Voltammetry in the pharmaceutical analysis: a review

Sergey Aronbaev[1*], *Dmitry* Aronbaev[1], and *Dilnosa* Isakova[2]

[1] Samarkand State University named after Sh.Rashidov, Department of Inorganic Chemistry and Materials Science, 140104 Samarkand, Uzbekistan
[2]Uzbek-Finnish Pedagogical Institute, 140107 Samarkand, Uzbekistan

Abstract. Due to its sensitivity, selectivity, simplicity and cost-effectiveness, the role of electrochemical analysis methods increases from year to year. This also applies to the use of various voltammetry options in the analysis of medicines. This mini-review is devoted to the analytical capabilities of cyclic voltammetry used in manufacturing technologies and clinical diagnostics of antihypertensive drugs. The main goal pursued by the authors of this article is to attract the attention of specialists to the problem of analytical control of medicines, and, first of all, antihypertensive drugs, using methods of voltammetric analysis. According to the authors, this will allow a deeper understanding of the cause of hypertension and the subsequent eradication of this disease, which will certainly affect the duration of a healthy human life.
Keywords: electrochemical methods of analysis, antihypertensive drugs, determination by cyclic voltammetry.

1 Introduction

According to the World Health Organization, there are almost a billion people with hypertension on Earth. It is known that high blood pressure is a trigger for such cardiovascular diseases as myocardial infarction, angina pectoris, ischemia and cardiac arrhythmias [1]. Therefore, the use of antihypertensive drugs, the main task of which is to normalize blood pressure, plays an important role in minimizing the consequences of hypertension.

Currently, the pharmaceutical industry produces a wide range of antihypertensive drugs, the range of which is constantly expanding. The therapeutic effect of the use of these drugs is achieved at a minimum dosage, if exceeded, a fatal outcome is possible. That is why information about the active component of the drug, which often has a narcotic effect, as well as about its pharmacokinetic and pharmacodynamic effects in the composition of the dosage form is extremely necessary for pharmacists and clinicians.

Thus, drug analysis is an integral part of the overall process of developing new pharmaceuticals and their commercial forms. A mandatory requirement for the analysis of pharmaceutical preparations is the mandatory analytical determination of the active component, excipients and the presence of undesirable impurities. In addition to the above, an important stage of pharmaceutical control is to obtain additional information about the stability of the

* Corresponding author: diron51@mail.ru

active substance, intermediate or final products, as well as other parameters such as uniformity of composition, solubility and dissolution rate [2].

Currently, various physico-chemical and instrumental methods are widely used in the practice of pharmaceutical analysis of medicines. These are gas and high-performance liquid chromatography [3,4], direct mass spectrometry and in combination with liquid chromatography [5,6], UV and IR spectrometry [7, 8] and some electrochemical methods [9-11]. All these analytical methods have gained sufficient fame in pharmacognosy and can be recommended for practical use.

It should be noted here that of all the listed methods of control of pharmaceutical products, in particular particularly popular antihypertensive drugs, preference is given to voltammetric methods using both traditional indicator electrodes (Pt, Au, glass carbon) and modified noble metal nanoparticles, their oxides and carbon nanotubes. Recently, electrodes made by screen printing have been used as such sensors. To modify such sensors, methods similar to modification of carbon graphite electrodes are used. [12].

Such a wide application of voltammetric analysis methods is due to its high sensitivity and selectivity, and their simplicity and low cost of measuring equipment ensure its use in small laboratories [13]. Moreover, voltammetric analysis methods allow measurements to be carried out in colored and turbid solutions and without preliminary sample preparation, which distinguishes them favorably from spectrophotometric analysis methods [14,15]. The use of modified electrodes in combination with cyclic voltammetry makes this advantage even more noticeable [16-18].

Many analytical reviews have been devoted to the analysis of pharmaceutical preparations using electrochemical analysis methods [19-23]. At the same time, the use of cyclic voltammetry for the analysis of antihypertensive drugs is not widely represented in these reviews [24-29].

The main purpose of this mini-review is to provide information about the analytical capabilities of cyclic voltammetry in the analysis of antihypertensive pharmaceuticals.

2 Analytical capabilities of voltammetric analysis for the determination of pharmaceuticals

Voltammetric analysis methods are based on measuring an analytical signal in the form of a direct electric current with continuous scanning of the potential applied at the electrode-solution interface. [30].

The analytical signal is displayed in the form of a voltammogram, the shape of which is similar to the spectrum in optical analysis methods, that is, the voltammogram is able to give information about the dependence of the current on the scanning potential energy [31].

Voltammetric methods of analysis have found their application in the study of stability, solubility of various forms of pharmaceuticals, as well as a number of metabolic processes that occur in the body when they are used. And this allows us to better understand the cause of the interaction between the drug and the living organism, that is, to establish the pharmaceutical effect of this drug.[32-35].

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Voltammetric methods of analysis are applicable to study the solubility and stability of various forms of drugs, as well as a number of metabolic processes that occur in a living organism when they are used. And this allows us to better understand the cause of the drug's effect on the body, that is, to establish the pharmaceutical effect of this drug [32-35].

Currently, voltammetry has significantly expanded its scope of application due to improved techniques for removing voltammograms and automating the process of measuring an analytical signal. Indicator electrodes based on modification of their surface or volume by noble metal nanoparticles have played a huge role in the development of voltammetric methods [18, 36, 37, 38], carbon nanoforms [39-43], organic compounds [17, 44-46]. Carbon-containing electrodes modified with hexacyanocomplexes of transition metals [47,48], MnO_2, Cu(I), W(V) and others with a catalytic response are of interest, which significantly increases the sensitivity of the determination of a number of organic compounds and reduces overvoltage.

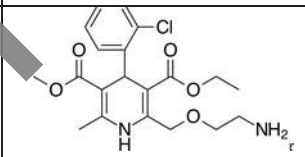
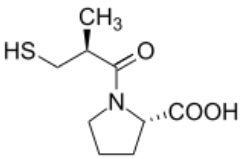
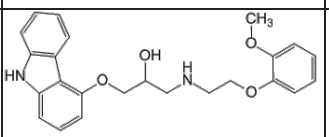
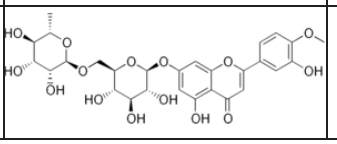
Using cyclic voltammetry, a number of researchers analyzed auxiliary ingredients in medicines, for example acetaminophen in tablets with paracetamol [55,56] or locarbef in the presence of cephalosporins in the concentration range of the main drug 6×10^{-6} to 2×10^{-4} M.

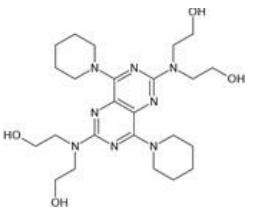
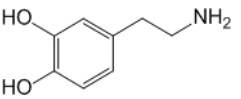
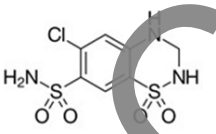
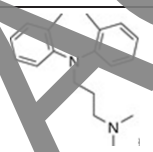
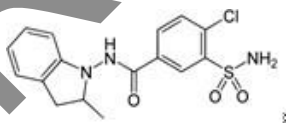
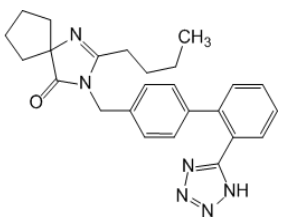
Other researchers have determined the monoglycoside preparation and isoramnetin in the ranges of their concentrations of 1×10^{-6} - 1×10^{-5} microns and 1×10^{-7} - 4×10^{-6} microns, respectively, using cyclic voltammetry and conventional and modified glass-carbon electrode [57].

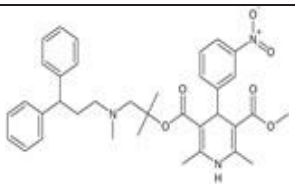
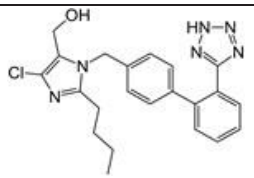
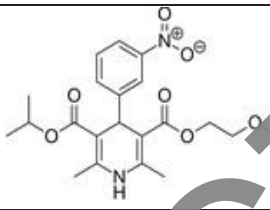
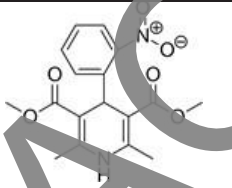
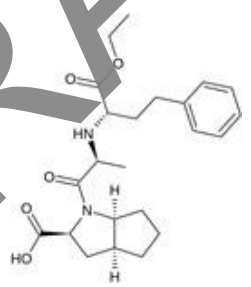
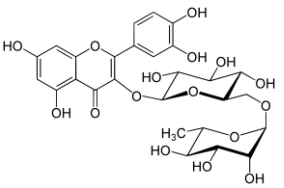
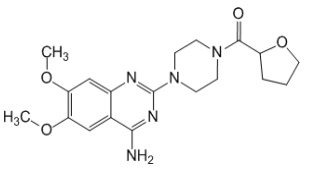
Further, P. Norouzi and his colleagues [58] also used cyclic voltammetry to develop a method for determining rantidine, which belongs to anti-ulcer drugs and belongs to the group of H2-histamine receptor blockers. They were able to determine the content of this substance in a pharmaceutical preparation with a detection limit of just over 20 picograms per milliliter.

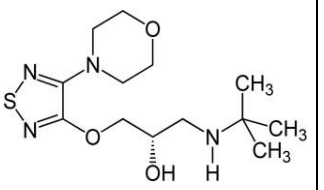
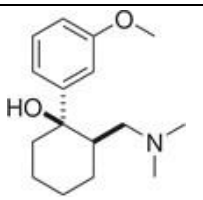
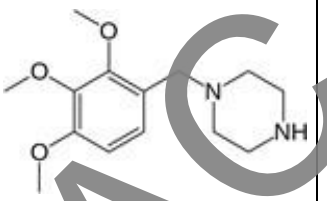
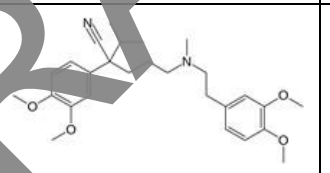
Table 1 provides information from the authors' article [31] on the definition of certain antihypertensive drugs, which gives an idea of the analytical capabilities of cyclic voltammetry.

Table 1. Examples of the use of cyclic voltammetry in the analysis of antihypertensive pharmaceutical drugs

Name of the drug	Pharmacological effect and purpose	Structural formula	Electrode	LOD and range of measured concentrations
Amlodipine	It is prescribed to reduce blood pressure in case of cardiac ischemia.		GCE	—
Captopril	It is prescribed for severe hypertension and heart failure. It belongs to the group of inhibitors for lowering blood pressure.		MCPE	1.0×10^{-6} M
Carvedilol	The drug belongs to the group of α- and β-blockers.It has no intrinsic sympathomimetic activity.		GCE	0.12 μg/mL
Diosmin	The drug has a venotonic effect. It is prescribed for violation of venous circulation.		GCE	3.0×10^{-8} M

Dipyridamole	The drug acts as a vasodilator, antiplatelet, antiadhesive, arteriodilating effect. It has a positive effect on primary and secondary platelet aggregation.		Pt; Pd; Au; C	-
Dopamine	The drug has a hypotensive and cardiotonic effect. It stimulates dopaminergic receptors. in high doses, it stimulates alpha- and beta-adrenergic receptors. It has diuretic properties		Modified. GCE	5 μM
Hydrochlorothiazide	It is prescribed for the treatment of high blood pressure. It is used as a diuretic to eliminate edema due to fluid accumulation		GCE	0.10 μg/mL
Imipramine	Along with amitriptyline, it belongs to the main representative of tricyclic antidepressants.		Au microelectrode	4.0 pg/mL 15-20000 pg/mL
Indapamide	The drug has a hypotensive effect similar to thiazide diuretics. It is prescribed for hypertension and edema due to heart failure.		MCPE	5 nM
Irbesartan	The drug has a pronounced antihypertensive effect. Reduces the concentration of aldosterone and reduces the symptoms of heart failure. It acts on angiotensin II receptors (AT1 subtype), blocking them, thereby eliminating its vasoconstrictive effect.		HMDE GCE	5.0×10^{-6} – 1.0×10^{-4} M 5.5×10^{-7} M
Lercanidipine	The drug has a vasodilating and long-lasting antihypertensive effect. It belongs to the derivatives of dihydropyridine, which inhibits the trans-		**GCE**	0.02-3.00 μg/mL

	membrane flow of calcium ions into cardiomyocytes and myocardial smooth muscle cells.			
Losartan	It is prescribed as a hypotensive drug. It belongs to the group of antagonists - blockers of angiotensin type II AT1 receptors.		Au-disk micro-electrode	
Nimodipine	The antagonist of Ca^{2+} mainly affects the tone of the cerebral vessels and has a nootropic, vasodilating effect. It is prescribed for chronic migraines		HMDE Modified GCE	7.3 ng/mL 0.06 - 2.0 µg/mL
Nifedipine	The antagonist of Ca^{2+}, is a derivative of dihydropyridine, has a hypotensive effect.		GCE	2 0 µM
Ramipril	The drug is used to treat and maintain high blood pressure at a normal level. It belongs to angiotensin converting enzyme (ACE I) inhibitors.		DME. Pt- electrode	4.0×10^{-8} M
Rutin	An angioprotective drug of the flavonoid group with pronounced antioxidant properties that improves the absorption of vitamin C and strengthens capillaries.		HMDE	5.0×10^{-9} M
Terazosin	The drug is used as a hypolipidemic, vasodilator, antidiuretic agent		GCE	6×10^{-7}M

Timolol	Timolol in the form of eye drops is used to treat glaucoma and is included in the list of vital and essential medicines. It is a beta-blocker.		Au-DME SMDE	1.4 ng/mL 2.0 ppb
Tramadol	The drug has a high analgesic activity, gives a quick and long-lasting effect. It refers to psycho-tropic opioid analge-sics, opioid receptor agonists.		Au-DME	0.30 pg/mL
Trimetazidin e HC1	It belongs to the group of antianginal drugs. Normalizes the energy metabo-lism of cells that have undergone hypoxia or ischemia. It is prescribed for the prevention of angina pectoris, Meniere's disease, disorders of cerebral circulation, accom-panied by tinnitus and dizziness.		GCE	2.2×10^{-8} M
Verapamil	The drug belongs to the group of slow calcium channel blockers and has antianginal and antiarrhythmic ef-fects		DME.CPE	5.0×10^{-10} M

Abbreviations: GCE - glass-carbon electrode; DME - mercury drop electrode; HMDE - electrode with a hanging mercury drop; SMDE - stationary mercury electrode on a conductive substrate; MCPE - modified paste carbon electrode; CPE-paste carbon electrode; Au-DME- Au-disk micro-electrode/

3 Conclusion

Over the past ten years, cyclic voltammetry has proven itself well in the analysis of pharmaceuticals in general, and antihypertensive drugs in particular. The review reveals the analytical capabilities of voltammetry using new sensor systems based on carbon-containing electrodes modified with noble metal nanoparticles, oxides, carbon nanoforms, organic substances, hexacyanocomplexes of transition metals, allowing to obtain electrodes with a catalytic response, improving the sensitivity and reproducibility of the analysis results, reducing overvoltage. when determining a large number of organic compounds and their derivatives. In many cases, voltammetry with linear, square-wave, differential pulse and cyclic potential scanning allows the analysis of pharmacological preparations with a limit of detection of micro-, nano-, and sometimes pico-molar concentrations in a wide range of their contents. Characteristics such as sensitivity, selectivity, simplicity and low cost of analysis allow voltammetric methods of analysis to compete with spectrophotometric and biological methods of analysis traditionally used in pharmacology. This makes it

possible to widely use voltammetric methods, especially cyclic voltammetry, in pharmacological practice in the creation of new medicines and in clinical diagnostics, which studies the effectiveness of the use of these pharmaceuticals in the treatment of a number of diseases. The emphasis placed on the analysis of antihypertensive drugs using voltammetric analysis methods will allow a deeper understanding of the cause of hypertension and subsequently eradicate this disease, which will certainly affect the duration of a healthy human life.

4 Conflict of interest

The authors declare that there are no conflicts of interest.

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