressive damage in cardio-surgery, transplantation of tissues and organs and lungs surgery. Oxidative stress contributes to adverse effects on the skin, expressed as erythema, edema, wrinkling, photoaging[4], inflammation, autoimmune manifestation, hypersensitivity, keratinization abnormalities, preneoplastic lesions and skin cancer[5], psoriasis[2,6,7], vitiligo[8,9] seborrheic dermatitis[10].

The negative role of free radicals in human health is described in[2,11,12]. On the other hand, reactive oxygen (ROS) and reactive nitrogen (RNS) substances play a crucial role in the body, ensuring good metabolism and performance of vital functions in cells. Previous studies in this field[13-16] allow thinking that AOA/OA (antioxidant/oxidant activity) of the skin can provide information on AOA/OA of the whole body. Thus, developing a method of evaluating this parameter will enable to create a noninvasive method of assessing human health.

Antioxidant determination methods are widely reported in the literature[17-19]. Actually, proposed methods are invasive: they require blood taking or homogenate preparations of the analyzed tissue. The data about non-invasive methods used for determining antioxidant activity of biological objects are limited[19–21].

Because of inductor of oxidative stress is an overall deficit of electrons accessible to cells, AOA/OA body balance has the electrochemical nature that is why electrochemical methods of evaluating this parameter are naturally should be considered as fully corresponding with the nature of the phenomenon.

In[22] we described a potentiometric method of skin AOA/OA measurement. Advantages of the proposed approach are as follows: skin AOA/OA can be measured as

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integrated parameter by a direct, highly sensitive, user friendly and selective method. However, the following problem arises: the investigated 'skin-gel-electrode' system is complicated in comparison with the 'water solution-electrode' system used in the early described method[15–16] and it is not obvious, that the same approach and calculations can be used in applying a new method.

To justify the correctness of approach and conformity assessment of the measured value of AOA/OA to actually existing in the sample, it is essential to provide theoretical background to the processes occurring in the system, to create a mathematical model that takes into account a range of parameters such as the thickness of the the gel containing the mediator system; the rate of the chemical reaction between skin antioxidants/oxidants and compounds of the mediator system in the gel.

2. Theoretical Considerations

The method proposed in[22] is based on the interaction between antioxidants/oxidants diffusing from the skin epidermis into the gel and the mediator system introduced into the gel which is applied on the skin. The information source with regard to AOA/OA is the electrode potential shift in the mediator system $K_3[Fe(CN)_6/K_4[Fe(CN)_6]$, which is observed when the gel comes into contact with the skin as a result of changing concentration of oxidized or reduced forms of the mediator system in the gel. These changes in the concentration result from reaction (1) for antioxidants and reaction (2) for oxidants:

$$Fe(III) + AO = Fe(II) + AO_{Ox} \quad (1)$$

$$Fe(II) + OA = Fe(III) + OA_{Red} \quad (2)$$

where AO – antioxidant; AO_{Ox} – antioxidant oxidation product; OA – oxidant; OA_{Red} – oxidant reduction product.

The initial potential of the system E is determined by the following equation (3):

$$E = E_0 + b \cdot \log \frac{C_{Ox}}{C_{Red}} \quad (3)$$

where E_0 – standard potential of mediator system, C_{Ox} – concentration of oxidized form of mediator system, M; C_{Red} – concentration of reduced form of mediator system, M, b=2.3RT/nF.

The signal measured at any times depends on the concentration ratio of Fe(III)/Fe(II) at the electrode surface, wherein the change in Fe(II) concentration equals to the concentration of antioxidants, and the change in Fe(III) concentration equals to the concentration of oxidants.

After the sample containing antioxidants, is introduced in the system, the potential of the mediator system is described by applying Equation (4):

$$E_1 = E_0 + b \cdot \log \frac{C_{Ox} - X}{C_{Red} + X} \quad (4)$$

where E_1 – end potential, V; X – concentration of antioxidants, that come to the gel from skin, M.

After the sample containing oxidants is introduced in the system, the potential of the mediator system is described by Equation (5)

$$E_1 = E_0 + b \cdot \log \frac{C_{Ox} + Y}{C_{Red} - Y} \quad (5)$$

where Y -concentration of oxidants, that come to the gel from skin, M,

AOA=X and OA=Y are expressed in mole-eq/l (M-eq), if mentioned mediator system is used. Because in this case one electron participates in reaction Fe(III)+e= Fe(II). AOA and OA are calculated applying Equations 6 and 7:

$$C_{AOA} = \frac{C_{Ox} - \alpha C_{Red}}{1+\alpha}; \quad \alpha = (C_{Ox} / C_{Red}) \cdot 10^{(E_1 - E)nF/2.3RT} \quad (6)$$

$$C_{OA} = \frac{\alpha C_{Red} - C_{Ox}}{1+\alpha}; \quad \alpha = (C_{Ox} / C_{Red}) \cdot 10^{(E_1 - E)nF/2.3RT} \quad (7)$$

Proposed a physical model of the process is shown in Fig 1.

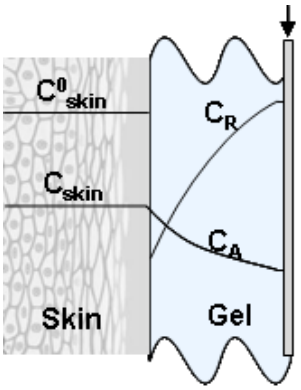

Figure 1. Physical model of the process: C^0_{skin} – initial concentration of antioxidants/oxidants in epidermis; C_{skin} – current concentration of antioxidants/oxidants in epidermis; C_A – concentration of antioxidants/oxidants in gel, C_R concentration of reagent (reduced form of mediator system Fe(II) or oxidized form of mediator system Fe(III) in gel

A mathematical model of the process is as follows: concentrations of antioxidants in epidermis (AOA=C_{skin}), reduced form of the mediator Fe(II) – C_R, resulting from Reaction (1) taking place in the space between skin surface and electrode, are determined by the solution of respective one-dimensional diffusion problems where the spatial coordinate x counts from the electrode surface (x=0) through gel layer to skin surface ($x=\delta_{gel}$). The coefficients of substances diffusion in the gel $D[cm^2 \cdot s^{-1}]$ is taken as a first approximation equal. Reactions 1 and 2 are considered first-order reactions with rate constant k. Antioxidant or oxidant penetrates from the epidermis into the gel through the skin surface. where its concentration is the desired time function with an initial value equal C^0_{skin}. For simplicity sake, we consider in calculations given below changes in the concentration of Fe(II) in Reaction (1) or Fe(III) in Reaction (2), as its concentrations. The electrode surface is

impenetrable to substances AO and R, δ in equations below is equal to δ_{gel}.

The diffusion problems for calculating concentration distribution of substances AO and R in the gel layer are as follows:

$$\frac{\partial C_A}{\partial t} = D \cdot \frac{\partial^2 C_A}{\partial x^2} - k \cdot C_A; \quad (8)$$

$$C_A(x,0) = 0; \quad \frac{\partial C_A}{\partial x}(0,t) = 0;$$

$$C_A(\delta,t) = C_{skin}(t);$$

$$\frac{\partial C_R}{\partial t} = D \cdot \frac{\partial^2 C_R}{\partial x^2} + k \cdot C_A; \quad (9)$$

$$C_R(x,0) = 0;$$

$$\frac{\partial C_R}{\partial x}(0,t) = \frac{\partial C_R}{\partial x}(\delta,t) = 0.$$

The mathematical model is added by the equation of the material balance of substance AO in the skin. The similar behavior is observed in the case of oxidants. The only difference is that the change in concentration of Fe(III) is considered instead of Fe(II).

$$\delta_{skin} \cdot \frac{dC_{skin}}{dt} = -D \frac{\partial C_A}{\partial x(\delta,t)}. \quad (10)$$

δ_{skin} – epidermis layer thickness,

An approximate solution of the problem was found by Laplace integral transformation along with Bubnov - Galerkin orthogonal method[23,24]. As a result, relative concentrations of antioxidant C_{skin}/C^0_{skin} in the skin and $C_{R(el)}/C^0_{skin}$ at the electrode surface were determined as a function of three dimensionless complexes:

$$Bi = \frac{k \cdot \delta^2}{D}; Fo = \frac{D \cdot t}{\delta^2}; \gamma = \frac{\delta}{\delta_{skin}}. \quad (11)$$

This representation allows us to analyze the effect of diffusion, the chemical reaction rate and the thickness of the gel layer on the dynamics of the processes.

$$\frac{C_{skin}}{C^0_{skin}} = e^{-F_1} \cdot \{\cosh(F_2)\} + \sinh(F_2) \cdot \frac{Bi + 2.5 \cdot (1-\gamma)}{f(Bi,\gamma)}; \quad (12)$$

$$F_1 = 0.5 \cdot Fo \cdot [Bi + (\gamma+1) \cdot 2.5];$$

$$F_2 = 0.5 \cdot Fo \cdot f(Bi,\gamma);$$

$$f(Bi,\gamma) = \sqrt{Bi^2 + 5 \cdot Bi \cdot (1-\gamma) + 6.25 \cdot (1+\gamma)^2};$$

$$\frac{C_{R(el)}}{C^0_{skin}} = \frac{d_1}{C^0_{skin}} + \frac{d_2}{C^0_{skin}}; \quad (13)$$

$$\frac{d_1}{C^0_{skin}} = \frac{Bi+15}{15 \cdot \gamma} - e^{-F_1} \left\{ \frac{Bi+15}{15 \cdot \gamma} \cdot \cosh(F_2) + \frac{F_3 - F_4}{\gamma \cdot f(Bi,\gamma)} \cdot \sinh(F_2) \right\} \quad (14)$$

$$F_3 = 2.5 \cdot (\gamma+1) + 2 \cdot Bi + 0.4 \cdot Bi^2;$$

$$F_4 = \frac{Bi \cdot (1-\gamma) + Bi^2}{3};$$

$$\frac{d_2}{C^0_{skin}} = F_5 \cdot e^{-10 \cdot Fo} - e^{-F_1} \cdot \{F_5 \cdot \cosh(F_2) + F_6 \cdot \sinh(F_2)\}; \quad (15)$$

$$F_5 = \frac{Bi \cdot (Bi-10)}{5 \cdot [30 - 10 \cdot \gamma - Bi \cdot (4-\gamma)]};$$

$$F_6 = \frac{Bi^3 - 2.5 \cdot (\gamma+3) \cdot Bi^2 + 25 \cdot Bi \cdot (\gamma+1)}{2.5 \cdot f(Bi,\gamma) \cdot (60 - 8 \cdot Bi - 20 \cdot \gamma + 2 \cdot \gamma \cdot Bi)}.$$

The solution enables to obtain the key correlation between the parameters which define characteristics of the processes occurring in this system, namely, to find the functions C_{skin}/C^0_{skin} and $C_{R(el)}/C^0_{skin}$ depending on the arguments δ_{skin}-epidermal thickness, δ_{gel}-thickness of the gel layer and t-time.

In this case C_R reflects C_{AOA}, as substance R (Fe(II)-reduced form of the mediator system) results from Reaction (1) which is running in the gel. In case of oxidants C_R will reflect C_{OA} as substance R (Fe(III)-oxidized form of the mediator system) results from Reaction (2) Let us once again focus on a very important fact: C_R is an increment (rather than an absolute value) of the concentration of reduced (Eq. 1) or oxidized (Eq. 2) forms of the mediator system.

$C_{R(el)}$ – increment (rather than an absolute value) of concentration at the electrode surface determines a measuring signal that is recorded as a shift of the electrode potential in the mediator system, initially introduced into gel.

Ideally, $C_{R(el)}/C^0_{skin}$ should approach to 1.

Since the mathematical model and calculations in the cases described by Equations (1) and (2) do not differ, the value of $C_{R(el)}$ will be used for further considerations.

The general profile of dependence of C_{skin}/C^0_{skin} and $C_{R(el)}/C^0_{skin}$ on non-dimensional parameters, including the above given arguments, is shown in Figure 2.

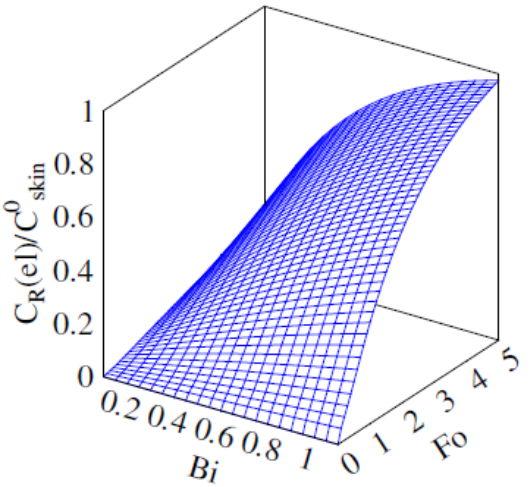

Figure 2. Dependence of $C_{R(el)}/C^0_{skin}$ on non-dimensional parameters Bi and Fo

Consequently, the values of C_{skin}/C^0_{skin} and $C_{R(el)}/C^0_{skin}$ that reflect the change in the concentration of the original substance (antioxidants) and reagent (the product of reaction (1)) at the interface of skin-gel and gel-electrode, are determined by the initial concentration of C^0_{skin} in skin; by the rate of AO diffusion and by the rate of chemical interaction of AO with the component of the mediator system (reaction 1) in the gel.

The aim of further research is to find the conditions when a recorded signal has a maximum correct reflection of C^0_{skin}.

For clarity and ease of comparison of the calculated and experimental data, C_{skin}/C^0_{skin} and $C_{R(el)}/C^0_{skin}$ are given as functions of t at different combinations of δ_{skin}, δ_{gel}, k and D.

It is apparent that C_{skin}/C^0_{skin} decreases whereas $C_{R(el)}/C^0_{skin}$ increases with time (Fig. 3). Moreover, at a given moment, the higher reaction rate constant, the lower C_{skin}/C^0_{skin}; but the bigger $C_{R(el)}/C^0_{skin}$. The diffusion coefficient affects neither C_{skin}/C^0_{skin} nor $C_{R(el)}/C^0_{skin}$.

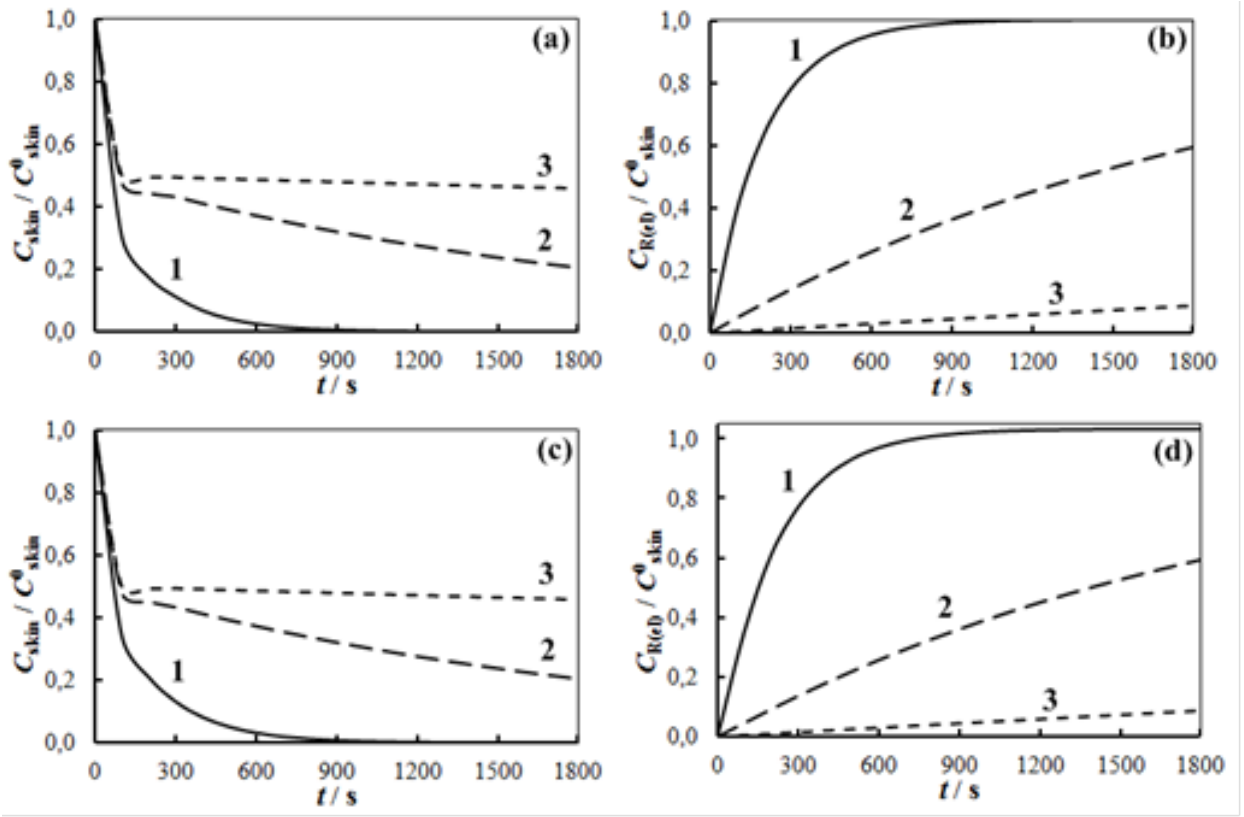

Figure 3. Calculated value of C_{skin}/C^0_{skin} (a, c) and $C_{R(el)}/C^0_{skin}$ (b,d) as functions of t for different D and k: D=10^{-4} cm^2s^{-1} (a, b); D=$2x10^{-6}$ cm^2s^{-1} (c, d) k =0.01 (1), 0.001 (2) and 0.001 (3) s^{-1}, δ_{skin}=0.1 mm; δ_{gel}=0.1 mm

Fig. 4 shows dependence of C_{skin}/C^0_{skin} and $C_{R(el)}/C^0_{skin}$ on the thickness of the gel and epidermal layers. It is also apparent that increasing duration of measurement and thinner gel layer lead to lower C_{skin}/C^0_{skin} but higher $C_{R(el)}/C^0_{skin}$. This relation is understandable since these parameters have an impact on exit of antioxidants from the skin and delivery of potential-determining substance R to the electrode surface. It is important to take into account the ratio of $\delta_{skin}/\delta_{gel}$, since the smaller δ_{skin}, the smaller the amount of antioxidants and, therefore, a potential-determining substance in gel, the smaller. The thicker the gel layer the lower the concentration of AO and R in it.

The calculations allow making an important practical conclusion: measurements should be long enough to ensure maximum exit of antioxidants from the skin into the gel; thickness of a gel layer should be minimum and close to thickness of epidermis. It should be reproducible in different experiments. The lower the rate constant of antioxidant/oxidant interaction with a corresponding component of the mediator system, the lower its contribution to the detected signal is.

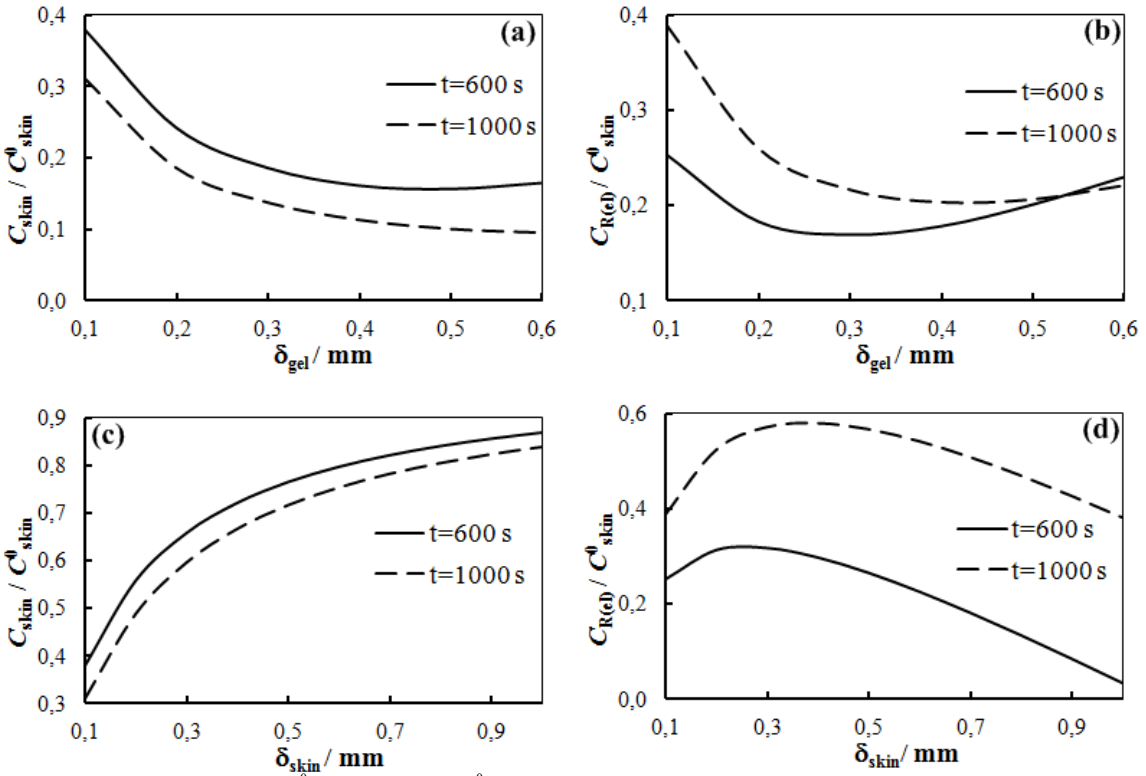

Figure 4. Calculated dependence of C_{skin}/C^0_{skin} (a,c) and $C_{R(el)}/C^0_{skin}$ (b,d) on thickness of gel layer (a,b) and skin (epidermis) layer (c,d). $D = 10^{-6}$ cm^2·s^{-1}; k=0.001 s^{-1}; δ_{skin}=0.1 mm (a,b), δ_{gel} =0.1 mm (c,d)

3. Experimental Section

3.1. Materials

- $K_4[Fe(CN)_6]$, $K_3[Fe(CN_6)]$, KH_2PO_4, $Na_2HPO_4 \cdot 12H_2O$, ascorbic and uric acids, cysteine and glutathione of high purity grade or chemically pure were obtained from Reachim, Russia.
- Mixture of $K_3[Fe(CN_6)]$ and $K_4[Fe(CN)_6]$ served as mediator system.
- Unimax, highly conducting gel (Geltek-Medica, Russia) and adhesive plaster Silkofix PE 2500 were bought in Pharmacy store.

3.2. Investigated Subject

The surface of human skin in the wrist area served as the subject of investigation. The investigated area of skin was washed with deionized water.

Gel, containing ascorbic acid, cysteine or glutathione served as model systems.

3.3. Instruments

Potentiometric measurements were performed using potentiometric analyser Taion (Tomanalyt Ltd, Tomsk, Russia) with a two-electrode electrochemical cell. Platinum screen-printed electrode (IVA, Ekaterinburg, Russia) and ecg electrodes H92SG Ag|AgCl, KCl (Arbo, Kendal, USA served as working and reference electrodes. Silver/silver chloride electrode (Ag/AgCl/3 M KCl), EVL -1M type (Gomel Measuring Equipment Plant, Gomel, Republic of Belarus) was used as reference electrode in kinetics experiments.

3.4. Methods

Measurements of chemical reactions rate using model systems

Four ml of the gel and 0.2 ml of an aqueous solution of the mediator system containing a mixture of 10^{-3} M $K_3[Fe(CN)_6]$) + 10^{-5} M $K_4[Fe(CN)_6]$ were placed in a glass cell. Electrodes were immersed in the mixture and the potential (E) was measured after 60 s. Then the electrodes were removed from the cell and 0.2 ml of an aqueous solution of an antioxidant was added. The concentrations of the solutions in the cell were $2 \cdot 10^{-5}$ M ascorbic acid or $4 \cdot 10^{-5}$ M glutathione. The electrodes then were again immersed in the cell and the change in the potential was recorded until its value stabilized. Concentration of antioxidants in gel was calculated using Equation 6 and assuming $\Delta E = E - E_1$, where E was the electrode potential in the gel containing the mediator system; E_1 was the potential in the gel containing the mediator system and antioxidant at a given time t. Value of found antioxidant concentrations at the end of the measuring process and at a half-time of that were used to calculate constants of chemical reaction rate. Form of the curves is shown on the Fig.6.

Skin investigation

In order to study the effect of thickness of a gel layer on potentiometric measurements two plates were placed on the tested skin area at a distance of 1cm from each other (Fig.5).

The gel containing mediator system, platinum screen-printed and ECG H92SG electrodes were placed in the space between the plates, as shown in Fig. 5. The layer thickness was controlled by the number of pieces of hypoallergenic adhesive plaster (from 1 to 5) located on each other. The thickness of plates were measured with a micrometer.

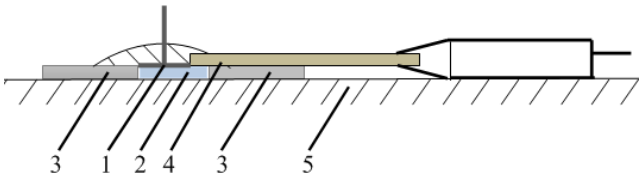

Figure 5. Design of a unit for measuring skin AOA: 1 – reference electrode; 2 – gel, containing mediator system (10^{-3} M $K_3[Fe(CN)_6]$+ 10^{-5} M $K_4[Fe(CN)_6]$), 3 – plates; 4 – platinum screen-printed electrode; 5 – skin

4. Results and Discussion

Fig. 6 presents the dependence of *E*-*t*, obtained experimentally and AOA-*t*, calculated applying Eq. 6. All experimental results given below were obtained in this way. Sudden changes in the potential and AOA were observed in the range 0–500 s, which is consistent with the results of the calculations (Fig. 3). After 600 s measurements the potential change in time was slow. For example, the difference between the experimental values of AOA (Fig. 6) during 600 s and 783 s was $0.3 \cdot 10^{-6}$ M-eq, or 0.8%. Further measurements were carried out during 600 s.

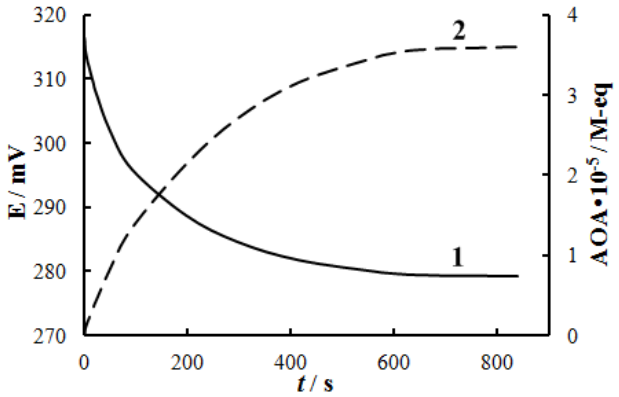

Figure 6. Time dependence of potential (1) and antioxidant activity (2) measured on human skin

Standard deviation of measurements on different areas of skin of the same person was within 5–6% The value $C_{R(el)}/C^0_{skin}$ required for the comparison of the experimental and calculated data was found as the ratio of AOA concentration at a given moment to concentration found after 600s measurements.

The search of the literature allowed to find the values only for water solutions in the range from $1.52 \cdot 10^{-5}$ $cm^2 \cdot s^{-1}$ (in the presence of 0.1 mM potassium ferricyanide in 0.1 M Na_2HPO_4)[25] to $7 \cdot 10^{-6}$ $cm^2 \cdot s^{-1}$ [26].

The value of the diffusion coefficient of ferri /ferrocyanides in the gel was calculated using the relation $D_{gel}=D_{water} \cdot \eta$. Gel viscosity ($\eta$) was taken close to 8-9 Pa·c[27] and density range equaled 1.02–1.05 $g \cdot cm^{-3}$. Further, D_{gel} was taken as $2 \cdot 10^{-6}$ $cm^2 \cdot s^{-1}$.

The rate constants of Reaction 1, determined by the above mentioned method, were 10^{-2} s^{-1} for ascorbic acid and $5 \cdot 10^{-4}$ s^{-1} for glutathione

Fig. 7 shows the calculated and experimental dependence of $C_{R(el)}/C^0_{skin}$ on the thickness of a gel layer. A thicker gel layer led to lower $C_{R(el)}/C^0_{skin}$. Two important conclusions are apparent from Fig. 7: (i) theory and experiment are in good agreement and (ii) thickness of a gel layer should be minimum and close to thickness of epidermis as follows from the theoretical calculations. It should be reproducible in different experiments.

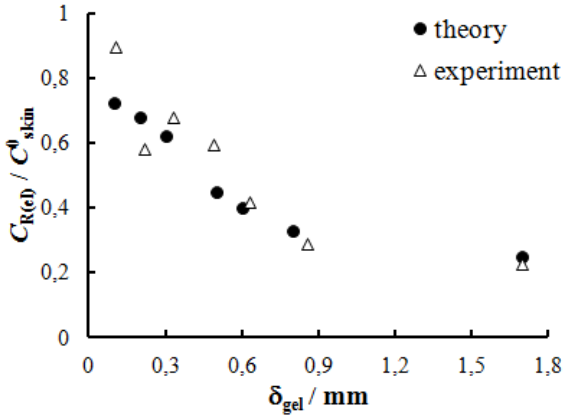

Figure 7. Calculated and experimental dependence of $C_{R(el)}/C^0_{skin}$ on thickness of gel layer; k=0.01 s^{-1}, δ_{skin}=0.1mm

Time dependence of (a) $C_{R(el)}$ (experimental measurements, volunteers 1-7); and (b) $C_{R(el)}/C^0_{skin}$: averaged experimental (Curve 1) and calculated curves (Curve 2, k =0.01 s^{-1} and Curve 3, k=0.0005 s^{-1}) are presented on Fig. 8.

Big differences in the values of AOA are due to a variety of volunteers' levels of health and nutrition/diets. For example, Curve 7 was obtained by taking measurements on the volunteer's skin who suffers from atopic dermatitis.

It is apparent that the expression of data as dependences $C_{R(el)}/C^0_{skin}$ lead to confluence of the curves: Figure 8b demonstrates averaged Curve 1 and a small scatter of the experimental data around it. The average curve is very close to the curve that was theoretically calculated for the case when a constant rate of the chemical reaction (1) between antioxidant and an oxidized form of the mediator system in the gel equaled $0.01s^{-1}$. As mentioned above, that was the rate of the reaction of ascorbic acid with $[Fe(CN)_6]^{3-}$. Glutathione reacts with $[Fe(CN)_6]^{3-}$ much slower (k=0.0005 s^{-1}). The result seems to be a less significant contribution of glutathione than of ascorbic acid to the formation of potential- determining substance and, therefore, to the signal. This would give significant errors in AOA determination if content of these antioxidants in the skin would be the same. Fortunately, ascorbic acid (70%) and uric acid (20%). prevail in epidermis. Cysteine and glutathione are present at low concentration (9%). The quantity of other antioxidants (including liposoluble antioxidants) does not exceed 1 – 2%[28]. Taking into account these data, the analysis results

of the proposed method can be considered as reflecting the real situation and the calculated and experimental results demonstrate good correlation.

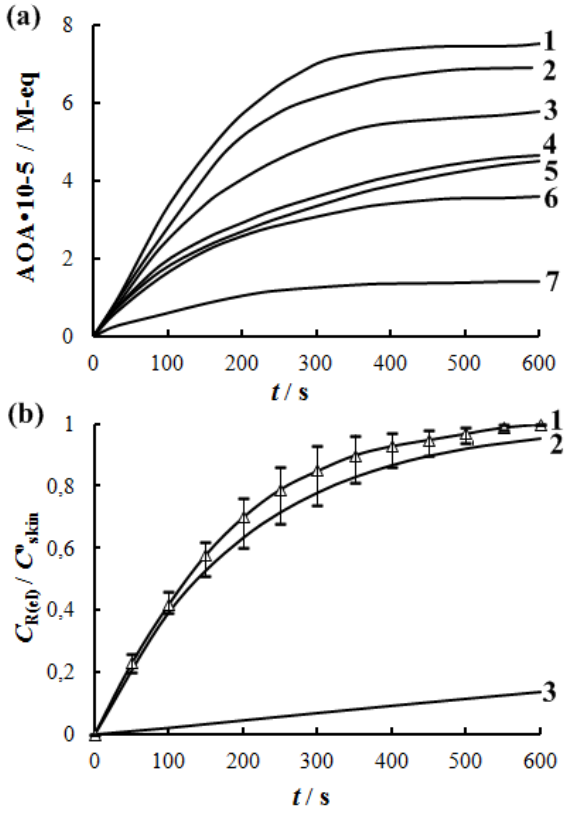

Figure 8. Time dependence of (a) AOA=$C_{R(el)}$ (experimental measurements, volunteers 1 – 7); and (b) $C_{R(el)}/C^0_{skin}$: averaged experimental (1) and calculated curves (2 – k =0.01 s^{-1} and 3 – k=0.0005 s^{-1})

Due to complexity of the mathematical models and calculations, lack of accurate data related to thickness of epidermis, AO diffusion in the skin, AO and R in the gel, and the rate constants of chemical reactions, it should be accepted that there is quite a good agreement between theory and experiment. This gives grounds to use the results of calculations as a source of information regarding selection of experimental conditions, evaluation and interpretation of the results.

5. Conclusions

The existing relationship between the internal state of a human body and skin pathology suggests that skin AOA/OA can be a source of information regarding common health problems. Skin AOA/OA can also constitute the basis for developing new methods of analytical chemistry that can be used for monitoring levels of human health and population screening in order to identify, in particular, groups of risk, and detect diseases in an early stage. Decreasing antioxidant content in the skin reflects the emergence of imbalances in the body's antioxidant defense system, i.e. oxidative stress. Oxidative stress has an electrochemical nature that is why electrochemical methods of evaluating this parameter may be considered as fully corresponding with the nature of the phenomenon.

Potentiometry is one of the most easily implemented electrochemical method. Moreover, it is widely used in sensors for medical diagnostics. The article elaborates upon the theory of non-invasive method of potentiometric determination of antioxidants and oxidants in the skin. The method is based on measuring an electromotive force produced when electrodes are placed in the gel applied to skin. A good agreement between theoretical and experimental results allows using the calculated results as a source of information regarding selection of experimental conditions, evaluation and interpretation of the results.

The advantages of the method are as follows: skin AOA/OA is measured as an integral parameter by direct method; results can be obtained quickly; the method is non-invasive and painless. The measurements are highly sensitive and show good selectivity. Hardware design is simple and accessible and provides possibility to work in the field, in the hospital or at the bedside.

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