ISSN 1070-3632, Russian Journal of General Chemistry, 2014, Vol. 84, No. 5, pp. 998–1009. © Pleiades Publishing, Ltd., 2014.
Original Russian Text © M.Sh. Khubutiya, A.Yu. Tsivadze, M.M. Gol'din, V.N. Andreev, G.R. Garaeva, A.A. Stepanov, Mikh.M. Gol'din, 2012, published in Rossiiskii Khimicheskii Zhurnal, 2012, Vol. 56, Nos. 5–6, pp. 30–42.

Electrochemically Controlled Methods for Removal of Endo- and Exotoxicants from Biological Media

M. Sh. Khubutiya[a], A. Yu. Tsivadze[b], M. M. Gol'din[a], V. N. Andreev[b], G. R. Garaeva[a], A. A. Stepanov[a], and Mikh. M. Gol'din[c]

[a] *N.V. Sklifosovsky Research Institute of Emergency Medicine, B. Sukharevskaya pl. 3, Moscow, 129090 Russia*
e-mail: markmgold@gmail.com; garaevagu@gmail.com; andreyastepanov@gmail.com

[b] *A.N. Frumkin Institute of Physical Chemistry and Electrochemistry, Russian Academy of Sciences, Leninskii pr. 31, Moscow, 119991 Russia*
e-mail: tsiv@phyche.ac.ru; vandr@phyche.ac.ru

[c] *Liberty University, 1971 University Blvd, Lynchburg, VA, 95653 USA*
e-mail: goldin03@gmail.com

Received November 1, 2012

Abstract—The electrochemical model of the system of electroconductive hemosorbent/biological medium was proposed to develop electro-chemically controlled medical detoxification technologies for treat-ment of diseases of certain etiology. It was obtained that the destruc-tion of blood cells as a result of a contact blood with hemosorbents is caused of hemosorbent potential. The potential region of hemosor-bent corresponding of hemocompatibility was determined. Hemo-compatible composite material based on activated carbon covered polypyrrole were synthesized. Certain electrochemical medical tech-nologies for selective removing of endo- and exotoxicants and dam-aged blood cells from biological media of organism were developed.

DOI: 10.1134/S1070363214050375

The existing methods for purification of biological media, including detoxification of the body (hemodialysis, infusion therapy with the use of oxidants, hemosorption etc.), have significant limitations and disadvantages. Therefore, one of the objectives aimed to improve biological media purification methods is to create a new generation of hemosorbents combining hemocompatibility and selectivity.

A possibility to use carbon materials as hemosorbents for emergency detoxification of the body is associated with their high adsorption activity in relation to organic and inorganic toxicants [1–3]. The main disadvantage of carbon sorbents is their lack of selectivity. In order to give carbon sorbents the desired adsorption properties it is usual to use modification methods, which are largely reduced to chemical interactions of different modifiers (oxidants, reducing agents, mineral acids etc.) with functional groups of carbon surface compounds [4, 5].

A rather promising line of research in the area of body detoxification technologies is the development of electrochemical methods for modification of carbon sorbents with a view to give them selective properties [6, 7].

The physiology friendly character of electrochemical medical technologies is related to the fact that many vital processes, taking place in the human body, are, in essence, electrochemical. There is a great number of examples of such biotic processes, including, for instance, transmission of nerve impulses, charge transfer in the electron transport chain of cellular respiration, trans-biomembrane ion exchange processes, membrane transport in blood cells, as well as metabolism of toxicants in the body [8–12]. Moreover, according to Nordenstrom's concept [12], the human body is a system of biologically closed electric circuits. Thus, blood vessels can be compared to electric wires, whereas blood and other liquid media of the body represent a conducting medium for transmission of signals and occurrence of many processes.

The development of theoretical ideas about the leading role of electrochemical processes in the

functioning of different systems of the body has led to an increase in electrochemical applications in modern medical technology. At present, methods to study different media of the body with the use of electrochemical sensors, which are able to determine the state and properties of biological objects, control their parameters, and assist to adjust the proposed medical treatment, are widely used in medical practice.

Let us briefly consider the principles of operation and creation of electrodes for electrochemical sensors, as these sensors form the basis for active development of detoxification electrochemical medical technologies using similar methods to treat the surface of the applied materials.

Detection techniques, involving the use of electrochemical sensors, are most often based on potentiometric, voltammetric, and conductometric methods [13, 14]. As a rule, measurements are taken in such liquid biological media as blood, blood plasma, and blood serum [15]. Methods to measure electric potentials directly in muscle tissues of the body, vascular walls etc. have been also developed. For example, the authors of work [12] measured potentials of platinum electrodes implanted in biological tissues in order to obtain information about the presence or absence of pathological processes in these tissues.

To give sensors the desired properties (high sensitivity and selectivity with respect to the test substance) electrodes are modified using various methods, for example, by depositing active substances with an affinity for the studied substrates on their surface [16].

There are biosensors based on polarographic biospecific methods [17]. Electrochemical sensors used to evaluate the state of the studied object on the basis of oxygen content in tissues [18] and aqueous media [19], or the content of glucose in blood [20] etc. have also become widespread.

One of the currently widely used electrochemical methods for general assessment of the state of the studied medium is based on measurements of redox potentials [21–25]. This technique is of a particular interest for the development of electrochemical detoxification methods, as it makes it possible to control the effectiveness of a conducted medical procedure and adjust the treatment process [26]. According to this method, the potential of a platinum or gold electrode, immersed in blood, plasma, or blood serum, is measured. However, it should be noted that in fact the measured value is not the redox potential of the tested medium; from the electrochemical point of view, it should be referred to as the open circuit potential. However, the "redox potential" term is long and deeply rooted in published medical works and, therefore, we will also apply this term in this article. As we demonstrated in work [27], the redox potential monitoring method applied to patients with a transplanted liver [28] or kidney [29] made it possible to develop diagnostic and prognostic criteria for timely diagnosis of complications in the course of treatment and signaling the necessity to change the treatment strategy.

At present, the most widely used detoxification technologies are hemodialysis and hemosorption. Hemosorption methods have certain advantages related to higher rates of adsorption processes as compared to dialysis processes [30, 31]. Moreover, the procedure of hemosorption detoxification is significantly simpler, less traumatic for patients, and much cheaper. However, the hemosorption process in its traditional form [30] cannot be controlled. Moreover, the existing hemosorbents based on carbon materials have no selectivity. However, if we take into account that adsorption of substances from aqueous solutions depends on electrochemical parameters of the electrode, real possibilities to create selective hemosorbents based on porous carbon materials with the help of electrochemistry become evident. It is important that electrochemical processes are easily automated. Therefore, the development of controlled detoxification technologies using electrochemical equipment seems, at first glance, quite attainable.

At the same time, the implementation of electrochemical detoxification processes requires the solution of several important problems. First of all, it is necessary to prevent decomposition of blood constituents upon contact with hemosorbents, which at present are based on porous carbon materials. The first works on hemosorption established that a contact of hemosorbents, made of activated carbons, with blood resulted in destruction or trauma of the formed elements of blood [30]. It is known [32] that the process of blood cell destruction upon contact with activated carbons can be suppressed if the carbon surface is modified with proteins (for example, albumin or haptoglobin [30, 33]). However, coating of carbon materials with proteins leads to a sharp decrease in the rate of adsorption of toxicants and the adsorption capacity of the sorbent. For example, in

Table 1. Density of electrical discharge of blood cells and their electrophoretic mobility in normal conditions

Formed element	Charge density, μC/cm^2	Electrophoretic mobility, μm cm^{-2} V^{-1} s^{-1}
Erythrocyte	–1.12 to –1.21	1.1–1.3
Platelet	–0.83 to –0.85	120–130
Leucocyte	–2.45	53000–58000

the presence of albumin adsorption of many natural compounds is reduced by a factor of 2–4 [34].

A similar effect on the rate of adsorption of exotoxicants was illustrated by an example of extraction of barbiturate drugs from aqueous and biological media with the use of SKT-6A carbon hemosorbent coated with albumin in our work [35].

The above facts stimulated a search of ways to use unmodified carbon materials as hemosorbents. In order to solve this problem it was necessary to establish the mechanism of interaction of activated carbons with the formed elements or blood cells (erythrocytes, leukocytes, and platelets).

The formed elements in the composition of the carbon/blood system have the following properties. Firstly, all formed elements are represented by colloidal particles with negatively charged membranes [36]. Secondly, under normal conditions, the charge density on the membrane of blood cells is constant, and, therefore, it can be used to diagnose certain diseases based on the magnitude of deviations of this parameter from the norm (Table 1) [37].

An assumption that it is the presence of the charge on blood cell membranes that can be the reason for their trauma or death has prompted us to look at the hemosorbent/blood system and to consider it from the electrochemical point of view. In fact, a hemosorbent based on activated carbons is a first-class conductor and upon its contact with blood it can be viewed as an electrode, as blood can be presented as an electrolyte, a 0.15 M aqueous solution of sodium chloride, containing the formed elements, proteins, and other natural compounds. Therefore, a double electric layer is formed on the surface of carbon immersed in blood and this surface acquires a certain charge. The magnitude and the sign of the carbon surface charge in the carbon/blood system depends entirely on the nature of carbon, as the electrolyte remains unchanged regardless of the conditions of the patient. Like the content of other blood constituents, the electrolyte composition of blood cannot significantly change even in case of pathological conditions of the patient.

Thus, the activated carbon/blood system is electrochemical, in essence; and carbon in this system acts as a porous electrode. Within the framework of this model, adsorption interactions in this system have to depend on the value of the potential of the carbon sorbent-electrode and the sign of the charge on its surface, as well as on the physicochemical properties of potential adsorbates, i. e. proteins, exo- and endotoxicants. A schematic picture of the proposed electrochemical carbon/blood model is given in Fig. 1.

As the surfaces of carbon and the membranes of blood cells are charged, attraction between the carbon

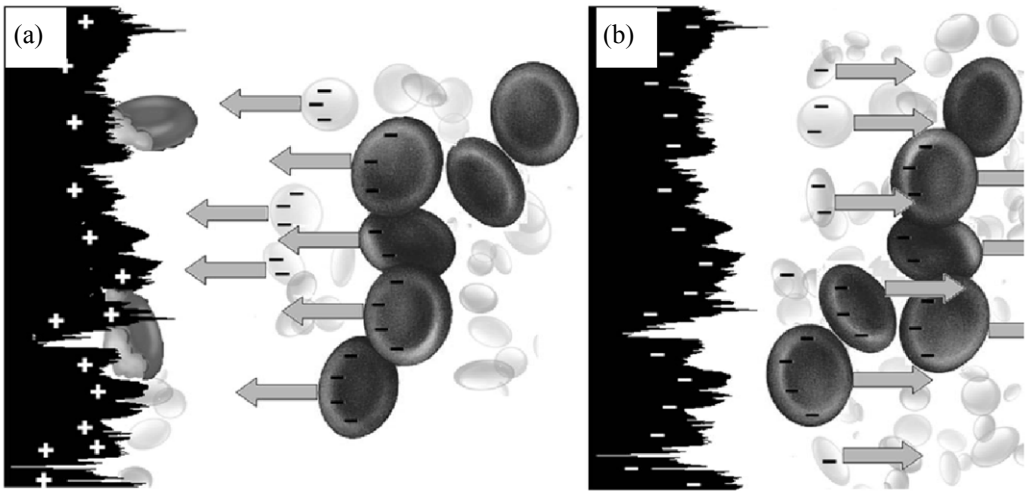


Fig. 1. Electrochemical model of interactions in carbon/blood system.

surface and blood cells has to take place if they are oppositely charged (Fig. 1a). In this case, the blood cell should be adsorbed on the carbon surface, and as a consequence of the contact between its charged membrane and a foreign surface destruction or trauma of the cell takes place. In case the carbon surface and the blood cell have charges of the same sign, repulsion of blood cells from the carbon surface has to take place (Fig. 1b), and this interaction can be minimized or brought to naught. As the membranes of blood cell always have a negative charge, interactions in the carbon/blood system have to depend on the sign of the carbon charge. It is clear that the degree of interaction in the carbon/blood system can be controlled by charging the carbon surface negatively. Thus, hemocompatibility can be achieved by external polarization of carbon, bringing the value of its potential into a range of potentials, corresponding to the absence of interactions between carbon and the formed elements of blood. Also, there is a possibility to give hemocompatible properties to activated carbons by means of chemical or electrochemical modification of the carbon surface, ensuring that the open circuit potential of the carbon is shifted into a range of potentials, corresponding to hemocompatibility.

The idea of a carbon sorbent as an electrode made it possible to make an unambiguous conclusion about the influence of the carbon potential on its adsorption activity. It should be noted that already in A.N. Frumkin's works [38] it was established that there was a dependence of adsorption of organic and inorganic substances on a metal electrode on the potential of the electrode.

In order to verify applicability of the proposed electrochemical model of the carbon/blood system the influence of the potential of the carbon electrode-hemosorbent on the decline of platelets in the process of hemosorption was studied. Correlation of values of the potentials of carbon hemosorbents under open circuit conditions with the decline of platelets in the carbon/blood system in the course of 60 min (Fig. 2) demonstrates that the more positive is the value of the carbon potential under open circuit conditions, the more damaging effect on platelets the carbon has. On the contrary, when values of the carbon potential are more negative than 0.05 V, no decline of platelets is observed (hereinafter values of the potential are given relative to a saturated silver chloride reference electrode).

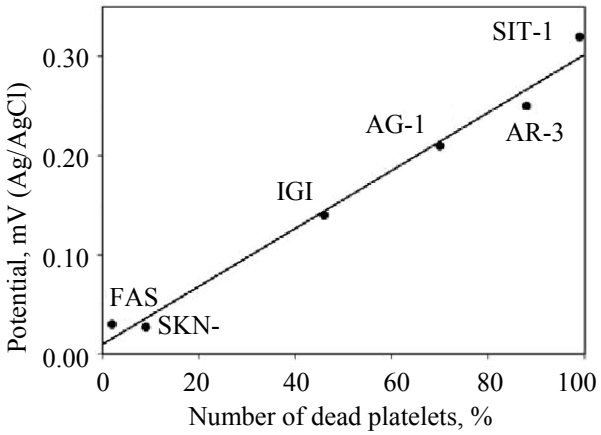


Fig. 2. Influence of the carbon sorbent potential on the death of platelets in the course of 60 min.

The results of works studying the influence of the potential of various carbon types on the decline of platelets, erythrocytes, and leukocytes after a 30-min period of contact between the carbons and blood are given in Table 2.

Table 2. Potentials of carbons and hematological indicators before and after 30 min of hemosorption

Carbon type	Potential, V	Hematological indicators			
		erythrocytes, units/L × 10^{12}	leucocytes, units/L × 10^{9}	platelets, units/L × 10^{9}	hemoglobin, g/L
No sorbent	–	4.9	6.3	280	156
SKT-6	0.04	4.8	6.1	180	156
IGI	0.06	4.0	5.5	170	148
BAU	0.12	3.2	5.2	110	134
SKT-6A	0.14	3.2	4.8	120	115
SKT-2B	0.20	2.9	3.6	100	122
AR-3	0.27	2.8	3.2	80	100

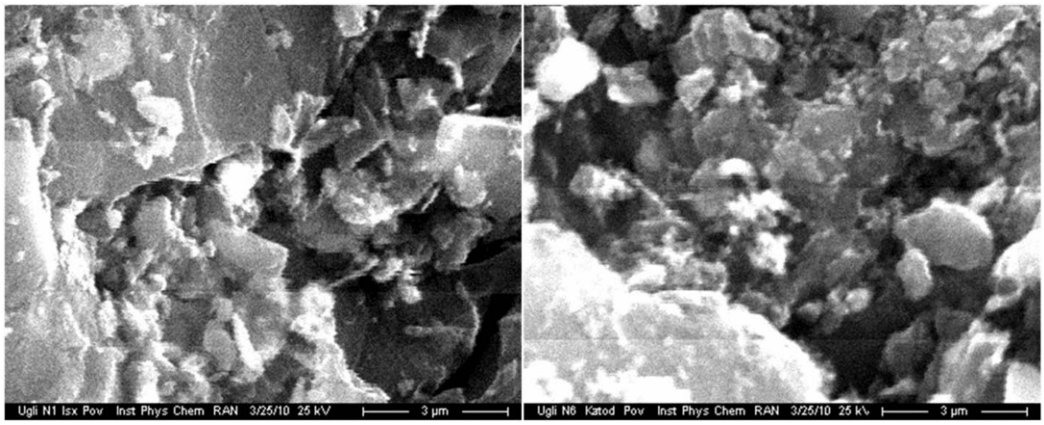


Fig. 3. Photomicrographs of AG-3 original carbon with the potential of E = 0.20 V and AG-3 carbon modified to the potential of E = –0.30 V.

As follows from the data presented in Fig. 2 and Table 2, there is a significant difference in the traumatic effect of the studied carbon materials on the formed elements of blood depending on the value of the carbon potential. The more positive is the value of the potential, the more platelets, erythrocytes, and leukocytes are destroyed. The maximal reduction in the number of the formed elements was observed for SIT-1 carbon, the potential of which was E = 0.38 V and for AR-3 carbon (E = 0.27 V). There was almost no decline in the number of the formed elements upon contact with FAS (E = 0.03 V) and SKN (E = 0.027 V) carbons.

The data of Table 2 also demonstrate that at positive values of the carbon potential (exceeding 0.20 V) there is significant blood hemolysis (rupturing of erythrocytes), and a decline in platelets is observed even upon contact with such carbons as FAS, SKN, and coconut-based carbon, which are little traumatic for the human body (Fig. 2). Thus, the carbon potential has an impact on interactions between blood and carbons of different nature. Moreover, the more positive is the value of the potential, the stronger is the interaction.

The obtained results make it possible to come to a conclusion about a rather significant effect of the carbon surface charge on interactions between carbons and blood cells. It should be emphasized that until present some researchers have interpreted destruction and death of blood cells upon contact with activated carbons as a result of cell collision with irregularities of microrelief of carbon materials, represented by sharp protrusions, often needle-shaped, and roughnesses of the surface [31, 39, and 40]. It is possible that sharp protrusions and roughnesses of the carbon surface are points of localization of the interaction between carbon and blood cells; however, in our opinion, the forces of interaction in the carbon/blood system and the reasons for cell destruction and trauma are related not to the presence of protrusions and roughnesses as such, but to the sign and magnitude of the carbon surface charge (i.e. to the electric potential of the surface).

It is evident that the question about the influence of the carbon potential on its interaction with blood cells is fundamental. The data presented in work [6] provide a clear evidence of the predominant influence of carbon potential on cell morphology. This work demonstrates that if the potential of SIT-1 carbon is 0.35 V, it almost completely destroys erythrocytes. However, when this carbon is polarized to a potential of –0.20 V, no destruction of erythrocytes or other blood cells is observed.

We studied the microrelief of many carbon types modified to different potentials using a scanning electron microscopy method; some of the obtained data are given in Fig. 3. The comparison of photomicrographs of carbons made before and after their modification convincingly demonstrates the absence of significant changes in the microrelief.

The presented data represent another argument in favor of our previously expressed point of view about the predominant role of the carbon surface charge (potential) in interactions between carbon and blood cells.

In this connection, it is interesting to measure hematological parameters of blood after contact with externally polarized activated carbon [41].

Table 3. Blood indicators after contact with AG-3 carbon polarized to different potentials

Blood elements and their content measurement units	No sorbent used	Potential of the sorbent, V			
		0.50	0.20	0.00	–0.30
Erythrocytes, units/L × 10^{12}	3.5	2.4	2.9	5.0	5.5
Leucocytes, units/L × 10^{9}	7.2	3.2	3.8	6.8	7.6
Hemoglobin, g/L	144.0	105.0	115.0	128.0	140.0
Free hemoglobin, μg %	0.0	300.0	150.0	0.0	0.0

As seen from the data presented in Table 3, significant deviations in the number of blood cells from the initial values take place only in case of anodic polarization of AG-3 carbon (0.20 V, 0.50 V); minor deviations are observed at a potential of E = 0.00 V. Cathodic polarization of AG-3 carbon to a potential of E = –0.30 V leads to insignificant deviations in the number of blood cells as compared to the initial blood sample. It should be noted that free hemoglobin appears as a result of contact of blood with AG-3 carbon, polarized to positive potentials. The presented data also demonstrate a significant influence of the electrode charge on its interaction with blood cells.

Summarizing the data presented in Fig. 2 and Tables 2 and 3, it is possible to make an important practical conclusion that for activated carbons a range of potentials from –0.15 to 0.05 V is a range of hemocompatibility.

As indicated above, the electrochemical model of the carbon/blood system makes it possible to control the adsorption process parameters by changing the electrode-sorbent potential. This possibility was confirmed by studying the adsorption of 1,2-dichloroethane on carbon sorbents with different potentials. The 1,2-dichloroethane was selected as the object of research because it is an extremely toxic exotoxicant and cases of poisoning with 1,2-dichloroethane are encountered in clinical practice of acute poisoning hospital departments [42]. It was found that a decrease in the concentration of 1,2-dichloroethane in a 0.15 M aqueous solution of NaCl in case of adsorption on SKT-6A carbon, which was widely used as a hemosorbent [30], amounted to 52% at a carbon potential of 0.16 V, whereas at a potential of 0.20 V a decrease in the concentration increased up to 84%. In work [42] the results of measurements of SKT-6A carbon potential in saline (0.15 M aqueous solution of NaCl) and in blood are also presented. It is established that the carbon potential remains almost unchanged in these media, which confirms the justification of using saline as a blood model.

Thus, it is proved that by changing the potential of activated carbons it is possible to achieve a reduction in the traumatic effect of carbons on the formed elements of blood, simultaneously increasing the adsorption activity of hemosorbents in relation to exotoxicants [41, 43].

In order to determine the reason for the shift of the carbon potential resulting from electrochemical modification of carbons it was attempted to find out the mechanism of action of cathodic and anodic modification of carbons, using the data of energy dispersive spectrum analysis. It was established that carbons of various nature had different oxygen content (Fig. 4).

These data aroused even more interest when open circuit potentials of carbons were measured. It was found that there was a clear correlation between the content of oxygen in surface functional groups of carbon and the value of its potential. As can be seen

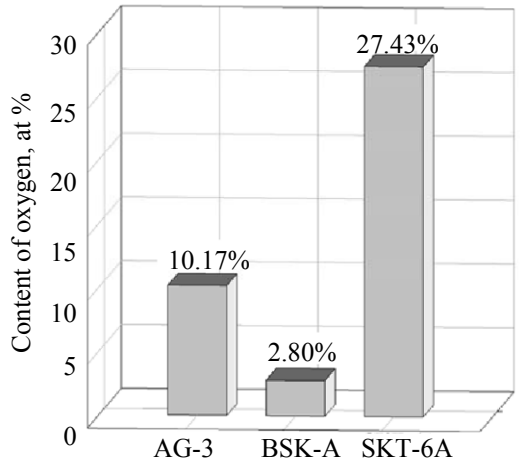


Fig. 4. Oxygen content in different types of activated carbons.

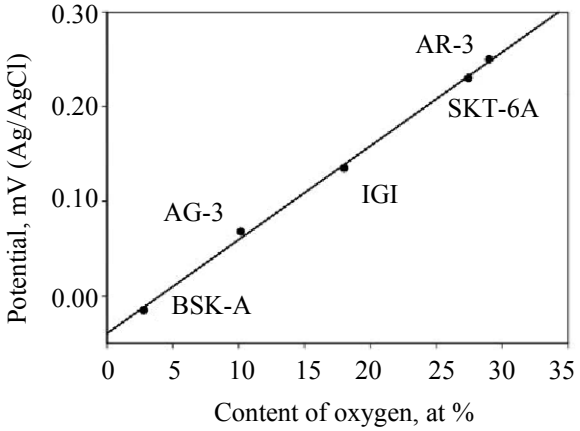


Fig. 5. Dependence of carbon potential on oxygen content.

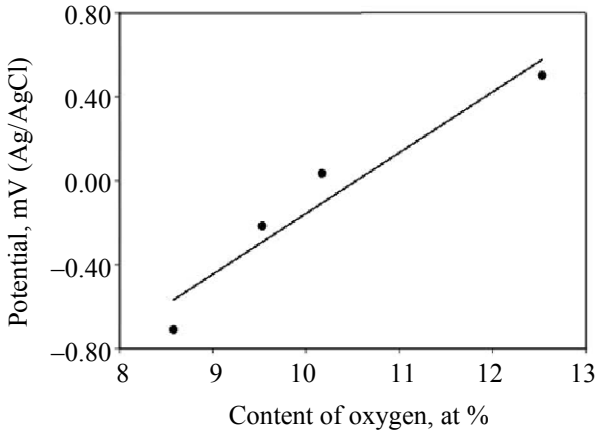


Fig. 6. Dependence of the potential of AG-3 modified carbon on oxygen content.

from Fig. 5, with an increase in the content of oxygen the carbon potential is shifted into a positive range.

This function is linear and has quite a high correlation coefficient (R^2 = 0.9981). It should be emphasized that the connection between the value of the potential of activated carbons and the content of oxygen atoms in their structure is discovered for the first time.

The resulting correlation between the value of the carbon potential and the content of oxygen in the carbon was confirmed in studies of AG-3 carbon, samples of which were electrochemically modified to various positive and negative potentials within a range from 0.70 to –0.50 V (Fig. 6).

Thus, important connections between the content of oxygen and the value of the potential of carbons were established and assumptions about the mechanism of electrochemical modification of carbons through redox reactions, taking place on the surface of carbons and leading to irreversible changes in the composition of surface compounds and electrochemical properties of carbons, were justified.

Table 4. Results of studies of the influence of electrochemical modification of carbons on the composition of surface groups

Type of treatment	Concentration of the group (mg-eq/g)		
	carboxyl	lactone	phenol
No treatment	0.47	0.10	0.18
Cathodic, i = 60 mA/g	0.00	0.00	0.00
Anodic, i = 60 mA/g	0.41	0.30	0.32
Cathodic, i = 12 mA/g	0.15	0.04	0.20
Anodic, i = 12 mA/g	0.51	0.16	0.20

Determination of the composition of surface compounds based on the Boehm titration method [44] in crushed samples of SIT-1 carbon before and after reactions of electroreduction and electrooxidation were carried out on the surface of the samples [37] demonstrated that as a result of electrochemical modification the surface compounds were actually reduced or oxidized (Table 4). In this case, shifts in values of the potential of the reduced or oxidized samples into a negative or positive range, respectively, are observed.

Thus, reactions of electroreduction on the surface of activated carbons lead to the desired effect, shifting the value of the potential into a negative range as a result of reduction of carbon surface compounds, whereas electrooxidation of the carbon surface is an undesirable process in terms of production of hemosorbents from such carbons.

The determination of the mechanism for electrochemical modification of carbons opened up new possibilities for targeted synthesis of carbons aimed to give them the desired properties. The choice of carbon electromodification method makes it possible not only to obtain adsorbents with the target value of the potential, but also to produce cathodes and anodes for fuel cells and supercapacitors.

Two types of devices were developed to carry out an electrochemically controlled hemosorption process.

A device for external polarization [37, 43] is represented by a cylindrical detoxification column with a capacity of 250 ml made of Teflon with several stainless steel meshes (0.2 mm thick, mesh size of 0.3 mm). The column is filled with granular activated carbon. Using this device it is possible to achieve equipotentiality of carbon granules. Due to a reduction in the column resistance an electric current less than 0.8 mA is required to achieve the potential of 1.0 V.

For body detoxification with the help of an electrochemical detoxification column it is possible to use sorbents based on activated carbons, which traumatize blood cells, but possess high sorption characteristics. For example, original SIT-1 carbon with a potential of 0.35 V completely destroys erythrocytes after several min of contact with blood, whereas polarization of this carbon to a potential lying within a range from –0.20 to 0.05 V in the detoxification column eliminates the risk of trauma or death of blood cells; at the same time, the adsorption activity of the carbon in relation to exotoxicants is not reduced. Thus, polarized SIT-1 carbon has been successfully used as a hemosorbent in medical treatment of cases of acute exogenous poisoning at N.V. Sklifosovsky Research Institute of Emergency Medicine for many years [6, 37].

The disadvantage of the electrochemical detoxification column for the process of hemosorption is the necessity for sophisticated equipment. There is an alternative. It is possible to use standard equipment for hemosorption and apply aggressive-to-blood carbons, pre-modified to potentials corresponding to the range of hemocompatibility, as hemosorbents.

As demonstrated above, cathodic modification of the carbon surface causes a shift in the carbon potential into the range of hemocompatibility.

An electrolyser developed for cathodic modification of carbons, which is designed to treat 2 kg of granular carbon in 30 min, is equipped with a peristaltic pump to ensure a continuous flow of the electrolyte (0.15 M aqueous solution of NaCl) at an electric current density of 10 A/kg. After modification of SIT-1 carbon with the initial potential of 0.35 V the final value of the potential lies within a range of –0.05–0.2 V. Changes in the main blood parameters in case of hemosorption on the modified SIT-1 carbon are insignificant. The modified SIT-1 carbon has been used in the toxicology clinic of N.V. Sklifosovsky Research Institute of Emergency Medicine for more than 10 years.

In works [45, 46] physicochemical and structural properties of samples subjected to cathodic electrochemical modification were studied. An important output of these works is evidence of preservation of the porous structure of carbons subjected to the process of electrochemical modification. This fact was established on the basis of the standard porosimetry method [47], which also made it possible to characterize hydrophobic and hydrophilic properties of carbons. It was found that cathodic modification of carbons led to a pronounced hydrophobization of the carbon surface (wetting angle of the original sample was 0°, whereas for the cathodically modified sample this figure was close to 90°). These data are also very important, as it is known that a hydrophobic surface prevents cell membranes from interacting with the surface [48].

Thus, cathodic treatment of activated carbons leads to a reduced interaction between blood cells and the modified carbon surface as a result of the shift in the carbon potential into the range of hemocompatibility and the effect of hydrophobization of the surface.

However, the acquired negative values of the potential drift in the opposite direction and reach the values characteristic for the initial carbon after a period of 60–80 h, i.e. long-term storage of carbons after modification is impossible, as with the return of the acquired potential to the initial values the property of hemocompatibility is also lost.

In connection with the above-described drawback, a search for new modification methods was continued. It was suggested that modification of activated carbons with conductive biocompatible materials could lead to the creation of new indifferent-to-blood composites.

The discovery of the property of biocompatibility in some conductive polymers, in particular, polypyrrole provoked an active interest in these materials as a basis for the creation of biocompatible medical coatings. Along with studies dedicated to the methods of synthesis of such polymers as poly(*p*-phenylene), polyaniline and its derivatives [49], and polypyrrole [50], there are a lot of works on the creation of other classes of conductive biocompatible polymers [51–53]. As a rule, the common feature of such polymers is the presence of poly-conjugation of π-bonds in the primary chain.

The electron conductivity property is achieved by doping, i.e. introduction of small amounts of a dopant, for example, Cl^- anions, into the matrix of the source polyconjugated polymers [54]. By regulating the doping level it is possible to vary the conductivity of polymers in a wide range.

Polypyrrole, which is a conductive hemocompatible polymer, was selected as a modifying agent in order to give activated carbons the property of hemocompatibility. Due to the above-described characteristics polypyrrole is widely used in the development of materials contacting with blood for a long period of time, for example, endoprostheses [55].

Joint implementation of electrochemical methods aimed to give biocompatible properties to carbon materials using polarization and modifying abilities of polypyrrole is a new promising direction in the development of hemo- and plasmasorbents, combining biocompatibility with high adsorption activity. In view of the fact that, like the majority of polymers, polypyrrole is a very inert material, it is also possible to count on long-term preservation of useful properties of carbons modified with this polymer.

The surface of AG-3 activated carbon, as a potentially possible hemosorbent, was modified, taking into account its high adsorption activity. Electropolymerization of pyrrole on the surface of AG-3 carbon was carried out in a potentiostatic mode at a potential of 1.0 V for 3 min. The potential of the carbon covered with polypyrrole was slowly moving towards negative values during a period of several days, reaching a value of –0.05 V.

During storage of polypyrrole-coated carbons their potentials shifted just slightly. Carbon samples treated in an aqueous solution of NaCl (120 g/L), containing 10 ml/l of pyrrole, for 3 min at a potential of 0.825 V were found optimal. The total shift in the potential in relation to the initial carbon reached approximately 0.20 V. After one year of storage the carbon potential remained at a level at which the carbon caused no trauma to the formed elements of blood, specifically, –0.03 V [37]. After two years of storage the value of the carbon potential shifted to 0.12 V, not reaching the initial figure of 0.22 V (characteristic for untreated AG-3 carbon).

Long-term preservation of these new properties given to carbons is undoubtedly a very important quality of the synthesized carbon/polypyrrole composite material as a potential hemosorbent. The stability of the composite can be explained by the formation of stable complexes, consisting of surface groups and polypyrrole chains, on the carbon surface in the course of pyrrole electropolymerization.

Experiments studying interactions between modified carbons and packed red blood cells were carried out using a sample of the composite material (carbon/polypyrrole) polarized to a potential of –0.01 V. It was found that when this composite made contact with packed red blood cells, no free hemoglobin was formed, whereas the contact of the initial sample of AG-3 led to the destruction of erythrocytes (hemolysis rate reached 30%).

An experimental comparison of the adsorption activity of the AG-3/polypyrrole composite with a potential of –0.01 V, carbon polarized to a potential of –0.01 V, and the original carbon with respect to a model toxicant, represented by a psychotropic medication Chlorprothixene, was carried out. The results of the comparison made it possible to conclude that modification of AG-3 carbon with polypyrrole did not interfere with the adsorption of Chlorprothixene; on the contrary, there was a 25% increase in adsorption as compared to the source carbon material.

The presence of biocompatible properties in activated carbons and other adsorption materials is the primary requirement for development of new adsorption materials for body detoxification and purification of biological media from toxicants. However, another necessary requirement for sorbents is selectivity to the extraction of target compounds. These requirements can be met only by biocompatible affinity sorbents.

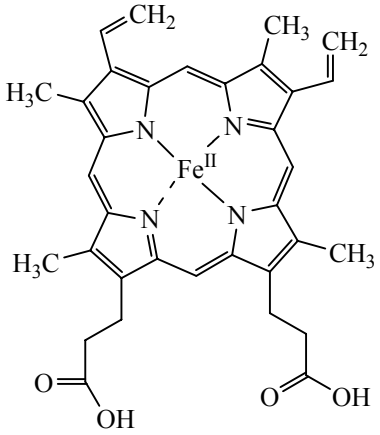
An example of such an affinity sorbent is based on carbon sorbents modified through electrochemical polymerization of pyrrole on their surface, which is aimed to clean blood plasma from free hemoglobin.

Acute blood loss resulting from injuries of various etiologies is one of the major factors determining the severity of the patient's condition [56]. In such cases it is necessary to quickly restore the circulating blood volume, which is the first priority in the complex of medical measures. Reinfusion, i.e. the return of the patient's own blood effused into serous cavities as a result of injuries of the internal organs into the bloodstream, has a number of indisputable advantages over transfusion of foreign plasma. However, me-

chanical destruction of a part of erythrocytes and contamination of the collected plasma with free hemoglobin, which is known to be toxic for the human body, is possible in the course of the reinfusion process [57–59]. Thus, it is a very urgent task to develop a method for purification of auto blood plasma from free hemoglobin.

Within the framework of this problem, adsorption of free hemoglobin from an aqueous solution on unmodified activated carbons of VSK-A and SKT-6A grades was studied. Adsorption of hemoglobin from aqueous solutions on carbons is insignificant; moreover, low adsorption rates make it impossible to count on the use of unmodified carbons for blood purification (Table 5), as in clinical conditions the reinfusion process has to take not more than 1 h.

There was an attempt to increase the rate of adsorption of free hemoglobin on carbons through immobilization with agents with a specific affinity to the hemoglobin molecule.



The heme molecule is represented by a complex of soft complex-forming iron ion and soft porphyrin ligand. This indicates that there is a possibility to give selective properties to carbons by immobilizing soft ligands, which can coordinate with iron ion of heme, on their surface.

The iodide ion was selected from the group of soft ligands [60, 61], as it has a high affinity to the iron ion in the composition of heme. Modification of the surface of SKT-6A carbon with iodide ion indeed led to an increase in the carbon adsorption activity in relation to free hemoglobin. However, the rate of adsorption of hemoglobin from aqueous solutions on the modified carbon did not increase much and amounted to only 3.10 mg g^{-1} h^{-1} against 2.34 mg g^{-1} h^{-1} for the initial SKT-6A carbon.

Table 5. Adsorption of free hemoglobin from an aqueous solution on VSK-A and SKT-6A carbons within 1 h

Carbon type	Decline in hemoglobin	
	%	mg Hb g^{-1} h^{-1}
VSK-A	2.23	0.71
SKT-6A	6.26	2.34

To strengthen the effect of iodide it was introduced into the matrix of a conductive polymer polypyrrole [62]. This decision, which seems paradoxical at first glance, was caused by the fact that we discovered electrocatalytic properties of polypyrrole deposited on the carbon surface [63].

Electrodeposition of polypyrrole with iodide ion as a dopant was carried out on SKT-6 and VSK-A carbons. We measured the amount of electricity spent on electropolymerization of pyrrole, assuming a current efficiency of 100%, and calculated the share of the activated carbon surface occupied by polypyrrole [64]. This share was found to be very small (less than 1%).

The maximal hemoglobin adsorption rate is characteristic for the SKT-6A/polypyrrole/I^- composite. It reaches 8.00 mg g^{-1} h^{-1}, which is 3.4-fold higher than the rate of adsorption on unmodified SKT-6A carbon. The maximal rate of adsorption on modified VSK-A carbon/polypyrrole/I^- was 2.90 mg g^{-1} h^{-1}, which is 4 times as high as the adsorption rate on unmodified VSK-A carbon.

Thus, occupying less than 1% of the activated carbon surface, polypyrrole doped with iodide ion significantly increases the rate of free hemoglobin adsorption as compared to unmodified activated carbons, on the surface of which iodide ion is applied directly. Examination of durability of the discovered effect in case of hemoglobin adsorption from blood plasma demonstrated that the rate of adsorption of hemoglobin from plasma on unmodified SKT-6A carbon decreased to 0.73 mg g^{-1} h^{-1} against 2.34 mg g^{-1} h^{-1} in an aqueous solution. The rate of hemoglobin adsorption on the composite, containing polypyrrole doped with iodide, remained almost unchanged, i.e. 8.30 mg g^{-1} h^{-1} in blood plasma against 7.70 mg g^{-1} h^{-1} in an aqueous solution.

It should be noted that there is a significant increase in the rate of hemoglobin adsorption from blood plasma as compared to unmodified carbon (11-fold).

This effect is probably associated with the catalytic action of polypryrrole doped with iodide ion.

It is also important that the rate of hemoglobin adsorption on the SKT-6A/polypyrrole/I^- composite remains almost unchanged in blood plasma as compared to adsorption from aqueous solutions. However, there is also in increase in the adsorption of proteins from plasma in the presence of free hemoglobin. Although a decline in proteins is insignificant and this effect does not interfere with the application of the method for purification of blood plasma from free hemoglobin in clinical practice, additional research works were carried out in order to find out the mechanism of protein adsorption on plasmasorbents that we synthesized. It is shown that initially the hemoglobin-haptoglobin complex, which is able to competitively adsorb plasma proteins, is adsorbed on the surface of modified carbons. Schemes of the adsorption process stages were proposed [64].

Let us summarize the results of works on the development of electrochemical medical detoxification technologies. The electrochemical model of interactions in the sorbent/biological medium system proved to be quite operational. It was possible to study the mechanisms of interactions taking place in the carbon/blood system, to develop applicability criteria for hemosorbents, and to create a number of methods for the synthesis of sorbents for selective removal of exo- and endotoxicants from biological media on the basis of the proposed concepts. Devices for electrochemically controlled body detoxification proved to be applicable for clinical practice.

In our opinion, electrochemical modification of porous carbon materials with the use of conductive polymers containing affinity agents is a promising direction for the synthesis of new sorbents for medical purposes.

REFERENCES

1. Tarasevich, M.R., *Elektrokhimiya uglerodnykh materialov* (Electrochemistry of Carbon Materials), Moscow: Nauka, 1984.
2. Marsh, H. and Rodrigues-Reinoso, F., *Activated Carbon*, Oxford: Elsevier Ltd., 2006.
3. Bansal, R.C. and Goyal, M., *Activated Carbon Adsorption*, Boca Raton, FL: CRC Press, 2005.
4. Shannon, M.A., Bohn, P.W., Elimelech, M., et al., *Nature*, 2008, vol. 452, no. 7185, pp. 301–310.
5. Qu, J., *J. Environ. Sci*., 2008, vol. 20, no. 1, pp. 1–13.
6. Tarasevich, M.R., Gol'din, M.M., Luzhnikov, E.A., and Bogdanovskaya, V.A., *Itogi Nauki i Tekhn. VINITI, Ser. Elektrokhimiya*, 1990, vol. 31, pp. 127–150.
7. Grimm, J., Bessarabov, D., and Sanderson, R., *Desalination*, 1998, vol. 115, no. 3, pp. 285–294.
8. Bullock, T.H., *Annu. Rev. Physiol*., 1951, vol. 13, pp. 261–280.
9. Bezanilla, F., *Nat. Rev. Mol. Cell Biol*., 2008, vol. 9, no. 4, pp. 323–332.
10. Gadsby, D.C., *Nat. Rev. Mol. Cell Biol*., 2009, vol. 10, no. 5, pp. 344–352.
11. Franco, R., Bortner, C.D., and Cidlowski, J.A., *J. Membr. Biol*., 2006, vol. 209, no. 1, pp. 43–58.
12. Nordenstrom, B., *Biologically Closed Electric Circuit*, Uitgever: Nordic Medical Publications, 1983.
13. Gong, K., Dong, Y., Xiong, S., et al., *Biosens. Bioelectron*., 2004, vol. 20, no. 2, pp. 253–259.
14. Ozkan, S., Uslu, B., Aboul-Enein, H., *Crit. Rev. Anal. Chem*., 2003, vol. 33, no. 3, pp. 155–181.
15. Wang, Y., Xu, H., Zhang, J., and Li, G., *Sensors*, 2008, vol. 8, no. 4, pp. 2043–2081.
16. Lambrechts, M. and Sansen, W., *Biosensors: Microelectrochemical Devices*, Bristol: Institute of Physics Publishing, 1992.
17. Schuhmann, W., Lammert, R., Hämmerle, M., and Schmidt, H.L., *Biosens. Bioelectron*., 1991, vol. 6, no. 8, pp. 689–697.
18. Lowry, J.P., Griffin, K., McHugh, S.B., et al., *Neuroimage*, 2010, vol. 52, no. 2, pp. 549–555.
19. Atkinson, M.J., Thomas, F.I.M., Larson, N., et al., *Deep Sea Research Part I: Oceanographic Research Papers*, 1995, vol. 42, no. 5, pp. 761–771.
20. Heller, A. and Feldman, B., *Chem. Rev*., 2008, vol. 108, no. 7, pp. 2482–2505.
21. Gol'din, M.M., Luzhnikov, E.A., Evseev, A.K., et al., *Aktual'nye voprosy ekstrakorporal'noi terapii* (Topical Problems of Extracorporeal Therapy), Moscow, 2007, pp. 129–130.
22. Gol'din, Mikhail M., Blanchard, G.J., Volkov, A.G., et al., *ECS Trans*., 2008, vol. 11, no. 20, pp. 19–28.
23. Gol'din, M.M., Blanchard, G.J., Evseev A.K., et al., *212 Meeting of the Electrochemical Society*, Washington, 2007, Abs. 0815.
24. Gol'din, M.M., Volkov, A.G., Khubutiya, M.Sh., et al., *ECS Trans*., 2008, vol. 11, no. 21, pp. 39–49.
25. Khubutiya, M.Sh., Krylov, V.V., Gol'din, M.M., et al., *Giperbaricheskaya Fiziologiya i Meditsina*, 2009, no. 4, pp. 1–12.
26. Khubutiya, M.Sh., Gol'din, M.M., Romasenko, M., et al., *ECS Trans*., 2010, vol. 25, no. 19, pp. 63–71.
27. Khubutiya, M.Sh., Evseev, A.K., Kolesnikov, V.A., et al., *Russ. J. Electrochem.*, 2010, vol. 46, no. 5, p. 537.

28. Khubutiya, M.Sh., Gol'din, M.M., Evseev, A.K., et al., *ECS Trans*., 2011, vol. 35, no. 35, pp. 45–50.
29. Khubutiya, M.Sh., Pinchuk, A.V., Aleksandrova, I.V., et al., *Transplantologiya,* 2011, nos. 2–3, pp. 29–33.
30. Lopukhin, Yu.M. and Molodenkov, M.N., *Gemosorbtsiya* (Hemosorption), Moscow: Meditsina, 1985.
31. Nikolaev, V.G., *Metod gemokarboperfuzii v eksperimente i klinike* (Hemocarboperfusion Method in Experimental and Clinical Conditions), Kiev: Naukova Dumka, 1984.
32. Chang, T.M., *Iskustvennye kletki* (Artificial Cells), Kiev: Naukova Dumka, 1979.
33. Lopatkin, N.A. and Lopukhin, Yu.M., *Efferentnye metody v meditsine* (Efferent Methods in Medicine), Moscow: Meditsina, 1989.
34. Chang, T.M.S., *Can. J. Physiol. Pharmacol*., 1969, vol. 47, no. 12, pp. 1043–1045.
35. Luzhnikov, E.A., Gol'din, M.M., and Strakhova, N.M., *Farmatsiya*, 1983, no. 1, pp. 40–43.
36. Kharamonenko, S.S. and Rakityanskaya, A.A., *Elektroforez kletok krovi v norme i patologii* (Blood Cell Electrophoresis in Normal and Pathological Conditions), Minsk: Belarus', 1974.
37. Gol'din, M.M., Volkov, A.G., Goldfarb, Yu.S., and Gol'din, Mikhail M., *J. Electrochem. Soc*., 2006, vol. 153, no. 8, pp. J91–J99.
38. Frumkin, A.N., *Izbrannye trudy: Elektrodnye protsessy* (Selected Works: Electrode Processes), Moscow: Nauka, 1987.
39. Surovikin, V.F., P'yanova, L.G., Luzyanina, L.S., and Dolgikh, V.T., *Efferentnaya Terapiya*, 2008, vol. 14, nos. 1–2, pp. 4–8.
40. Surovikin, V.F., Surovikin, Yu.V., and Tsekhanovich, M.S., *Ros. Khim. Zh. (Zh. Ros. Khim. Ob–va im. D.I. Mendeleeva),* 2007, vol. LI, no. 4. pp. 111–118.
41. Luzhnikov, E.A., Gol'din, M.M., and Suslova, I.M., *Farmatsiya,* 1980, no 3, pp. 65–66.
42. Gol'din, M.M. and Luzhnikov, E.A., *Elektrokhim.*, 1979, vol. 4, no. 9, p. 1419.
43. Gol'din, M.M., Luzhnikov, E.A., and Suslova, I.M., *Elektrokhim*., 1980, vol. 16, no. 11, pp. 1667–1669.
44. Boehm, H.P., *Advances in Catalysis*, Eley, D.D, Pines, H., and Weisz, P.B., Eds., Academic Press, 1966, pp. 179–274.
45. Borover, G.Yu., Gol'din, M.M., Shkol'nikov, E.I., et al., *Elektrokhim*., 1989, vol. 25, no. 5, pp 565–569.
46. Bogdanovskaya, V.A., Tarasevich, M.R., and Gol'-din, M.M., *Itogi Nauki i Tekhniki VINITI, Ser. Elektrokhimiya,* vol. 31, pp. 151–166.
47. Vol'fkovich, Yu.M., Bagotskii, V.S., Sosenkin, V.E., and Shkol'nikov, E.I., *Elektrokhim.*, 1980, vol. 16, no. 11, pp. 1620–1652.
48. Raicu, V. and Popes, A., *Integrated Molecular and Cellular Biophysics*, Springer, 2008.
49. Feng, B., Su, Y., Song, J., and Kong, K., *J. Mater. Sci. Lett.*, 2001, vol. 20, no. 4, pp. 293–294.
50. Sadki, S., Schottland, P., Brodie, N., and Sabouraud, G., *Chem. Soc. Rev*., 2000, vol. 29, pp. 283–293.
51. Nishizawa, M., Nozaki, H., Kaji, H., et al., *Biomaterials,* 2007, vol. 28, no. 8, pp. 1480–1485.
52. Jiang, X., Marois, Y., Traore, A., et al., *Tissue Engineering*, 2002, vol. 8, no. 4, pp. 635–647.
53. George, P.M., Lyckman, A.W., LaVan, D.A., et al., *Biomaterials*, 2005, vol. 26, no. 17, pp. 3511–3519.
54. Epstein, A.J. and MacDiarmid, A.G., *Macromol. Chem., Macromol. Symp*., 1991, vol. 51, no. 1, pp. 217–234.
55. Goddard, J.M. and Hotchkiss, J.H., *Prog. Polym. Sci*., 2007, vol. 32, pp. 698–725.
56. Urman, M.G., *Travma zhivota* (Abdominal Trauma), Perm': IPK Zvezda, 2003.
57. Dement'eva, I.I., Morozov, Yu.A., and Charnaya, M.A., *Kardiologiya i Serdechno-Sosudistaya Khirurgiya*, 2008, no. 6, pp. 60–63.
58. Lopukhin, Yu.M., Molodenkov, M.N., and Shurkalin, B.K., *Gemosorbtsiya, Sb. Trudov II MOLGMI im. N.I. Pirogova:* (Hemosorption, Collection of Works of N.I. Pirogov Russian National Research Medical University), 1977, pp. 64–69.
59. Hamburger, J., *Presse méd*., 1960, vol. 68, pp. 279–281.
60. Pearson, R.G., *J. Chemical Education*, 1968, vol. 45, pp. 581–587.
61. Pearson, R.G., *J. Chemical Education*, 1968, vol. 45, pp. 643–648.
62. Rodríguez, F.J., Gutiérrez, S., Ibanez, J.G., et al., *Environmental Science and Technology*, 2000, vol. 34, no. 10, pp. 2018–2023.
63. Khubutiya, M.Sh., Gol'din, M.M., Stepanov, A.A., et al., *Carbon*, 2012, vol. 50, pp. 1146–1151.
64. Khubutiya, M.Sh., Tsivadze, A.Yu., Garaeva, G.R., et al., *Makrogeterotsikl.,* 2012, vol. 5, nos. 4–5, pp. 321–326.