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Electrochemical Behavior of Tryptophan and 5-hydroxytryptophan on an Electrode Modified with Multi-Walled Carbon Nanotubes and Polyfolic Acid

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Abstract. A possible mechanism for the concentration and oxidation of tryptophan and 5-hydroxytryptophan on an electrode modified with carbon nanotubes and polyfolic acid has been proposed. The influence of the pH of the solution, the accumulation potential, and the potential sweep speed on the analytical signals of amino acids has been investigated. When the pH increases, the potentials of the anode peaks shift to the region of negative values; the I – pH dependence passes through the maximum with the pH of 6.8. Based on the processing of the dependences of the peak current and the peak potential on the potential sweep speed, it has been found that tryptophan and 5-hydroxytryptophan oxidize with the participation of two electrons and two protons. The transfer process of the first electron limits the electrochemical reaction. The process is controlled by diffusion and adsorption. The diffusion coefficients are equal to $9.7 \cdot 10^{-6}$ cm^2/s and $7.4 \cdot 10^{-6}$ cm^2/s for tryptophan and 5-hydroxytryptophan, the maximum adsorption value for tryptophan has been $1.63 \cdot 10^{-10}$ mol/cm^2 and for 5-hydroxytryptophan it has been $6.41 \cdot 10^{-1}$ mol/cm^2. The optimal parameters of concentration and oxidation of tryptophan and 5-hydroxytryptophan in the compresence have been established: the pH of 6.8; the accumulation potential of 0.1 V, the electrolysis time of up to 120 s, the optimal scanning velocity of 120 mV/s. The limit of quantification has been $5 \cdot 10^{-8}$ M.

Keywords: stripping voltammetry, tryptophan, 5-hydroxytryptophan, polyfolic acid, modified electrode.

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Электрохимическое поведение триптофана и 5-гидрокситриптофана на модифицированном многостенными углеродными нанотрубками и полифолиевой кислотой электроде

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Аннотация. В работе предложен возможный механизм концентрирования и окисления триптофана и 5-гидрокситриптофана на электроде, модифицированном углеродными нанотрубками и полифолиевой кислотой. Исследовано влияние pH раствора, потенциала накопления, скорости развертки потенциала на аналитические сигналы аминокислот. При повышении pH потенциалы анодных пиков смещаются в область отрицательных значений, зависимость I – pH проходит через максимум при pH 6,8. На основании обработки зависимостей тока пика и потенциала пика от скорости развертки потенциала установлено, что окисление триптофана и 5-гидрокситриптофана происходит при участии двух электронов и двух протонов. Лимитирует электрохимическую реакцию процесс переноса первого электрона. Процесс контролируется диффузией и адсорбцией. Коэффициенты диффузии равны $9{,}7 \cdot 10^{-6}$ см^2/с и $7{,}4 \cdot 10^{-6}$ см^2/с для триптофана и 5-гидрокситриптофана, величина предельной адсорбции для триптофана составила $1{,}63 \cdot 10^{-10}$ моль/см^2, а для 5-гидрокситриптофана – $6{,}41 \cdot 10^{-11}$ моль/см^2. Установлены оптимальные параметры концентрирования и окисления триптофана и 5-гидрокситриптофана при совместном присутствии: pH 6,8; потенциал накопления –0,1 В, время электролиза до 120 с, оптимальная скорость развертки 120 мв/с. Нижняя граница определяемых концентраций составила $5 \cdot 10^{-8}$ М.

Ключевые слова: инверсионная вольтамперометрия, триптофан, 5-гидрокситриптофан, полифолиевая кислота, модифицированный электрод.

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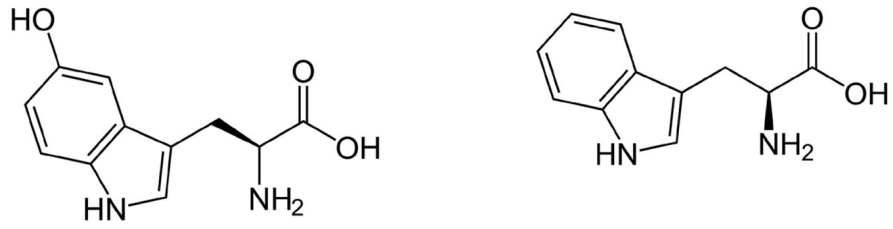
Introduction

Tryptophan (β- (β-indolyl) -α-aminopropionic acid (Fig. 1a) represents an aromatic alpha-amino acid that exists in two optically isomeric forms, L and D, and in the form of racemate (racemic mixture) (DL) [1]. L-tryptophan is a proteinogenic amino acid that is included in the proteins of all known living organisms. It belongs to a number of hydrophobic amino acids as it contains an aromatic indole ring. L-tryptophan participates in hydrophobic and stacking interactions [2]. 5-hydroxytryptophan (Fig. 1b) is a chemical precursor and metabolic intermediate in the biosynthesis of the serotonin



(a) (b)

Figure 1. Structural formulas of tryptophan (a) and 5-hydroxytryptophan(b)

neurotransmitter. Tryptophan is a precursor in the metabolism of 5-hydroxytryptophan and serotonin. A small proportion of tryptophan is used for synthesizing protein and producing neurotransmitters. The remaining part, more than 95 % of free tryptophan released during food digestion, is a substrate for the kynurenine cycle of tryptophan, which generates several metabolites with different biological activities [3–4].

Since amino acids enter the human body mainly through food, medicines and biologically active supplements (BAS), reliable methods of their control in these objects are needed.

There are various methods that allow assessing the content of tryptophan and 5-hydroxytryptophan in a wide range of concentrations: capillary electrophoresis [5], fluorescence spectroscopy [6], chromatographic methods [6–10], mass spectrometry [11], NMR [12]. However, the application of the mentioned methods requires long-term sample preparation, expensive equipment and reagents, thorough cleaning of the latter. In this connection, electrochemical methods attract much attention of experts because of their simplicity, high selectivity, sensitivity and low cost of equipment. Voltammetric methods provide massive opportunities for specifying amino acids [13]. In these electrochemical studies, carbon electrodes that are characterized by a low background current, a wide area of ideal polarizability are widely used. They are chemically inert, cheap and suitable for determining organic and biologically important compounds.

When using voltammetric methods on inert electrodes, the detection limit is high enough; therefore, the electrodes are modified to increase sensitivity. Nanoparticles, metal oxides [14–16], carbon nanotubes and fullerenes [17–20], cyclodextrins [21–22], graphene and graphene oxide [23–24], amino acids [25] are most commonly used for this purpose. In [26], a glassy-carbon electrode modified with AuNPs and carbon nanotubes was used. The linear range of determined concentrations is from 5.0×10^{-6} M to 100.0×10^{-6} M with a detection limit of 3.0×10^{-6} M. In [27], the authors presented the identification of tryptophan using an electrode, in the manufacture of which ionic liquid and multi-walled carbon nanotubes (MCNT) were used as the main components. The electrode surface was activated by potential cycling. The region of working concentrations is 5.0×10^{-6}–1.0×10^{-3} M. A highly selective electrochemical sensor representing a hybrid structure of aluminum oxide, graphene and copper is presented in [28]. This electrode was prepared by electrodeposition of copper nanoparticles on aluminum oxide nanofibers encapsulated in graphene. The electrode was used for the simultaneous determination of adrenaline, acetaminophen and tryptophan with a low detection limit of 0.027; 0.012; 0.009 μM, respectively. One of the methods for determining tryptophan on a glassy-carbon electrode modified with argentum was described in [29]. Under optimal experimental conditions, the peak current linearly depends on the Trp

concentration in the range from 1.0×10^{-7} to 1.0×10^{-4} M with a detection limit of 4.0×10^{-8} M. All the methods presented above have their own advantages, but they are also not free from shortcomings associated with expensive materials and a long process of forming the active layer surface. An available determination method is the application of films of the vitamin B complex and amino acids [30]. In [31], a technique was proposed for the simultaneous determination of tryptophan and 5-hydroxytryptophan on a carbon-containing electrode modified with MCNT and a vitamin B_9 film (polyfolic acid). Proposing this technique for determining amino acids, we have proceeded from the fact that folic acid takes part in the kynurenine cycle as an enzyme. It is necessary to clarify the mechanism for optimizing the electrochemical process with a view of increasing the resolving power of this method and reducing the detection limit of tryptophan and 5-hydroxytryptophan.

Materials and methods

All electrochemical measurements were carried out on a TA-LAB voltammetric analyzer (NPO "Tomanalit") in a direct current mode in a three-electrode cell. An indicator electrode is modified carbon–containing, auxiliary and reference – silver chloride in 3 M KCl. Folic acid (vitamin B_9) (Sigma), tryptophan, 5-hydroxytryptophan (Sigma, USA) were used in the work. MCNT were purchased from the "Aldrich" company. All the reagents were prepared using deionized water obtained from "Sartorius" of the "arium®pro" brand. All the experiments were carried out at room temperature.

Preparation of the modified electrode

The MCNT suspension was prepared in the following way: the MNT sample was oxidized in a mixture with the 1:1 ratio of HNO_3(conc) and H_2O_2(conc) until the complete evaporation of the solution. Then the oxidized nanotubes were washed with deionized water and dissolved in dimethylformamide. The suspension aliquot (5 mcl) was applied to the electrode surface and dried until the complete evaporation of the solvent. The folic acid film was applied by cyclic voltammetry in the range of potentials equal to – 1.4 V ÷ 0.5 V.

Results and discussion

The process of concentrating tryptophan and 5-hydroxytryptophan is significantly influenced, in addition to the electrode, by the composition of the background electrolyte, pH, conditions of concentration on the electrode and the concentrate electrodissolution. The process of simultaneous oxidation of tryptophan and 5-hydroxytryptophan is shown in the Fig. 2.

pH influence

To study the electrochemical behavior of tryptophan and 5-hydroxytryptophan, voltamperograms were recorded in the Britton-Robinson solution in the pH ranges from 1.75 to 9.18. Fig. 3(a) shows the dependences of the anode currents of tryptophan and 5-hydroxytryptophan on pH. The highest sensitivity is observed at pH = 6.8. The state diagrams [31] have shown that tryptophan and 5-hydroxytryptophan are in the form of zwitter ions at such pH value. Since COO^-groups are present in polyfolic acid at such pH value, amino acids concentrate due to the electrostatic interaction between COO^- and NH_3^+. During the transition to a more alkaline region, these amino acids deprotonate, as a result of which the electrostatic interaction is impossible. In the acid medium, polyfolic acid is protonated, which slows down the electrostatic interaction between the film and amino acids.

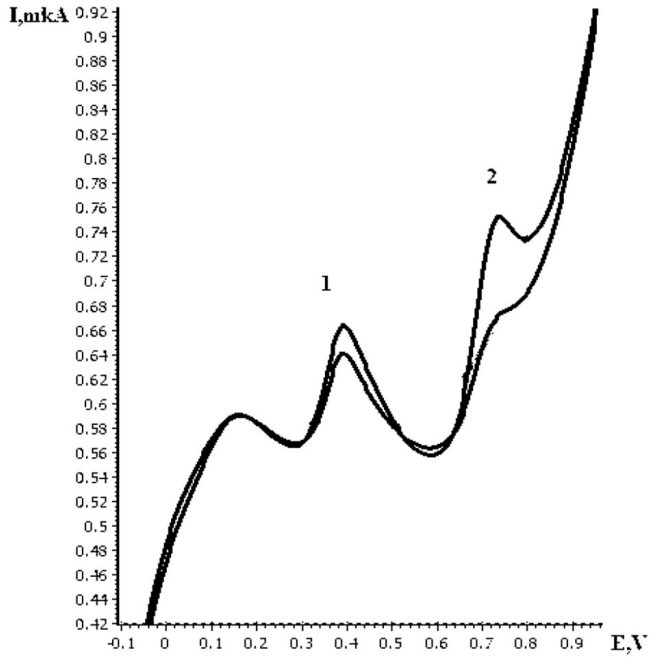


Figure 2. Voltamperograms of tryptophan (TRP) and 5-hydroxytryptophan (5-HTP): 1) 0,5 μM TRP и 0,2 μM 5-HTP, 2) 0,7 μM TRP и 0,5 μM 5-HTP

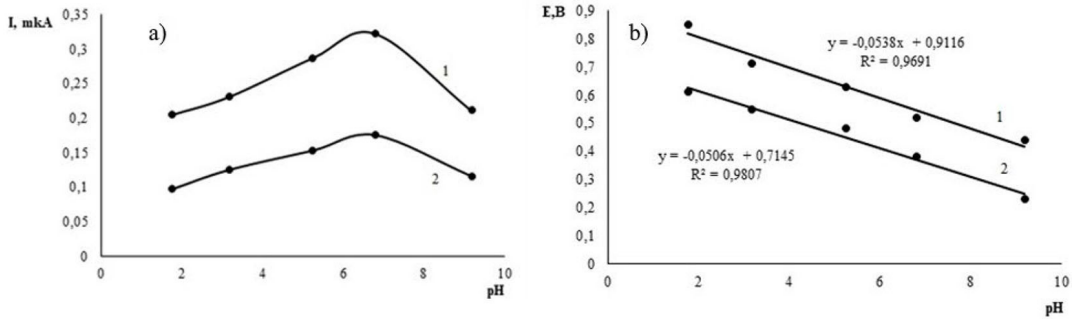


Fig. 3. Dependence of anode current (a) and peak potential (b) of tryptophan and 5-hydroxytryptophan on pH

When the pH of the buffer solution increases, the peak potentials shift to values that are more negative. The linear dependences can be observed between the peak potentials and pH as shown in Fig. 3(b).

The slope values of 53.8 mV/pH for tryptophan and 50.6 mV/pH for 5-hydroxytryptophan are close to the Nernst slope (59.0 mV/pH), which indicates an equal number of electrons and protons involved in the electrochemical process.

The influence of the potential sweep speed on the currents and potentials of anode peaks

The ratio between the peak current/potential and the potential sweep speed provides constructive information about the mechanism of the electrochemical reaction. The electrochemical behavior of

tryptophan and 5-hydroxytryptophan was studied by the voltammetry method at various potential sweep speeds in the range from 25 to 280 mV/s.

An acceleration in the potential scanning velocity increased the currents of electrooxidation of tryptophan and 5-hydroxystryptophan. The dependences of the peak current on $W^{1/2}$ were plotted to evaluate the oxidation mechanism (Fig. 4).

Linear dependences in these coordinates are typical of both reversible and irreversible processes. The peak potentials shift to more positive values when the potential sweep speed increases for both amino acids, which indirectly confirms the irreversibility of the oxidation process [32]. The proof of such irreversibility is also the linear dependence between the peak potential and lgW (Fig. 5c).

The linear dependence of the current on the potential sweep speed (Fig. 5a) indicates that the process is controlled by either diffusion or adsorption.

The linear dependence of the peak potential on the square root of the potential sweep speed is typical of the processes accompanied by diffusion control [33] (Fig. 5b). The diffusion coefficients were calculated using the Randles-Sevcik equation and equaled $9.7 \cdot 10^{-6}$ cm^2/s and $7.4 \cdot 10^{-6}$ cm^2/s for tryptophan and 5-hydroxytryptophan, respectively. Based on the slope angle of the dependence of lgI on lgW (Fig. 5d), the value of the Semerano criterion was 0.64 for tryptophan and 1.04 for 5-hydroxytryptophan. For the processes controlled purely by diffusion, this criterion should be 0.5. Since the Semerano criterion is greater than 0.5, it is possible to conclude that this process is also of adsorption nature.

To assess the influence of adsorption, the dependences of the peak current on the potential sweep speed were plotted (Fig. 5a). The linearity of these dependences indicates the contribution of adsorption to the electron-transfer process. The maximum adsorption was calculated according to the following equation [33]:

$\Gamma_\infty = \frac{b}{9.4 \cdot 10^5 An}$", where b is a tangent of the slope angle $I - W$, A is an electroactive surface area of the electrode, n is the number of electrons involved in the process.

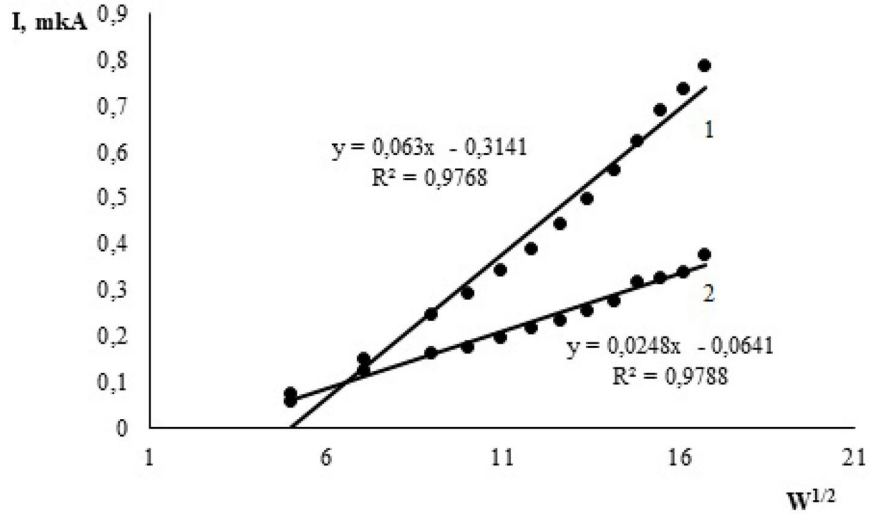


Fig. 4. Dependences of the electrooxidation current of tryptophan (1) and 5-hydroxytryptophan (2) on the square root of the sweep speed $W^{1/2}$

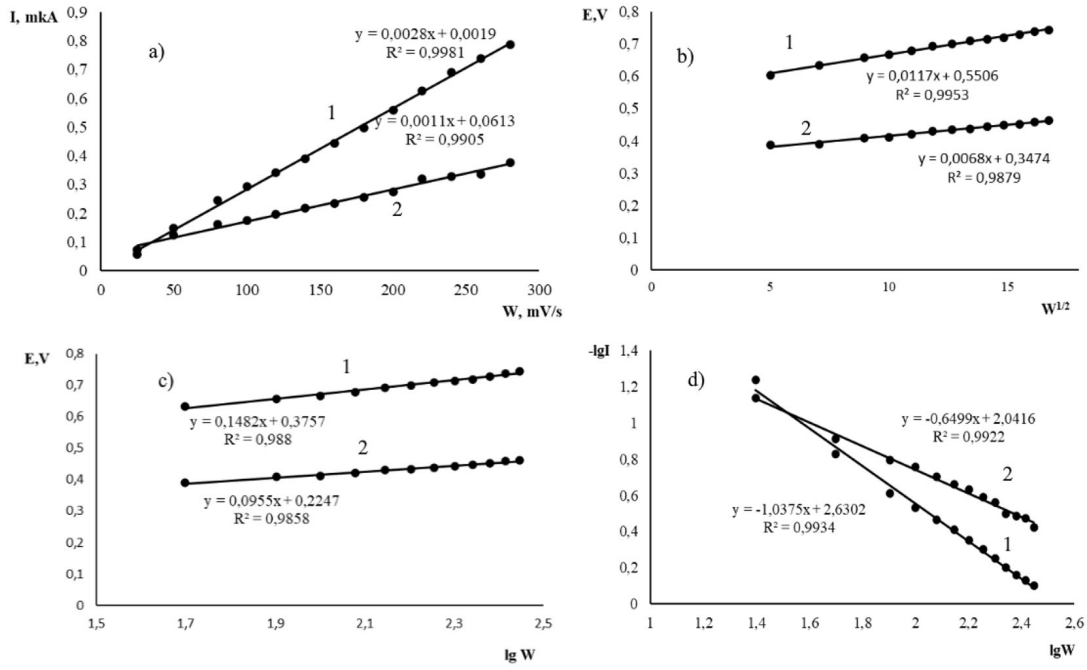


Figure 5. The influence of the potential sweep speed on the electrochemical behavior of 7.0 × 10^{-7} M tryptophan (1) and 5-hydroxytryptophan (2)

The maximum adsorption value for tryptophan was 1.63·10^{-10} mol/cm^2, and for 5-hydroxytryptophan it was 6.41·10^{-11} mol/cm^2. This fact may explain the higher sensitivity coefficient when determining 5-hydroxytryptophan.

The proposed adsorption mechanism of concentration is in good agreement with the mechanism of electrooxidation of tryptophan on graphite electrodes, which was reported in [34–35].

To determine the number of electrons and the limiting stage of the electrode reaction, the transfer coefficient for the irreversible process (oxidation of tryptophan and 5-hydroxytryptophan) was calculated using the Tafel dependence according to the formula: $b = \frac{\alpha F}{RT}$, where b is a tangent of the slope angle of the dependence ln|I_{ox}| – Ep, α is a transfer coefficient.

As a result of the calculations, the values of effective transfer coefficients equal to 1.47 and 1.52 for tryptophan and 5-hydroxytryptophan, respectively, were obtained.

For the irreversible process, the number of electrons was calculated according to the formula: $|E_п - E_{\frac{п}{2}}| = \frac{47.7}{\alpha n}$. The values equal to 1.94 and 2.18 were obtained for tryptophan and 5-hydroxytryptophan; that is, they are close to 2.

The calculated values of the effective transfer coefficients that are close to 1.5 indicate that the limiting stage is the process of transferring the first electron.

The above-mentioned results confirm the mechanism of concentration and oxidation of tryptophan and 5-hydroxytryptophan on electrodes modified with MCNT and vitamin B_9 that we proposed earlier [31].

Selection of optimal conditions for recording an analytical signal

To select the optimal conditions for recording an analytical signal, the influence of the potential and accumulation time was studied. The values of the analytical signals practically do not depend

on the electrolysis potential in the range from –1.0 to + 0.2 V, which proves the fact of adsorption concentration of amino acids on the electrode modified with polyfolic acid. Let us propose a potential of –0.1 V as an optimal one for simultaneous determination of amino acids. When accumulating more than 120 s, the analytical signals reach the limit, which may be conditioned by the complete filling of the electrode surface with adsorbed precipitate; therefore, 120 s was chosen as the optimal time.

The dependences of peak currents on the concentration are linear in the range of (0.5–50) × 10^{-7} and obey the equations I = 0.017C – 0.012 and I = 0.003C+0.001 for tryptophan and 5-hydroxytryptophan, respectively.

In the compresence of tryptophan and 5-hydroxytryptophan, analytical signals are not distorted even at a ratio of 1:250, 250:1. The influence of other amino acids on the results of the determination of tryptophan and 5-hydroxytryptophan was studied. The ultimate transfer concentration was determined as a maximum concentration of a substance-obstacle that causes an error in determining amino acids of no more than 5 % [36, 37]. Accordingly, at least a 10-fold excess of ascorbic acid, dopamine, histidine, glycine, methionine, arginine, cysteine and tyrosine does not have any noticeable distorting effect on the determination.

Some metrological characteristics of the procedure for determining tryptophan and 5-hydroxytryptophan

According to ISR 61–2010, the indicators of repeatability, intermediate precision, and accuracy were calculated (Tables 1, 2).

Table 1. Metrological characteristics of the procedure for determining tryptophan (p = 0.95, n = 2, l = 15)

Concentration ×10^{-7}, mol/dm^3	Repeatability indicator, σ_r^*,%	Intermediate precision indicator, σ_{Rl}^*,%	Accuracy indicator (limits of relative error at P = 0.95), ±Δ,%
10	9.14	9.97	20.85
20	8.66	8.91	19.96
30	7.63	7.70	19.53
40	7.21	7.67	19.15
50	6.89	7.39	18.79

Table 2. Metrological characteristics of the procedure for determining 5-hydroxytryptophan (p = 0.95, n = 2, l = 15).

Concentration ×10^{-7}, mol/dm^3	Repeatability indicator, σ_r*,%	Intermediate precision indicator, σ_{Rl}*,%	Accuracy indicator (limits of relative error at P = 0.95), ±Δ,%
10	8.24	8.74	20.35
20	8.16	8.25	19.26
30	7.93	8.04	19.03
40	7.81	7.92	18.95
50	7.69	7.85	18.89

Based on the obtained metrological characteristics of the developed procedure for determining tryptophan and 5-hydroxytryptophan, it is possible to conclude that the accuracy figure does not exceed 21 % for tryptophan and 5-hydroxytryptophan, and the repeatability and intermediate precision indicators do not exceed 10 % for tryptophan and 9 % for 5-hydroxytryptophan.

Conclusions

The regularities of electrooxidation of tryptophan and 5-hydroxytryptophan on modified electrodes have been investigated. Amino acids oxidize with the participation of two electrons and two protons. The transfer process of the first electron limits the electrochemical reaction. The process is controlled by diffusion and adsorption. According to the Randles-Sevcik equation, the diffusion coefficients have been calculated: $9.7 \cdot 10^{-6}$ cm^2/s and $7.4 \cdot 10^{-6}$ cm^2/s for tryptophan and 5-hydroxytryptophan. The maximum adsorption value has been $1.63 \cdot 10^{-10}$ mol/cm^2 for tryptophan and $6.41 \cdot 10^{-11}$ mol/cm^2 for 5-hydroxytryptophan. The optimal conditions for the determination of amino acids in the compresence have been chosen: the accumulation potential is –0.1 V, the electrolysis time is up to 120 s, the potential sweep speed is 120 mV/s. Some metrological indicators have been established for the procedure of determining tryptophan and 5-hydroxytryptophan: accuracy indicators, repeatability and intermediate precision. The lower limit of the determined concentrations has been $5 \cdot 10^{-8}$ M.

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