Current Topics in Analytical Chemistry
Vol. 8, 2011

Review

Determination of catecholamines in pharmaceutical formulations

Alexey E. Poliakov[*,#], Svetlana V. Muginova[*,$], and Tatiana N. Shekhovtsova

Department of Chemistry, M. V. Lomonosov Moscow State University, Leninskie Gory, Moscow 119991 GSP-1, Russia

ABSTRACT

This review presents the data published during 1990-2010 (161 references) dealing with the application of modern instrumental methods for analysis of catecholamine-based drugs. Such pharmaceuticals are widely used for the treatment of neuroblastoma, hypertension, bronchial asthma, schizophrenia, Parkinson's disease and for the diagnostics of cardiac diseases. Hence, it is very important to control the quality of the catecholamine-based drugs. The present review is organized primarily according to analytical method type. Sensitivity, selectivity, precision, and other analytical characteristics of the developed procedures for the determination of natural and synthetic catecholamines in different pharmaceutical formulations are discussed. Particular attention has been paid to flow injection pharmaceutical analysis. The specific features of pretreatment of liquid and solid dosage forms are described. The problems and prospects of the chemical analysis of the officinal catecholamine-based drugs are considered.

KEYWORDS: catecholamines, electrochemistry, spectroscopy, kinetic and biochemical methods, biosensors, chromatography, capillary electrophoresis, flow injection analysis, pharmaceutical analysis.

*Corresponding authors
[#]a.e.polyakov@gmail.com
[$]muginova@analyt.chem.msu.ru

1. INTRODUCTION

Nowadays, frequent cases of falsification of drugs (when the concentration of an acting component of a drug does not correspond to the data indicated on packing) [1-2], their improper transport and storage have led to the necessity of the operative control of quality of pharmaceuticals in pharmacy depots and within pharmacy.

The major problems of counterfeiting of pharmaceuticals [1, 2] and their improper storage and transportation conditions require developing new methods for rapid screening of their quality, including determination of active ingredients directly at warehouses and drugstores. The problem becomes especially challenging if counterfeited are such pluripotential drugs as catecholamines (CAs), which actively participate in the nervous activity of humans. Catecholamine-based drugs are widely used for the treatment of neuroblastoma, hypertension, bronchial asthma, anorexia, schizophrenia, Parkinson's disease and for the diagnostics of cardiac diseases [3-5]. Moreover, sportsmen are known to receive some CA-containing pharmaceuticals or food supplements as energy stimulators [6].

The aspects of the determination of CAs and their metabolites in biological liquids (blood, urine, cerebral- and amniotic-fluids) for timely diagnosis of the mentioned diseases are described in detail in the reviews and articles prepared by Tsunoda [7] (2006), Nicolajsen [8] (2001), Dziedzic [9], and Jacob [10] (1982). Methods of CA determination in pharmaceuticals were mentioned in reviews

devoted to the application of flow injection methods (Solich [11, 12], 2001 and Evgen'ev [13], 2001) and electrochemical biosensors (Gil [14], 2010) in pharmaceutical analysis. A recent review (Perry [15], 2009) dealing with the methods of the determination of neurotransmitters has not provided enough details. No special review considering the methods for the determination of CAs in officinal drugs has been found. The goal of this paper is to present an overview of the numerous procedures proposed for the determination of CAs in pharmaceuticals and thus complement and update the information provided earlier in the sources cited above [7-15]. In our opinion, it is desirable to estimate critically the main features and application of the methods concerning this issue. We will restrict ourselves to the consideration of the papers concerning modern instrumental methods of quantitative analysis of catecholamine-based drugs in different dosage forms that were published between 1990 and 2010. We hope that this review will contribute to the better understanding of the current status of analytical methods for the determination of CAs in pharmaceuticals.

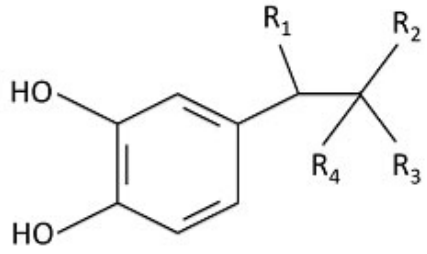
2. General information on catecholamines and catecholamine-based drugs

CAs are known to be derivatives of catechol containing an amino group in a radical bound to the benzene ring. The structural formulae of CAs (dopamine (DA), adrenaline (epinephrine) (AD), noradrenaline (norepinephrine) (NAD), α-methyldopa (MD), levodopa (L-dopa) (LD), carbidopa (CD), dobutamine (DB), isoprenaline (isoproterenol in some papers) (IPA)), which usually may be found in drugs and mentioned in this review, are presented in Fig. 1.

It should be noted that the components of officinal drugs are the salts (hydrochlorides or tartrates) of CAs (Fig. 1). They are readily soluble in water and hardly soluble in esters and chloroform. In contrast, initial CAs, being phenolic compounds, are soluble in alkaline solutions but poorly soluble in water. Further in the text, the term “CAs” implies their water-soluble salts.

The freshly prepared aqueous solutions of CAs are colorless; they absorb in the UV region of spectrum (Table 1). The UV and infrared spectra are widely used for the identification of CAs in simple pharmaceutical forms, for instance in injections.

As a rule, catecholamine-based drugs are liquid (injection) or solid (tablet, capsule, and powder) dosage forms. Aeriform preparations (aerosol, spray) contain generally AD or IPA and occur rather rarely (Table 1). No mull pharmaceutical formulations (creams, gels, and etc.) have been found. Injections, aerosols, or sprays are the



	DA	AD	NAD	MD	LD	CD	DB	IPA
R_1	H	OH	OH	H	H	H	H	OH
R_2	H	H	H	COOH	COOH	COOH	H	H
R_3	NH_2	$NHCH_3$	NH_2	NH_2	NH_2	$NHNH_2$	$NHCH(CH_3)EtPhOH$	H
R_4	H	H	H	CH_3	H	CH_3	H	$NHCH(CH_3)_2$

Fig. 1. The structural formulae of CAs mentioned in the review.

Table 1. The molar absorptivity of the solutions of CAs (ε, $M^{-1} \cdot cm^{-1}$) at the wavelengths of their maximum absorbance

CA	Medium	$\varepsilon \cdot 10^{-3}$ (λ_{max}, nm)	Typical commercial pharmaceutical form
DA	0.05 M H_2SO_4	2.037 (279.5) [16]	Injection
AD	0.01 M HCl	2.75 (280) [16]	Injection, aerosol, spray
NAD	0.01 M HCl	2.6 (279) [17]	Injection
MD	H_2O	2.79 (280) [18]	Tablet, powder
LD	0.001 M HCl	2.63 (280) [19]	Tablet, capsule
DB	CH_3OH	4.77 (280) [20]	Tablet, powder
IPA	No data	No data	Tablet, aerosol, spray

solutions of CAs in certain acids (in most cases, HCl or H_2SO_4). Powders or capsules contain the active pharmaceutical ingredients, which should be dissolved in the mentioned acids before the analysis. In addition to CA, tablets contain excipients such as starch, talc, magnesium stearate, stearic acid, ethyl cellulose, etc. Here it should be mentioned that except for LD, MD, and CD-based tablets, pharmaceutical formulations usually contain only one CA.

The analysis of some databases (see http://scopus.com, http://sciencedirect.com) has shown that the percents of the publications devoted to the analysis of liquid and solid forms containing CAs are 78% and 22% of the total number of the published data, respectively. Depending on a pharmaceutical formulation, the concentrations of CAs may vary in a rather wide range (1 μM - 1 mM). Thus, it is preferable to use such analytical procedures that can provide the determination of CAs in as many pharmaceutical forms as possible.

3. Instrumental methods of analysis of catecholamine-based drugs

European and US Pharmacopeias (and Russian Pharmacopeia as well) recommend determining concentrations of CAs in pharmaceuticals by potentiometric titration with $HClO_4$ in anhydrous formic or acetic acid medium containing acetic anhydride [21, 22]. Nowadays, more and more strict regulations related to the quality control of pharmaceuticals lead to increasing demands on analytical assays. Innovative procedures of analysis of pharmaceuticals should combine sensitivity, selectivity, and precision with simplicity, rapidity, low cost, and possibilities of automation [11-14]. The listed requirements to procedures of pharmaceutical analysis along with the significant biological role of DA and its derivatives have initiated many studies devoted to the development of novel procedures for the determination of CAs. The procedures described in scientific literature have been summarized and characterized according to the type of a method.

Fig. 2 shows a diagram, which illustrates the distribution of the publications considering the use of different procedures of analysis of catecholamine-based drugs by the type of the analytical method. This diagram demonstrates that electrochemistry and spectroscopy are the most widely used methods for the determination of CAs in pharmaceutical formulations. Both groups of the methods have been successfully applied for the detection of CAs by FIA procedures, the fraction of which is rather high among the reviewed methods (Fig. 2). Other instrumental methods have been applied less frequently. Before the discussion of the groups of methods presented in Fig. 2, some aspects of a pretreatment of the different pharmaceutical forms should be considered.

3.1. Pretreatment

In the case of injections, the content of one or several ampoules (depending on the concentration

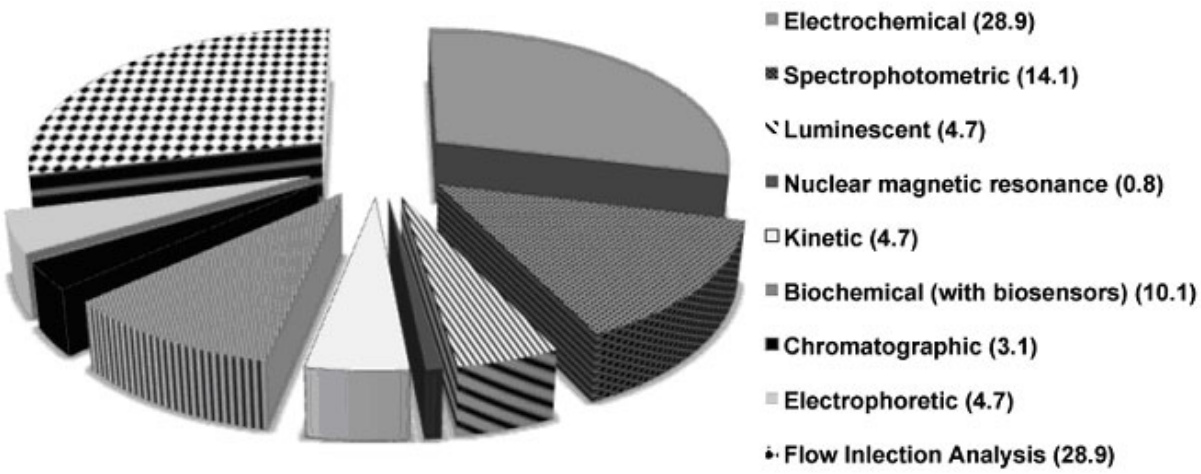


Fig. 2. Statistics of the use of different instrumental methods in the analysis of officinal catecholamine-based drugs (numbers in parentheses correspond to the percentage of data published between 1990 and 2010).

of CA in a sample) is transferred carefully into a volumetric flask, diluted to a certain volume by water, and thoroughly mixed. Analyzed tablets are weighed and ground into fine powder. A precisely weighed portion of the resultant powder (or the whole portion of the powdered sample) is dissolved in water, shaken thoroughly for a certain time to ensure the dissolution of CA, filtered to a calibrated flask, and subjected to the procedures described below for injections. Powders are often dissolved in certain inorganic acids and then are added to the reaction mixture. Aerosols (sprays) are diluted in appropriate solvents. The obtained solutions of samples are stored in tightly closed vessels before the analysis. Direct contact with light should be avoided.

3.2. Electrochemical methods

Since CAs are electroactive compounds, electrochemical methods are often applied for their determination (Fig. 2). The reported electrochemical procedures for the analysis of catecholamine-based drugs are systematized in Table 2.

The data of Table 2 show that the methods of CV and DPVA are more frequently used for the determination of CAs. The analysis of drugs is based on the redox properties of CAs resulting from the presence of quinone groups in the chemical structures of their molecules (Fig. 1). GC electrode is widely applied as an indicator electrode. Various inorganic and organic compounds were used as modifiers of the indicator electrode surface although GC electrode demonstrated high response to an analyte without any modification [23-25]. Usually, the electrodes are modified with some polymers in the absence [26, 30, 31, 33, 35, 36, 40, 56] or in the presence [27-29, 38] of a subsidiary component (for instance, metal nanoparticles, hematoxylin). Such modified electrodes are stable for a long time (up to 60 days) and may be applied for several determinations of CAs without loss of the signal intensity, but it is necessary to perform the regeneration of the electrode surface. The procedures employing cysteamine with gold nanoparticles [34], β-cyclodextrine [45], and TiO_2 film [54] for an electrode's modification differed from that mentioned above by better analytical characteristics and easy techniques for the indicator electrode preparation. Unfortunately, it is impossible to make a correct estimation of the advantages of the application of nanomaterials (Pt, Au, or Fe nanoparticles, MWCNT, SWCNT, Au-carbon nanotubes) [27, 28, 34, 37, 38, 42, 46, 48] and hydrophobic ionic liquids (imidazolium-, phosphonium-, or pyridinium-based [43, 47]) as the modifiers of the electrode surface because the authors have not compared the analytical characteristics of the procedures obtained using modified and non-modified electrodes.

Voltammetric techniques for the determination of CAs in drugs [34, 50, 54] are the most sensitive electrochemical procedures. However, to achieve

Table 2. The analytical characteristics of the electrochemical procedures for the determination of CAs in injections

Type of electrode	Method	Modification agent	Analyte	ACR, μM	Interferents (tolerance ratio), RSD	Ref.
Voltammetric						
Glassy carbon	CVA	None	DA AD	65 - 5400 16 - 1100	No interferents were studied; RSD - 1-3%	[23]
	DPVA	None	LD* CD*	110 - 1300 31 - 470	Multivariate calibration is necessary for the determination; RSD - 2.5% (LD) and 3.4% (CD)	[24]
	DPVA	None	IPA	10 - 10000	Glucose, Zn^{2+}, Mg^{2+}, and Hg^{2+} ions interfere, Ca^{2+}, Cd^{2+}, Co^{2+}, Ni^{2+}, Pb^{2+}, fructose, and magnesium stearate do not interfere; RSD - 1.2%	[25]
	DPVA	PAAD	DA	1 - 100	Ascorbic and uric acids and adenine do not interfere; RSD - 3.5%	[26]
	CVA DPVA	Nanostructured Pt and Nafion	DA	3 - 60	No interferents were studied; RSD - 4.5%	[27]
	DPVA	Nafion and nanoparticles of Fe(III) with chitosan	DA	2 - 60	DB, uric, ascorbic and citric acids do not interfere; RSD - 2.2%	[28]
	DPVA	Mixture of chitosan and CPB	DA	40 - 5000	Ascorbic acid interferes; RSD - 2.6%	[29]
	CVA	Poly(caffeic acid) film	AD	2 - 300	DA, ascorbic acid (2), Ca^{2+} ions, uric acid (5) interfere; RSD - 2.9-3.2%	[30]
	DPVA	PEPA nanofibers	NAD	0.3 - 10	DA, AD, ascorbic and uric acids do not interfere; RSD - 2%	[31]
	CVA	Valine	AD	4.6 - 10 10 - 140	K^+, Na^+, Ca^{2+}, NH_4^+, Mg^{2+}, Cl^-, β-alanine (100); glucose, tartric acid (10) do not interfere; RSD - 3%	[32]
	CV, DPVA	PASA	DA	0.1 - 100	Ascorbic acid does not interfere; RSD - 2.5-3.0%	[33]
	CVA	Cysteamine + Au nanoparticles	DA	0.01 - 25	KNO_3, NaCl, Mg^{2+}, SO_4^{2-}, CO_3^{2-} (1000), NH_4Br (500), uric acid (200) do not interfere; RSD - 2.8%	[34]
	CVA, DPVA	PXSP	AD	2 - 390	Zn^{2+}, Ca^{2+}, Mg^{2+}, glucose, fructose, carbonate, and starch do not interfere; aspirin, methionine, cysteine, citric acid and Cu^{2+} interfere; RSD - 2.3%	[35]
	DPVA	Polytaurine	DA AD	1 - 800 2 - 600	Na^+, K^+, Cl^- (500); glucose, lysine, cystine, glycin, citric acid, hippuric acid (100) do not interfere; RSD - 1.2-2.1% (DA) and 2.2-2.8% (AD)	[36]
	DPVA	MWCNT	DA	3 - 200	NADH, ascorbic and uric acid do not interfere; RSD - 1.7%	[37]
	DPVA	Hematoxylin + MWCNT	AD	0.2 - 80 80 - 320	Ascorbic and uric acids do not interfere; RSD - 3%	[38]

Table 2 continued..

	DPVA	Electrochemically pretreated	AD	1 - 40	KCl (1000), NH_4^+ (300), Mg^{2+} (100) ions, glycine (30), L-lysine (25), L-aspargine, glucose, glutamic acid (15), fructose, ascorbic acid (5) do not interfere; RSD - 2.3%	[39]
	DPVA	CDDA	DA	5 - 280	Zn^{2+}, Ca^{2+}, Mg^{2+} ions, glucose, fructose, carbonate, starch, oxalate, lysine, urea, ascorbic, citric and uric acids do not interfere; aspirin, cysteine, Cu^{2+} ions, tyrosine interfere; RSD - 5%	[40]
	CVA	OsO-RuCN film	DA AD NAD	0.5 - 1000 1 - 1000 1 - 1000	Chloride and tartrate ions do not interfere; RSD - 2% (DA), 4% (AD), and 5% (NAD)	[41]
Print-screen	CVA	Gold nanoparticles	LD*	100 - 1200	RSD - 4%	[42]
	CVA	Ionic liquid	DA AD DB	3.9 - 100 0.29 - 100 0.17 - 100	Ascorbic acid does not interfere; Short living-time of electrode; RSD - 1.5%	[43]
Graphite	CVA	None	DA AD	65 - 1600 22 - 1800	No interferents were studied; RSD - 1-4%	[23]
	DPVA	SDS	DA	10 - 200	Ascorbic acid does not interfere; RSD - 2.5%	[44]
	CVA, AdDPVA	β-Cyclodextrine	DA AD NAD	0.5 - 500 1 - 500 2.3 - 500	Ascorbic and uric acid, K_2SO_4, KCl, KBr do not interfere; RSD - 1.8% (DA), 0.9% (AD), and 3.9% (NAD)	[45]
	DPVA	Au-carbon nanotube	LD**	0.1 - 150	Glucose, urea (100), and NO_3^-, Cl^-, PO_4^{3-}, SO_4^{2-}, NH_4^+, K^+, Na^+, Mg^{2+}, Ca^{2+} (1000) ions do not interfere; RSD - 1.53-1.84%	[46]
Carbon-paste (ceramic)	CVA	N-butylpyridinium hexafluorophosphate	DA	1 - 800	Ca^{2+} (0.2) ions interfere, K^+, Cl^-, Zn^{2+} (0.2) ions, L-cysteine (1.7), glucose and citric acid (1) do not interfere; RSD - 3.46%	[47]
	DPVA	MWCNT	DA	0.5 - 100	Ascorbic and uric acids do not interfere; RSD - 1.9%	[48]
	DPVA	CTAB	AD	10 - 270	Ascorbic (40) and uric (50) acid do not interfere; RSD - 6%	[49]
	DPVA	Zirconium phosphated amorphous silica gel	DA	0.04 - 50 50 - 400	Mg^{2+}, Na^+ (500), Ca^{2+}, K^+ (300), acetic acid, glucose, phenyl alanine (200), glutamic acid, tartaric acid, 5-hydroxytryptamine (100), glycine (50), phenylacetic acid (25), dihydroxyphenylacetic acid, cysteine (10) do not interfere; RSD - 4.55%	[50]
	SWVA	Methyltrimethoxysilane	DA AD	0.5 - 20 5 - 100	Ascorbic and uric acids do not interfere; RSD - 2.4% (DA) and 2.8% (AD)	[51]

Table 2 continued..

	DPVA	Triiodide ions immobilized in an anion-exchange resin	AD	20 - 310	A 20% decrease of the initial analytical signal was observed only after 300-400 determinations; RSD - 2.6%	[52]
Gold	CVA	*N*-acetylcysteine	DA	1 - 200	Ascorbic acid does not interfere; RSD - 3.9%	[53]
Si electrode	DPVA	TiO_2 nanostructured film	DA AD NA	0.01 - 100 0.03 - 100 0.05 - 100	RSD – 1% (DA), 2% (AD), 4% (NAD)	[54]
Amperometric						
Print-screen	AM	Iridium oxide (III) film	DA AD	0.1 - 70 0.1 - 15	Uric acid (1000) does not interfere; RSD - 2.5% (DA) and 4% (AD)	[55]
Carbon paste (ceramic)	AM	PAMT	DA	0.02 - 1.56	Ascorbic acid and serotonin do not interfere; RSD - 2.4%	[56]
	AM	MPS + $Cu(NO_3)_2$	DA	7.3 - 2200	Ascorbic acid does not interfere; RSD - 4.0%	[57]
Glassy-carbon	ChAM	PXSP	A	2 - 390	Zn^{2+}, Ca^{2+}, Mg^{2+}, glucose, fructose, carbonate, and starch do not interfere; aspirin, methionine, cysteine, citric acid and Cu^{2+} interfere; RSD - 2.6%	[35]
Gold	ChAM	L-cysteine	DA	0.1 - 15 40 - 1100	Na^+, K^+, Cl^- (150), dextrose, citric acid (100), uric acid (80) do not interfere; RSD - 2.3%	[58]
Potentiometric						
PM Teflon cylindrical	PM	TPB membrane	DA AD DB*	100 - 10000 5700- 5×10^5 50 - 10000	Mg^{2+}, Ca^{2+}, Li^+, Na^+, K^+ do not interfere; Cs^+, NH_4^+ ions interfere; RSD - 3.4% (DA), 4.1% (AD), and 4.0% (DB)	[59]
Coulometric						
CM Electrogenerated halogen	CM	Cl_2, Br_2, I_2	DA AD	-	RSD - 1%	[23]

* - analysis of a tablet, ** - analysis of a capsule, ACR - applicable concentration range; CVA - cyclic voltammetry, DPVA - differential pulse voltammetry, AdDPVA - adsorptive differential pulse voltammetry, SWVA - square wave voltammetry, AM - amperometry, ChAM - chronoamperometry, PM - potentiometry, CM - coulometry; PAAD - poly-4-amino-1-1'-azobenzyl-3,4'-disulfonate acid, CPB - cetylpyridinium bromide; PEPA - poly-ethylenedioxypyrrole dicarboxylic acid, PASA - poly-*p*-aminobenzene sulfonic acid, PXSP - poly-*p*-xylenolsulfonephthalein, MWCNT - multi-wall carbon nanotubes, CDDA - poly-3-(5-chloro-2-hydroxyphenylazo)-4,5-dihydroxynaphthalene-2,7-disulfonic acid, SDS - sodium dodecylsulfate, CTAB - cetyltrimethyl ammonium bromide, PAMT - poly-2-amino-5-mercapto-thiadiazole, MPS - (3-mercaptopropyl)trimethoxysilane, TPB - 3-(4-tolylazo)phenylboronic acid.

high sensitivity of the determination, it is necessary to use special apparatus permitting measurement of nanoampere currents. The selectivity of the determination of CAs has been studied in all considered electrochemical procedures. However, in most papers, the reasons for selecting one or another interfering compound were not discussed. At the same time, the interference of such typical subsidiary components as chloride, carbonate, tartrate, sulfite, and metabisulfite ions, and amino acids has been studied only by a few authors [32, 35, 40, 50].

All the electrochemical procedures except those described in the articles [24, 42, 46, 59] have been developed for the determination of CA in injections. Generally, RSD of the results of the determination of CAs in pharmaceutical formulations does not exceed 6% (Table 2).

3.3. Spectroscopic methods

3.3.1. Spectrophotometric methods

Due to its simplicity, sensitivity, selectivity and cost efficiency, spectrophotometry is still widely used in pharmaceutical analysis including the assay of CAs (Table 3). Spectrophotometric procedures are based on redox [60-63], oxidative-coupling [64-68], diazocoupling [69, 70], binary-complex formation [71-76], and ion-pair complex formation [77, 78] photometric reactions (Table 3).

The procedures based on redox reactions involving CAs [60-63] are least sensitive; nevertheless, they are the most simple and rapid ones. Application of the native enzyme, polyphenol oxidase (PPO), in such type of photometric reactions, does not provide the increase in the sensitivity and selectivity of the determination of DA and MD [63].

On the whole, products obtained as a result of other photometric reactions are characterized by better absorptivity than the initial CAs (Tables 1, 3). Such strong oxidizers as $NaIO_4$, K_2CrO_4, $K_2S_2O_8$ are often used to obtain quinoid dyes which may be further transformed by the substances containing primary amino-group, in our case by CAs. The most sensitive procedures were developed on the basis of photometric reactions of oxidative-coupling [65-68] and ion-pair complex formation [77, 78]. However, the procedure [78] requires a long time for the formation of the photometric compounds. The application of sulphanillic acid [67, 70] allowed increasing the absorptivity of the obtained quinodes. However, the maximal values of molar absorptivity were observed in the system Fe(III) - *o*-phenantroline for MD, LD, and CD. Molar absorptivity of the majority of the colored species used in spectrophotometric procedures lies in the range $n \cdot 10^4$ - $1.3 \cdot 10^5$ $M^{-1} \cdot cm^{-1}$ at the wavelengths of maximum absorbance. The most selective procedures are based on the application of complex formation photometric reactions (Table 3).

It is to be noted that the majority of spectrophotometric procedures (Table 3) provides the same results as the pharmacopeia-recommended methods, their precision being comparable as well. The values of RSD of the results obtained using spectrophotometric procedures do not exceed 5.2%.

3.3.2. Luminescent methods

Luminescent procedures for CAs determination presented in the literature may be divided into three groups. The first group of procedures employs native fluorescent signal of CAs. Wang *et al.* [79] developed a fluorescent procedure for DA determination in the presence of methanol which enhanced the intensity of a signal. The applicable concentration range (ACR) of DA was 0.4 - 230 μM. Such ions as Na^+, K^+, SO_4^{2-}, HPO_4^{2-}, PO_4^{3-} (1000-fold molar excesses), Zn^{2+}, Al^{3+} (50-fold molar excesses), and Pb^{2+} (40-fold molar excesses) did not interfere with the analysis; ions Ca^{2+}, Mg^{2+} (20-fold molar excesses) and especially Cu^{2+}, Hg^{2+} (5-fold molar excesses) resulted in less error of DA determination. RSD of the results of the determination of 150 μM DA in an injection was 5%. Kim *et al.* [80] applied synchronous fluorescence for the determination of 0.1 - 10 μM of LD (RSD ≤ 1.8%) and CD (RSD ≤ 2.4%) in tablets. Use of Δλ scan mode (where $\Delta\lambda = \lambda_{em} - \lambda_{ex}$) enables the determination of the individual concentration of each CA in their mixture. At Δλ = 30 nm (a signal was observed at 288 nm), only CD provided a detectable signal that was independent on the presence of LD, while the signal of LD was not influenced by the presence of CD when Δλ = 65 nm was used (a signal was observed at 281 nm).

Table 3. The analytical characteristics of spectrophotometric procedures for the determination of CAs

Reagents	**Analyte**	**Sample type**	**λ_{max}, nm**	**ACR, μM ($\varepsilon \cdot 10^{-3}$, $M^{-1} \cdot cm^{-1}$)**	**Interference (Tolerance ratio[a])**	**Ref.**
$NaIO_4$	DA LD DB	Injection Tablet Injection	465-520	250 - 5680 250 - 5680 250 - 5680	Products are stable for 4 h; RSD - 0.9% (DA), 1.2% (LD), and 1.0% (DB)	[60]
Sodium bismuthate	AD NAD	Injection Injection	482-486	4.8 - 800 (*3.73*) 4.8 - 600 (*3.33*)	Products are stable for at least 60 min; No effect of any interferents was observed for the analyzed drugs; RSD - 1.9% (AD) and 1.35% (NAD)	[61]
	DA MD LD	Injection Tablet Tablet	429 428 429	50 - 720 (*1.07*) 40 - 620 (*1.14*) 45 - 560 (*1.34*)	Talc, glucose, starch, lactose, dextrose, magnesium stearate, sodium metabisulfite, NaCl do not interfere at their levels in dosage forms; RSD - 1.05% (DA), 1.16% (MD), and 0.87% (LD)	[62]
Polyphenol oxidase	DA MD	Injection Tablet	470 480	200 - 6000 (*0.11*) 200 - 6000 (*0.13*)	Sucrose, glucose, fructose, lactose, starch, polyethylene glycol, NaCl and magnesium stearate do not interfere; RSD - 1.68% (DA), 1.27% (MD)	[63]
NBS and isoniazide	DA MD LD	Injection Tablet Tablet	490 480 480	18 - 90 (*6.47*) 24 - 75 (*3.96*) 12 - 60 (*8.38*)	The coloured products were stable for 3-48 h at room temperature AD, NAD, vitamin C, and other components (100) interfere; RSD - 1.03% (DA), 0.90% (MD), and 0.74% (LD)	[64]
Sodium nitroprusside and hydroxylamine hydrochloride	DA	Injection	635	15 - 110 (*7.4*)	AD, NAD, vitamin C, and other components (100) interfere; RSD - 1.2%	[64]
$NaIO_4$ and 4-aminobenzoic acid	DA MD LD	Injection Tablet Tablet	458 460 456	1.3 - 113 (-*) 2.4 - 95 (-) 2.5 - 100 (-)	Glucose, lactose, fructose, talc, NaCl, magnesium stearate (1) do not interfere; RSD - 1.2% (DA), 1.0% (MD), and 1.1% (LD)	[65]
	LD CD	Tablet Tablet	410 390	2.5 - 50 1 - 45	Mean centering of ratio spectra is necessary for the determination; Na^+, K^+, Al^{3+}, Cl^-, NO_3^-, SO_4^{2-}, HPO_4^{2-} ions, ascorbic acid, glycine, lactose, glucose, fructose (up to 1000) do not interfere, Zn^{2+} (500), Mg^{2+} (50), PO_4^{3-} (20), Pb^{2+} and Cu^{2+} (10) ions interfere; RSD - 1.1% (LD) and 5.2% (CD)	[66]

Table 3 continued..

K_2CrO_4 and sulphanillic acid	DA MD LD	Injection Tablet Tablet	495 490 495	13 - 72 (*1.8*) 7 - 190 (*1.5*) 8 - 120 (*1.8*)	Talc, glucose, starch, lactose, sulfate, dextrose, acetate, phosphate, magnesium stearate do not interfere; Sodium metabisulfite, NaCl do not interfere with DA determination; RSD - 1.11% (DA), 1.12% (MD), and 1.11% (LD)	[67]
$K_2S_2O_8$ and semicarbazide hydrochloride	AD MD	Injection Tablet	460 470	0.5 - 131 (*8.1*) 0.5 - 114 (*26.2*)	Products are stable for 30-60 min; RSD - 1.14% (AD), 1.21% (MD)	[68]
Diazotised sulphanilamide and molybdate ions	DA AD MD LD	Injection Injection Tablet Tablet	500 500 500 500	1 - 16 (*36*) 5 - 30 (*36*) 5 - 30 (*29*) 2 - 12 (*53*)	Common excipients (10) do not interfere; phosphate ions (3) seriously interfere; RSD - 0.75% (DA), 0.95% (AD), 1.02% (MD), and 0.90% (LD)	[69]
Sulphanillic acid	DA AD MD LD	Injection Injection Tablet Tablet	475 475 507 475	4 - 100 (*9.27*) 5 - 150 (*8.12*) 4 - 80 (*9.47*) 8 - 100 (*7.09*)	Talc, glucose, starch, lactose, sulfate, dextrose, acetate, phosphate, and magnesium stearate do not interfere at ACR of CA; RSD - 0.92% (DA), 0.86% (AD), 0.92% (MD), and 0.69% (LD)	[70]
Ammonium molibdate	MD	Tablet	410	230 - 920 (-)	Sucrose, glucose, talc, fructose, lactose, poly(ethylene glycol), microcrystalline cellulose, croscarmellose sodium, starch, polyvinylpyrrolidone, and magnesium stearate (10) do not interfere; RSD - 1.7%	[71]
DQC	MD	Tablet	400	19 - 95 (*6.42*)	Hydrochlorothiazide does not interfere; RSD - 5.1%	[72]
Barbituric acid	MD	Tablet Injection	593	50 - 1200 (*2.97*)	Chloral hydrate, salicylic acid, acetyl salicylic acid, paracetamol, benzodiazepine, buscopan, lantanone, haloperidol, ephedrine, atrotine, brucine, hyoscine, barbitone, morphine, strychnine, quinine, caffeine, codeine do not interfere; RSD $\leq$ 1.1%	[73]
$CuSO_4$ and 4-AAP	DA	Injection	480	485 - 2700 (*29.79*)	Catechol, phenol, pyrogallol, resorcinol, hydroquinone seriously interfere; ascorbic acid and glucose do not interfere; RSD - 1.7%	[74]

Table 3 continued..

4-AAP and $[Cu(NH_3)_4]^{2+}$ ions	LD CD	Tablet Tablet	525 520	100 - 350 (*2.4*) 80 - 240 (*1.8*)	Glucose and maltose (10) slightly interfere; 2-nitrophenol, phenol, pyrogallol, resorcinol, and pyrocatechol interfere; RSD - 4.4% (LD) and 2.8% (CD)	[75]
	DA DB	Injection Injection	505 480	310 - 2700 (*29.79*) 220 - 1340 (*10.36*)	Glucose, acetone or urea (10) do not interfere; ascorbic acid, catechol, phenol, pyrogallol, resorcinol, and hydroquinone interfere with DA determination; No organic substances and ions interfere with DB determination; RSD - 0.75% (DA) and 0.52% (DB)	[76]
Fe(III) – *o*-phenantroline mixture	AD MD	Injection Tablet	510 510	0.06 - 4.5 0.2 - 44	RSD - 1.06% (AD) and 0.85% (MD)	[77]
	MD LD CD	Tablet Tablet Tablet	510 510 510	0.23 - 11 (*129*) 0.25 - 12.3 (*126*) 0.43 - 17 (*102*)	Required heating (50°C); reaction time – 40-50 min; the colour of the obtained product is stable for at least 24 h; RSD – 0.86% (MD), 1.23% (LD), and 1.06% (CD)	[78]

a. Tolerance ratio - the maximum ratio of the interfering ion concentration to the analyte concentration which caused an approximately ±5% relative error in the determination of this analyte. NBS - N-bromsyccinimide, DQC - 2,6-dichloroquinone-4-chlorimide, 4-AAP - 4-aminoantipyrine; * - no data.

The procedures of the second group are based on the formation of a luminophore through oxidation of CAs (DA, NAD, AD) by Hg(II) ions [81, 82] or $K_3Fe(CN)_6$ in borate buffer solution with pH 9.5 [83] and the following condensation of the obtained products with ethylendiamine [81, 82] or formaldehyde in acidic medium [83], respectively. The limits of detection (c_{min}) of DA and NAD were 80 and 2.5 nM in the presence of ethylendiamine, and 0.24 nM for AD in the presence of formaldehyde. The exipients did not interfere with the determination of CAs. RSD of the results of the determination of DA, NAD, and AD were 4.3, 2.3, and 2.5%, respectively.

The procedures of the third group are based on the enhancement of fluorescence of other substances in the presence of CA. So, Su *et al*. [84] proposed a procedure for AD determination based on the increase in the electrochemiluminescence (anodic potential sweep) of luceginin system (c_{min} = 24 nM, RSD ≤ 1.8-2.2%). The developed procedure was successfully applied for the determination of AD in injections.

3.3.3. Other spectroscopic methods

Nuclear magnetic resonance

The procedures utilizing ^1H nuclear magnetic resonance [85] were developed for the confirmation of the identity and quantity of MD, LD, and CD in the pharmaceutical formulations. These procedures are based on resonance characteristics of the functional groups in the structures of CAs and the integral ratio of selected signals belonging to different compounds with respect to those of an internal standard. The ACRs of MD, LD, and CD were 0.15 - 40, 0.4 - 120, and 0.2 - 50 μM, respectively.

Infrared (IR) spectroscopy

Currently, due to such advantages of IR spectroscopy as rapidity, simplicity, and the possibility of analysis of pharmaceutical formulations directly in the package (blister pack, plastic, ampoule, carton etc.), this method is widely used for an authentication of some pharmaceutical formulations including catecholamine-based drugs [86, 87]. In the last few years there has been considerable interest in the development of the procedures for quantitative pharmaceutical analysis by method of IR spectroscopy [88]. However, to our best knowledge, no procedures of analysis of catecholamine-based drugs can be found in the literature.

3.4. Kinetic and biochemical methods

Afkhami *et al*. [89] developed a kinetic method based on the inhibition of the reaction of nitrite with neutral red in acidic media by CAs. The calibration plots were linear in the following concentration ranges of DA, AD, MD, and LD: 2.61 - 26.7, 1.59 - 32.7, 1.8 - 13.3, and 3.05 - 16.2 μM, respectively. The same sensitivity was observed when the reactions of CA oxidation by potassium periodate in acidic medium [90] were used for their indirect kinetic determination in the model solutions. Then, the quantity of potassium periodate not reacted with CA was detected spectrophotometrically (665 nm) after the addition of methylene blue and KI to the indicator reaction. ACRs of AD, LD, and MD were 3 - 40 μM. Very simple kinetic method for MD determination was proposed by Tubino *et al*. [91]. The addition of MD into the indicator system Fe^{3+}- salicylate ions decreased the maximum absorbance of this complex (525 nm) due to the reduction of Fe^{3+} to Fe^{2+}. ACR was 0.2 - 1.8 mM (RSD ≤ 0.8%). However, no data on selectivity were presented.

Chamsaz *et al*. [92] developed the kinetic-spectrophotometric procedures for the determination of MD, CD, and LD by their oxidation by iron(III) in the form of tris(1,10-phenanthrolinate). The ACRs of MD, CD, and LD were 0.4 - 28, 0.9 - 31, and 1 - 30 μM, respectively. Gotardo *et al*. [93] proposed the indicator system where MD reacted with *p*-chloranil. This reaction was accelerated by H_2O_2 and resulted in the production of the violet-red compound (λ_{max} = 535 nm). ACR of MD was 210 - 2480 μM (RSD ≤ 3.2%). No interferences were observed from starch, talc, magnesium stearate, tartaric acid, polyethylene glycol, polypropylene glycol, hydroxypropyl-methyl cellulose, ethyl cellulose, cellulose, lactose, silicon dioxide and sodium croscarmelose when their concentrations were comparable to or 10 times higher than MD concentration. Pagani *et al*. [94] used the differences in the reaction rates of LD and CD oxidation by Ce(III) in sulfuric acid medium for the kinetic fluorescent determination of these CAs without preliminary separation (λ_{ex} = 255 nm, λ_{em} = 355 nm) with the

ACRs of 5 - 1000 and 4 - 360 μM, respectively. The authors chose the parameters of the reaction in order to maximize the selectivity (20°C and 0.02 M H_2SO_4).

Biochemical methods of CA determination include enzymatic methods and biosensors.

Poliakov *et al*. [95] developed the rapid enzymatic procedures for the determination of DA, AD, and MD. As the indicated CAs are the substrates of native horseradish peroxidase, the reactions of their enzymatic oxidation by H_2O_2 in the presence of L-thyroxine have been proposed for their determination. Spectrophotometry at 480 (DA, AD) and 481 (MD) nm was applied to follow the indicator reaction rates. ACRs of DA, AD, and MD were 0.5 - 300 (RSD: 4.3%), 4 - 300 (RSD: 4.1%), and 100 - 400 (RSD: 5.4%) μM, respectively. Common excipients of pharmaceutical formulations did not interfere with the determination of the CAs.

Zhu *et al*. [96] used the inhibition effect of NAD, AD, DA, and LD on the catalytic activity of native horseradish peroxidase in the reaction of *p*-chlorophenol with 4-AAP, the rate of which was followed spectrophotometrically (505 nm). ACRs of NAD, AD, DA, and LD were 6 - 120, 1 - 25, 2.5 - 25, and 2 - 80 μM, respectively. In these procedures, the selectivity was achieved by preliminary separation of CAs by liquid chromatography.

The traditional scheme of the enzymatic action in the procedures using biosensors is presented in Fig. 3, where E_{Ox}, E_{Red}, S_{Ox}, and S_{Red} are the oxidized and reduced forms of the enzyme and its substrate (H_2O_2 for peroxidase, and O_2 for laccase and PPO), respectively.

A novel biosensor for DA determination based on peroxidase from zucchini extract was developed by Lupetti *et al*. [97]. Electrochemical reduction of dopamine-*o*-quinone was realized at a potential of -0.02 V. The limit of detection of DA employing cyclic voltammetry was 26 μM. However, the presence of sodium metabisulfite caused an error in the results of DA determination (RSD ≤ 4.1%).

A novel biosensor based on immobilization of a bean sprout peroxidase on a gold electrode modified with self-assembled monolayers of *L*-cysteine was created for the determination of DA using SWVA [98]. The calibration curve was linear at 10 - 220 μM concentration of DA when

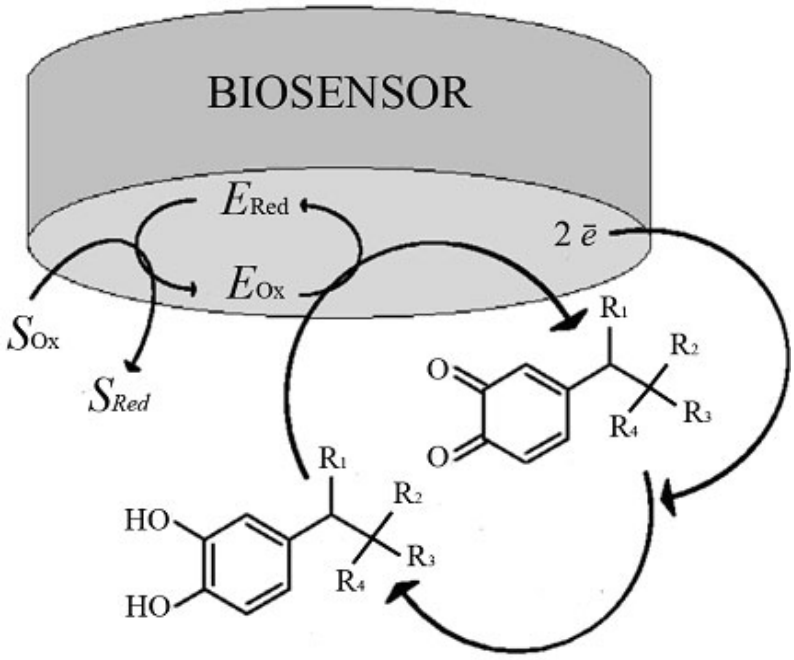


Fig. 3. The scheme of a biosensor action.

using phosphate buffer solution (pH 6.0; pulse amplitude of 80 mV). Brondani *et al*. [99] developed a biosensor for AD determination based on 1-butyl-3-methylimidazolium hexafluorophosphate and corn peroxidase. When determining DA, AD, MD, CD, and LD, the best biosensor response was obtained for AD. The ACRs employing SWVA were 2 - 106 (RSD $\leq$ 6.6%) and 1 - 122 (RSD $\leq$ 5.3%) μM with and without ionic liquid, respectively. However, the indicator system should be purged with nitrogen to eliminate the interference of metabisulphite ions.

The application of laccase [100] immobilized on a graphite electrode employing DPVA did not result in any increase in the sensitivity of the determination of CAs. The limits of detection of AD and DA were 7.9 and 9.8 μM. Using the platinum nanoparticles dispersed in 1-butyl-3-methylimidazolium hexafluorophospate and laccase allowed Brondani *et al*. [101] to construct the biosensor employing SWVA for the determination of AD (Fig. 3) with an ACR of 10 - 213 μM. This biosensor was notable for a better stability (90 days on the air), as compared to the sensor described above.

Mataveli *et al*. [102] constructed an amperometric biosensor for AD determination based on the modification of an electrode by polyphenol oxidase from banana extract. The ACR of AD was 0.008 - 800 μM. The enzyme was isolated in the laboratory, and no interference study was performed.

Yan *et al*. [103] developed a selective biosensor for the determination of DA in the presence of a 5000-fold molar excess of ascorbic acid. The biosensor was based on a graphite electrode modified with AgCl nanoparticles and polyaniline. The analytical signal was measured employing CVA and SWVA in phosphate buffer solution (pH 7.0). The limit of detection of DA was 0.2 μM in the presence of 1 mM ascorbic acid.

A novel approach in analytical chemistry consists in an application of an analogue of the enzymes, also known as mimetic enzymes. This is a class of synthetic organic compounds, which are similar to an active site of an enzyme.

A novel and simple amperometric biosensor for DA determination was proposed by Sotomayor *et al.* [104]. A graphite paste electrode modified by copper phthalocyanine (CoI) and histidine in 0.1 M phosphate buffer was utilized as a biosensor. Coupling of CoI and histidine gave a compound, which acted similar to dopamine-β-monooxidase. The ACR of DA was 40 - 290 μM (c_{min} = 11 μM). Ascorbic acid and acetoaminophen interfered with DA determination but uric acid did not. The application of GS electrode coated by Nafion membrane doped with bis(2,2'-bipyridil) copper(II) chloride complex [105] as a biomimetic catalyst resulted in increasing the sensitivity for DA determination: ACR was 35 - 240 μM (c_{min} = 8 μM). This sensor had a reproducible response for at least 40 successive measurements.

A novel biomimetic sensor coated by Fe-complex (analogue of uteroferrin) was proposed for DA determination employing SWVA [106]. This binuclear Fe-complex had a bulky ligand. The advantages of this biosensor were a long-term stability and rapid response. The calibration curve for DA determination was linear from 50 to 6500 μM. Sodium chloride, citric acid, starch, polyethylene glycol, magnesium stearate, lactose, and sucrose did not interfere.

Using complexes of Mn(III) with porphyrin derivatives as modification reagents for carbon and diamond paste microelectrodes allowed Balasoiu *et al*. [107] to develop highly sensitive biosensor for DA determination in the concentration ranges of 0.001 - 1×10^6 and 0.1 - 100 nM. A 10-fold molar excess of ascorbic acid slightly interfered with the determination of DA; 10-fold molar excess of uric acid did not interfere, with RSD < 1%.

However, despite the low cost of the proposed mimetic biosensors, the sensitivity of CAs determination was lower (except for [107]) than the sensitivity of the enzymatic procedures. At the same time, the selectivity of these biosensors is quite high for the pharmaceutical analysis. Thus, the application of such sensors is a promising approach for solving the problems of pharmaceutical analysis.

3.5. Chromatographic and relative methods

3.5.1. Chromatographic procedures

Due to high selectivity combined with high sensitivity, chromatographic method is used for

the determination of CAs in both biological and pharmaceutical samples [7, 108, 109]. However, the application of chromatographic procedures is preferable for the monitoring of purity of the initial substances as well as final pharmaceuticals, i.e. for the determination of impurities in pharmaceutical formulations. For this reason, not many chromatographic procedures for the determination of CAs in officinal drugs have been found in scientific literature.

Camanas *et al*. [110] proposed HPLC method with the micellar mobile phase containing SDS (0.1 M), 1-propanol (5% v/v), and phosphate buffer (25 mM, pH 3) for the determination of DA, AD, NAD, LD, MD, CD, and IPA in injections, tablets, and aerosols with UV-detection at 280 nm (RSD ≤ 0.3%). The column was C_{18} Spherisorb ODs-2 (12 cm × 4.6 mm). SDS was added in order to increase the retention of CAs on C_{18} column. The limits of detection of the listed CAs were 0.05, 0.03, 0.03, 0.02, 0.02, 0.02, and 0.08 μM, respectively.

The procedure employing reversed-phase HPLC [111] with UV-detector (280 nm) was proposed in order to monitor the purity of AD-based liquid formulations. The mobile phase was water: methanol: acetic acid (85:10:5 v/v). The calibration plot for AD after separation on C_{18} column was linear in the concentration range of 0.06 - 0.6 μM (RSD ≤ 0.3%). The purity of the pharmaceutical formulations was estimated by determining the AD concentration; possible impurities were not considered. Guan *et al*. [112] developed the procedures for the determination of CAs by ion-exchange chromatography with direct conductive detection: ACR of DA and AD were 0.6 - 300 μM and 0.05 - 300 μM for NAD. The separation was conducted on an IC column (Metrosep cation 1-2 4.0 × 125 mm) with a cationic pre-column, mobile phase was 1 mM nitric acid. The RSD of the obtained results did not exceed 2.1%.

A well-known approach used for the improvement of the analytical characteristics of procedures is derivatization of the initial substances with organic compounds in order to obtain the products giving better analytical signals. Khuhawar *et al*. [113] used gas chromatography with a flame ionization detector for DA and AD determination. The application of an inexpensive derivatizing reagent (ethyl chloroformate) and capillary column (30 m × 0.32 mm, coated with a 0.25 μM film of HP-5, J&W Scientific, USA) resulted in 0.9 and 2 μM detection limits for DA and AD, respectively. When DA and AD were determined in injections, RSD of the results varied in the range of 1-2.5%.

3.5.2. Electrophoresis

Capillary electrophoresis is a relatively new method in the analysis of pharmaceuticals, and, especially, catecholamine-based drugs. The examples of the application of this method for pharmaceutical analysis were described by Brown and Grushka [114] (1995), Morzunova [115] (2006), and Marsh [116] (2008).

De Griend *et al*. [117] developed an electrophoretic procedure for the separation and quantification of L- and D-adrenaline in anaesthetic injections. The analysis was performed in the buffer containing heptakis(2,6-di-O-methyl)-β-cyclodextrin (40 mM), phosphoric acid (0.1 M), and triethanolamine (0.05 M) at voltage of 30 kV. When UV-detection (200 nm) and high temperature (45°C) were used, the ACR of AD was 10 - 200 μM. The results of the analysis of the pharmaceutical samples were obtained with RSD of 10-15%. However, the procedure may be applied for the estimation of enantiomeric purity of AD-based pharmaceutical formulations.

Capillary electrophoresis with indirect chemiluminescent detection was applied for the determination of DA, AD, and NAD [118]. Quenching effects of these CAs in luminol-$K_3[Fe(CN_6)]$ system were observed in the following concentration ranges: 0.57 - 13 (DA), 0.92 - 28 (AD), and 0.85 - 24 μM (NAD). The separation was performed in $Na_2B_4O_7$ (15 mM) - luminol (2 mM) buffer solution (pH 9.5) at voltage of 20 kV. RSD of the results of CA determination in injections was less than 5.5%. Based on the same fluorimetric system, Zhao *et al*. [119] developed a rapid and simple procedure for the determination of LD. The ACR was 0.05 - 2.5 μM (RSD 4.1%) with 30 mM borate buffer (pH 9.4) at 16 kV of voltage. He *et al*. [120] did not improve the analytical characteristics of the procedure for LD determination

employing luminol - $K_3[Fe(CN_6)]$ system. Utilizing 100 mM borate buffer (pH 9.5) with voltage of 15 kV provided the analytical range for LD of 5 - 500 μM. However, this procedure seemed to be more reproducible (RSD ≤ 2.9% for the analysis of an LD tablet), as compared to the techniques mentioned above.

Zhang *et al*. [121] used the method of capillary electrophoresis with laser-induced fluorescent detection for the determination of 0.05 - 2 μM DA and NAD (10 mM borate buffer, pH 10.5, with 10% (v/v) acetonitrile, applied voltage 20 kV). Fluorescein isothiocyanate was used as a derivatizing agent that yielded a compound absorbing and emitting light in different ranges of the spectrum, as compared to the initial CAs (λ_{ex} = 488 nm, λ_{em} = 520 nm). The developed procedure is simple and sensitive but requires 4 h for a completion of the derivatization reaction. RSD of the results of DA determination in injections was 2.7%.

Capillary electrophoresis with amperometric detection (carbon disk electrode, E = 900 mV) was applied for the determination of LD and CD [122]. Under the optimum conditions, LD and CD were separated within 12 min and determined in the concentration ranges of 6 - 500 and 5 - 650 μM, respectively. The results of the analysis of tablet formulations were obtained with RSD of 2.6 (LD) and 2.3% (CD).

3.6. Flow injection analysis (FIA)

FIA with spectrophotometric, luminescent, electrochemical, and kinetic detection is widely used for the determination of CAs in pharmaceuticals (Fig. 2, Table 4). The last reviews devoted to the application of FIA in pharmaceutical control for the determination of different drugs were published in 2001 [11-13], 2007 (Tzanavaras [123]), and 2010 (Felix [124]). It should be noted that the constructions of the reported flow injection systems (flow cells) were similar to the schemes described in detail in the articles [123, 124]. Thus, we shall only indicate the analytical parameters of FIA procedures for the analysis of catecholamine-based pharmaceutical formulations (Table 4).

The data of Table 4 show that FIA with luminescent detection [139-154] is quite a sensitive method for the determination of CAs in the pharmaceutical formulations but the developed procedures require substantial dilution of the analyzed sample. The possibility to carry out up to 180-200 measurements per hour [132, 160] makes this method very attractive for pharmaceutical industry. Unfortunately, no study of the interferents was made and described in the majority of the papers.

Coupling FIA with spectrophotometric detection resulted in low cost simple procedures, beside those [135-137] where the construction of the reactors was complicated. The addition of the enzyme, PPO [128-131, 151, 157], did not improve the analytical characteristics. Furthermore, the enzyme preparations were extracted from different sources (palm tree fruits [128], sweet potato roots [129, 130], avocado [131], sour sop [151, 157]) in laboratory, which limited the application of these procedures by other researchers. Using kinetic method did not allow the authors [138] to develop a sensitive and simple procedure for MD determination. Significant dependence of the analytical signal on the concentrations of the indicator system components rather than on CA concentration or external conditions (temperature, etc.) [125, 126, 138, 152] made such procedures inappropriate for the precise analysis.

The application of gravimetric FIA analysis is quite preferable due to its simplicity, rapidity, high reproducibility, and selectivity although it is less sensitive, as compared to spectrophotometric, luminescent, or amperometric FIA (Table 4).

4. Future trends

Considering possible future trends in the analysis of catecholamine-based drugs, we can state that for the majority of chemists the high-priority direction is the improvement of the proposed procedures, the development of novel FIA techniques and their adaptation to wide pharmaceutical practice. It is worth to note that today most of the reported FIA procedures for the analysis of catecholamine-based drugs are sensitive, selective, accurate, simple, rapid, computer-assisted, and are characterized by excellent reagent economy, with sampling frequency approaching 200 h^{-1} (Table 4). Such procedures satisfy the requirements of pharmaceutical analysis even now. Unfortunately, despite the obvious advantages of the reported

Table 4. The analytical characteristics of FIA procedures for the determination of CAs

Reagents	Sample type: analyte	Parameters	ACR, μM	Sampling rate, h^{-1}	Remarks	Ref.
Spectrophotometric detection						
NaOH	Injection: DA AD	λ_{max} = 390 nm λ_{max} = 390 nm	20 - 200 20 - 200	130	Temperature 65°C; no interferents were studied; RSD - 4.2% (DA), 5% (AD)	[125]
$NaIO_4$	Injection: DA Tablet: MD	λ_{max} = 473 nm λ_{max} = 473 nm	20 - 200 20 - 200	130	Temperature of the reactor: 65°C (DA) and 45°C (MD); glucose, fructose, saccharose, NaCl, Na_2SO_3, starch do not interfere; RSD - 8.2% (DA), 6.4 (MD)	[126]
	Injection: AD IPA	λ_{max} = 491 nm λ_{max} = 491 nm	5 - 200 5 - 200	120	Signal is stable for 30 min; no interferents were studied; RSD - 10% (AD), 4.3% (IPA)	[127]
PPO	Injection: AD	λ_{max} = 486 nm	20 - 200	-*	Enzyme was extracted in a lab; RSD - 1.9-3.4%	[128]
	Tablet: LD CD	λ_{max} = 295 – 540 nm	290 - 2800 90 - 300	18	Complicated measurements; analysis of LD and CD in their mixture; enzyme was prepared in lab; RSD - 1.3-3.7%	[129]
	Tablet: LD CD	λ_{max} = 292 – 600 nm	5×10^3 - 3×10^4 700 - 4000	-	Analysis of LD and CD in their mixture; enzyme was prepared in lab; RSD - 5.5%	[130]
	Tablet: IPA	λ_{max} = 492 nm	120 - 740	36	Enzyme preparation was extracted in lab; RSD - 6-8%	[131]
$NaIO_4$ and *p*-toluidine	Injection: DA AD Tablet: MD	λ_{max} = 480 nm λ_{max} = 480 nm	12 - 310 25 - 400 4.5 - 200	180	Glucose, lactose, fructose, talc, NaCl, magnesium stearate do not interfere; RSD - 0.43% (DA), 0.54% (AD), 0.31% (MD)	[132]
p-Aminophenol	Tablet MD	λ_{max} = 608 nm	200 - 3000	48	The addition of ethanol is required; RSD - 1.6-2.6%	[133]
Fe(II)-citrate	Injection: AD Tablet: IPA	λ_{max} = 530 nm	30 - 1000 50 - 1400	120	None of the common excipients interfere; EDTA interferes at high concentration; RSD 2-4%	[134]

Table 4 continued..

Triiodide ion immobilized in a anion-exchange resin	Injection: AD	λ_{max} = 488 nm	6.4 - 300	80	Reactor is stable even after injection of more than 600 solutions; RSD - 2.7%	[135]
PbO_2 immobilized in a polyester resin	Injection: AD	λ_{max} = 486 nm	100 - 800	130	Required the preparation of the reactor; no interferents were studied; RSD - 1%	[136]
	Tablet: LD	λ_{max} = 520 nm	100 - 1000		RSD - 0.2%	[137]
FDNB and CTAB	Tablet: MD	Stopped-flow kinetic λ_{max} = 352 nm	10 - 200	40	Sensitivity depends on pH and concentrations of the reagents; RSD - 0.4-3.9%	[138]
Luminescent (Electro, chemi, and photo types) detection						
NaOH	Injection: AD	λ_{ex} = 330 nm λ_{em} = 510 nm	0.3 - 80 100 - 200	107	Heating at 73°C; picric acid and ZnO interfere, other components do not interfere; RSD - 2.7%	[139]
NaOH and CTAB	Injection: AD	λ_{ex} = 330 nm λ_{em} = 520 nm	6 - 2700	90	The tolerance levels for NaCl, EDTA, $Na_2S_2O_5$ were 2, 0.2, 0.05 mg/ml for the determination of 6 μM AD; RSD - 1.1%	[140]
MnO_2 and polyester resin	Injection: AD	λ_{ex} = 330 nm λ_{em} = 540 nm	3 - 100	65	$NaHCO_3$, H_3BO_3 interfere, other components do not interfere; RSD - 1.5-2.5%	[141]
DAPB	Injection: DA	λ_{ex} = 330 nm λ_{em} = 540 nm	10 - 100	24	Glycine and ascorbic acid interfere, other components do not interfere; RSD - 2.2%	[142]
Thionine blue and EDTA	Injection: DA Tablet: LD	λ_{ex} = 322 nm λ_{em} = 455 nm	12.5 - 500 10 - 500	35	Stable fluorescent signal; no interferents were studied; RSD - 2.1% (DA), 3.2% (LD)	[143]
Luminol	Injection: DA	E_{max} = 0.7 V PMT	0.05 - 10	60	Co^{2+} and Mn^{2+} ions interfere (eliminated by the addition of 0.1 mM EDTA), other components do not; RSD - 1.5-1.8%	[144]
Luminol - Ag(III)	Injection: AD	PMT E = -800 V	0.001 - 0.1	-	K^+, Na^+, Ca^{2+}, NO_3^{2-}, Cl^-, Zn^{2+}, SO_4^{2-}, PO_4^{3-}, Br^- ions and glucose do not interfere; RSD - 5.4%	[145]
	Injection: DA	PMT E = -800 V	0.0001 - 0.01	-	Equal amounts of glucose and starch slightly interfere, other components do not interfere; RSD - 2.3%	[146]

Table 4 continued..

Luminol - KIO_4	Injection: DA AD DB	PMT *E* = -600 V	0.007 - 6.5 0.006 - 5.5 0.003 - 3.3	-	K^+, Na^+, Cl^-, SO_4^{2-}, NO_3^-, SO_3^{2-}, PO_4^{3-}, Ba^{2+}, Mg^{2+} ions, glucose, lactose, $Na_2S_2O_5$, Ca^{2+}, ascorbic acid do not interfere in the tested concentrations; RSD - 2.1% (DA), 2.7% (AD), 2.3% (DB)	[147]
	Injection: DA AD NAD IPA	PMT *E* = -700 V	0.0007 - 0.07 0.0006 - 0.6 0.005 - 0.5 0.03 - 0.3	60	Mn^{2+}, Co^{2+}, Fe^{2+} ions interfere with the determination of DA, other components do not interfere; RSD - 1.7% (DA), 2.8% (AD), 3.6% (NAD), 1.1% (IPA)	[148]
	Injection: AD	PMT *E* = -600 V	0.05 - 1.5	130	One measurement takes about 27 s; Ca^{2+}, Mg^{2+}, SO_3^{2-} ions interfere, other components do not interfere; RSD - 1-2.3%	[149]
Luminol - $K_3Fe(CN)_6$	Injection: DA	Flow luminometer with spiral flow-cell	0.2 - 0.65 2.5 - 20	135	Common excipients do not interfere; RSD - 4.7%	[150]
Luminol and PPO	Injection: AD	PMT *E* = 1200 V	5 - 55 55 - 140	20	NaCl, H_3BO_3, EDTA $Na_2B_4O_7 \times 10H_2O$, citric, ascorbic, and picric acids, glucose, lactose, $NaHSO_3$ do not interfere; enzyme preparation is stable for 1 week; RSD - 2.1%	[151]
NaClO and DCF	Injection: DA AD Tablet: MD	*E* = 650 V	20 - 330 16 - 440 15 - 400	96 64 68	Different values of optimum pH for each CA; RSD - 1.25% (DA), 2.0% (AD), 0.85% (MD)	[152]
Lucigenin	Injection: IPA	PMT	0.1 - 100	3	Ca^{2+}, Cd^{2+}, Co^{2+}, Ni^{2+}, Pb^{2+}, V^{5+}, Zn^{2+}, Hg^{2+}, Cu^{2+}, Mg^{2+} ions, riboflavin and magnesium stearate interfere severely; RSD - 1.4 - 2.2%	[153]
Lucigenin and Fe(II)	Injection: DA	Luminometer with a spiral flow- cell	0.01 - 0.2	40	Thermostating at 30°C; sodium urate and SO_3^{2-} ion interfere, other components do not interfere; RSD - 4.6%	[154]

Table 4 continued..

Amperometric detection						
Glassy carbon electrode	Injection: DA AD Tablet: LD	E = 800 mV	7 - 50 7 - 50 7 - 50	100	No interferents were studied; RSD - 3.2% (DA), 8.1% (AD), 12.5% (LD)	[155]
Glassy carbon electrode with DTDB	Injection: DA	E = 200 mV	0.0005 - 500	-	Electrode is stable for 1 week; RSD - 4-11%	[156]
Carbon paste electrode with PPO	Injection: DA	E = 100 mV	200 - 20000	40	500 determinations in 60 days without considerable loss of enzymatic activity; no interferents were studied; RSD - <3.4%	[157]
	Injection: AD	E = -100 mV	50 - 350	60	Sulfite and mainly metabisulfite interfere; RSD - 3.0-4.2%	[128]
Gold (working) and platinum electrodes, $KMnO_4$	Tablet: LD	ΔE = 0 V (between two electrodes)	0.2 - 100	-	Fe^{3+} and Cl^- ions interfere, other components do not interfere; RSD - 3%	[158]
Gold screen-printed electrode	Tablet: LD	E = 800 mV	1 - 660	20	No interferents were studied; RSD - 4%	[42]
Cylindrical carbon fiber microelectrode modified with P3MT	Tablet: LD	E = 700 mV	10 - 800	-	Electrode does not absorb organic molecules; no interferents were studied; RSD - 3.2%	[159]
Potentiometric detection						
Metaperiodate BTPA	Injection: DA	I = 0	52 - 1700	200	Required a control of ionic strength, $Na_2S_2O_5$ interfere; RSD - 2.4%	[160]
Gravimetric detection						
Piezoelectric crystal with silver electrode and SDPS	Injection: AD Tablet MD	10 MHz	220 - 4600 180 - 3700	120	Glucose, lactose, sucrose, asparate, citrate, tartrate, antipyrine, berberine, pilocarpine, sparteine hydrochloride do not interfere; RSD - 0.24% (AD), 0.16% (MD)	[161]

* - no data; FDNB - 1-flouro-2,4-dinitrobenzene, DAPB - *m*-dansylaminophenylboronic acid, PMT - photomultiplier tube, DCF - 2,7-dichlorofluorescein, P3MT - poly-3-methylthiophene, DTDB - 5,5-ditetradecyl-2-(2-trimethylammonioethyl)-1,3-dioxane bromide, BTPA - bis(triphenylphosphoranylidene) ammonium, SDPS - sodium dodecyl phenylsulfonate.

procedures, the old techniques for the determination of CAs are still cited in the pharmacopeias of different countries.

The physical-chemical properties of CAs and the type of the chemical reaction used for their derivatization often predetermine the choice of a certain detection system in FIA. In our opinion, a promising approach is the integration of several different detectors into flow injection systems for CA determination. In the future, the application of such systems will make a significant contribution to the improvement of the precision of analysis, promoting modern procedures in pharmaceutical practice and analysis of multicomponent formulations.

CONCLUSIONS

The analysis of the published data allows concluding that the majority of the current instrumental methods for the determination of CAs in officinal drugs is advantageous over the pharmacopeia methods. Their advantages are sensitivity, non-interference from the other ingredients usually found in pharmaceutical formulations, simplicity, rapidity, precision, high throughput, and good agreement with the official methods. It is not our intention to suggest that the reviewed procedures replace potentiometric method of analysis for the determination of CAs. However, the presented methods may be more convenient as compared to the existing and recommended ones.

In our opinion, current advances of the pharmaceutical analysis of catecholamine-based drugs are as follows: increase in the number of reactions for spectrophotometric analysis, expansion of the choice of modification agents used for the indicator electrodes (nanoparticles, nanotubes, surfactants, ionic liquids, etc.) and the variety of enzymes (including mimetic enzymes) in biosensors, the application of novel approaches for CA determination by kinetic and enzymatic methods, the development of methodology of flow injection methods in the practice of pharmaceutical analysis.

ACKNOWLEDGEMENTS

This work was supported by Ministry of Education and Science of Russian Federation (contract № P868 of 25 May 2010) and Russian Foundation for Basic Research (grant № 09-03-00823-a).

REFERENCES

1. Jacobs, L., Samli, A. C., and Jedlik, T. 2001, Ind. Market. Manag., 30, 499.
2. Next Generation Pharmaceutical Europe. http://www.ngpharma.eu.com/article/Get-real/
3. Richard, J. and Wurtman, M. D. 1970, N. Engl. J. Med., 282, 45.
4. Factor, S. A. and Schneider, A. S. 1995, Exp. Neurol., 131, 64.
5. Bond, J. V. 1975, Arch. Dis. Child., 50, 691.
6. Neurotransmitters for Sport, http:// community.myprotein.com/content/sport-neurotransmitters-60/
7. Tsunoda, M. 2006, Anal. Bioanal. Chem., 386, 506.
8. Nikolajsen, R. P. H. and Hansen, Å. M. 2001, Anal. Chim. Acta, 449, 1.
9. Dziedzic, L. M., Dziedzic, S. W., Cerqueira, S., and Gitlow, S. E. 1982, Clin. Chim. Acta, 125, 291.
10. Jacob, K. and Vogt, W. 1982, J. Clin. Chem. Clin. Biochem., 20, 644.
11. Solich, P., Sklenářová, H., Polášek, M., and Karlíček, R. Available online at http://www.flowinjection.com/Brochures/ solich.pdf.
12. Solich, P., Sklenářová, H., Polášek, M., and Karlíček, R. 2001, J. Flow Injection Anal., 18, 118.
13. Evgen'ev, M. I., Garmonov, S. Yu., and Shakirova, L. Sh. 2001, J. Anal. Chem., 56, 313.
14. Gil, E. S. and De Melo, G. R. 2010, Brazilian J. Pharm. Sci., 46, 375.
15. Perry, M., Li, Q., and Kennedy, R. T. 2009, Anal. Chim. Acta, 653, 1.
16. Pohloudek-Fabini, R. and Beyrich, Th. 1875, Organische Analsyse (Organic Analysis), Geest und Portig, Leipzig, 624.
17. Beaudouin, C., Haurat, G., Fraisse, L., Souppe, J., and Renaud, B. 1993, J. Chromatogr. Biomed. Appl., 613, 51.

18. Gadkariem, E. A., Ibrahim, K. E. E., Kamil, N. A. A., Haga, M. E. M., and El-Obeid, H. A. 2009, Saudi Pharm. J., 17, 303.
19. http://www.sigmaaldrich.com/etc/medialib/docs/Sigma/Product_Information_Sheet/d0676pis.Par.0001.File.tmp/d0676pis.pdf.
20. http://www.sigmaaldrich.com/etc/medialib/docs/Sigma/Product_Information_Sheet/d9628pis.Par.0001.File.tmp/d9628pis.pdf.
21. "Europian Pharmacopoeia 5.0", 2005, 5th Ed., Council of Europe, Strasbourg, France.
22. "United States Pharmacopeia", 1995, 23rd Rev., Twinbrook Parkway, Rockville, USA.
23. Ziyatdinova, G. K. and Budnikov, G. K. 2005, J. Anal. Chem., 60, 673.
24. Zapata-Urzúa, C., Pérez-Ortiz, M., Bravo, M., Olivieri, A. C., and Álvarez-Lueje, A. 2010, Talanta, 82, 962.
25. Al-Mayouf, A. M. and Al-Sulaim, A. M. 1999, J. King Saud. Univ., 11, 53.
26. Kumar, S. A., Tang, C.-F., and Chen, S.-M. 2008, Talanta, 74, 860.
27. Selvaraju, T. and Ramaraj, R. 2005, J. Electroanal. Chem., 585, 290.
28. Lai, G.-S., Zhang, H.-L., and Han, D.-Y. 2008, Microchim. Acta, 160, 233.
29. Cao, X., Luo, L., Ding, Y., Zou, X., and Bian, R. 2008, Sens. Actuators B, 129, 941.
30. Ren, W., Qun Luo, H., and Li, N. B. 2006, Sensors, 6, 80.
31. Seol, H., Jeong, H., and Jeon, S. 2009, J. Solid State Electrochem., 13, 1881.
32. Li, X., Chen, M., Ma, X., and Lin, X. 2010, Int. J. Chem., 2, 206.
33. Jin, G, Zhang, Y., and Cheng, W. 2005, Sens. Actuators B, 107, 528.
34. Hu, G.-Z., Zhang, D.-P., Wu, W.-L., and Yang, Z.-S. 2008, Colloids Surf. B, 62, 199.
35. Ensafi, A. A., Taei, M., and Khayamian, T. 2010, Colloids Surf. B, 79, 480.
36. Wang, Y. and Chen, Z.-Z. 2009, Colloids Surf. B, 74, 322.
37. Alothman, Z. A., Bukhari, N., Wabaidur, S. M., and Haider, S. 2010, Sens. Actuators B, 146, 314.
38. Zare, H. R. and Nasirizadeh, N. 2010, Sens. Actuators B, 143, 666.
39. Qiao, J. X., Luo, H. Q., and Li, N. B. 2008, Colloids Surf. B, 62, 31.
40. Ensafi, A. A., Taei, M., and Khayamian, T. 2009, J. Electroanal. Chem., 633, 212.
41. Shaidarova, L. G., Gedmina, A. V., Chelnokova, I. A., and Budnikov, G. K. 2008, J. Anal. Chem., 63, 891.
42. Bergamini, M. F., Santos, A. L., Stradiotto, N. R., and Zanoni, V. B. 2005, J. Pharm. Biomed. Anal., 39, 54.
43. Chernyshov, D. V., Shvedene, N. V., Antipova, E. R., and Pletnev, I. V. 2008, Anal. Chim. Acta, 621, 178.
44. Alarcón-Angeles, G., Corona-Avendaño, S., Palomar-Pardavé, M., Rojas-Hernández, A., Romero-Romo, M., and Ramírez-Silva, M. T. 2008, Electrochim. Acta, 58, 3013.
45. Izaoumen, N., Cubillana-Aguilera, L. M., Naranjo-Rodríguez, I., Hidalgo-Hidalgo de Cisneros, J. L., Bouchta, D., Temsamani, K. R., and Palacios-Santander, J. M. 2009, Talanta, 78, 370.
46. Hu, G., Chen, L., Guo, Y., Wang, X., and Shao, S. 2010, Electrochim. Acta, 55, 4711.
47. Sun, W., Yang, M., and Jiao, K. 2007, Anal. Bioanal. Chem., 389, 1283.
48. Habibi, B. and Pournaghi-Azar, M. H. 2010, Electrochim. Acta, 55, 5492.
49. Corona-Avendaño, S., Alarcón-Ángeles, G., Ramírez-Silva, M. T., Romero-Romo, M., Cuán, A., and Palomar-Pardavé, M. 2009, J. Electrochem. Soc., 156, J375.
50. Shams, E., Babaei, A., Taheri, A. R., and Kooshki, M. 2009, Bioelectrochem., 75, 83.
51. Salimi, A., MamKhezri, H., and Hallaj, R. 2006, Talanta, 70, 823.
52. Luetti, K. O., Vieira, I. C., Vieira, H. J., and Fatibello-Filho, O. 2002, Analyst, 127, 525.
53. Liu, T., Li, M., and Li Q. 2004, Talanta, 63, 1053.
54. Curulli, A. 2009, Sensors, 9, 2437.
55. Salimi, A., Alizadeh, V., and Compton, R.G. 2005, Anal. Sci., 21, 1275.
56. Wei, J., He, J.-B., Cao, S.-Q., Zhu, Y.-W., Wang, Y., and Hang, G.-P. 2010, Talanta, 82, 190.

57. Shankaran, D. R., Iimura, K., and Kato, T. 2003, Sens. Actuators B, 94, 73.
58. Hu, G., Liu, Y., Zhao, J., Cui, S., Yang, Z., and Zhang, Y. 2006, Bioelectrochem., 69, 254.
59. Nazarova, I. A., Starushko, N. V., Otkidach, K. N., Shvedene, N. V., Formanovski, A. A., and Pletnev, I. V. 2001, Mos. Univ. Bull., 42, 33.
60. El-Kommos, M. E., Mohamed, F. A., and Khedr, A. S. 1990, J. Assoc. Off. Anal. Chem., 73, 516.
61. Sorouraddin, M. H., Manzoori, J. L., Kargarzadeh, E., and Haji Shabani, A. M. 1998, J. Pharm. Biomed. Anal., 18, 877.
62. Sajjan, A. G., Melwanki, M. B., and Seetharamappa, J. 2001, J. Anal. Chem., 56, 827.
63. Vieira, I. C. and Fatibello-Filho, O. 1998, Talanta, 46, 559.
64. Nagaraja, P., Murthy, K. C. S., Rangappa, K. S., and Gowda, N. M. M. 1998, Talanta, 46, 39.
65. Madrakian, T., Afkhami, A., Khalafi, L., and Mohammadnejad, M. 2006, J. Braz. Chem. Soc., 17, 1259.
66. Madrakian, T. and Mohammadnejad, M. 2007, Chem. Pharm. Bull., 55, 865.
67. Gowda, B. G., Melwanki, M. B., and Seetharamappa J. 2001, Anal. Sci., 17, 533.
68. Nagaraja, P., Vasantha, R. A., Murthy, K. C. S., and Rangappa, K. S. 2001, Chem. Anal., 46, 569.
69. Nagaraja, P., Vasantha, R. A., and Sunitha, K. R. 2001, Talanta, 55, 1039.
70. Shaikh, S. M. T., Manjunatha, D. H., Harikrishna, K., Ramesh, K. C., Kumar, R. S., and Seetharamappa, J. 2008, J. Anal. Chem., 63, 637.
71. Ribeiro, P. R. S., Pezza, L., and Pezza, H. R. 2005, Eclectic Chem., 30, 23.
72. Gadkariem, E. A., Ibrahim, K. E. E., Kamil, N. A. A., Haga, M. E. M., and El-Obeid, H. A. 2009, J. Saudi Pharm., 17, 303.
73. Aman, T., Khan, I. U., Aslam, N., and Ahmad, I. 1998, Anal. Lett., 31, 1007.
74. Nour El-Dien, F. A, El-Nahas, R. G, and El-Nahas, A. G. 2006, J. Autom. Methods Manage. Chem., 2006, 1.
75. Nour El-Dien, F. A., Zayed, M. A., Mohamed, G. G., and El-Nahas, R. G. 2005, J. Biomed. Biotechnol., 1, 1.
76. Nour El-Dien, F. A., Frag, E. Y. A., and Mohamed, G. G. 2010, Drug Test. Anal., 2, 234.
77. Afkhami, A. and Nouri-Zadeh, A. 2002, Asian J. Chem., 14, 867.
78. Issopoulus, P. B. 1990, J. Anal. Chem., 336, 124.
79. Wang, H. Y., Sun, Y., and Tang, B. 2002, Talanta, 57, 899.
80. Kim, W. H., Karim, M. M., and Lee, S. H. 2008, Anal. Chim. Acta, 619, 2.
81. Wang, H. Y., Hui, Q. S., Xu, L. X., Jiang, J. G., and Sun, Y. 2003, Anal. Chim. Acta, 437, 93.
82. Karim, M. M., Alam, S. M., and Lee, S. H. 2007, J. Fluoresc., 17, 427.
83. Guo, Y., Yang, J., Wu, X., and Du, A. 2005, J. Fluoresc., 15, 131.
84. Su, Y., Wang, J., and Chen, G. 2005, Talanta, 65, 531.
85. Talebpour, Z., Haghgoob, S., and Shamsipur M. 2004, Anal. Chim. Acta, 506, 97.
86. Elizarova, T. E., Shtyleva, S. V., and Pletneva, T. V. 2008, Pharm. Chem. J., 42, 432.
87. Alvarenga, L., Ferreira, D., Altekruse, D., Menezes, J. C., and Lochmann, D. 2008, J. Pharm. Biomed. Anal., 48, 62.
88. Blanco, M., Coello, J., Iturriaga, H., Maspoch, S., and De la Pezuela, C. 1998, Analyst, 123, 135.
89. Afkhami, A., Nematollahi, D., and Khatami, H. A. 2002, Asian J. Chem., 14, 333.
90. Afkhami, A. and Khatami, X. A. 2003, J. Anal. Chem., 58, 157.
91. Tubino, M., Batista, D. C. D. V., and Rodrigues, J. A. R. 2006, Anal. Lett., 39, 327.
92. Chamsaz, M., Safavi, A., and Fadaee, J. 2007, Anal. Chim. Acta, 603, 140.
93. Gotardo, M. A., Lima, L. S., Sequinel, R., Rufino, J. L., Pezza, L., and Pezza, H. R. 2008, Eclectic Chem., 33, 7.
94. Pagani, A. P., Cabezón, M. A., and Ibáñez, G. A. 2009, Anal. Sci., 25, 633.

95. Poliakov, A. E., Dumshakova, A. V., Muginova, S. V., and Shekhovtsova, T. N. 2011, Talanta, 84, 710.
96. Zhu, M., Huang, X., Li, J., and Shen, H. 1997, Anal. Chim. Acta, 357, 261.
97. Lupetti, K. O., Ramos, L. A., Vieira, I. C., and Fatibello-Filho, O. 2005, Farmaco, 60, 179.
98. Moccelini, S. K., Fernandes, S. C., and Vieira, I. C. 2008, Sens. Actuators B, 133, 364.
99. Brondani, D., Dupont, J., Spinelli, A., and Vieira, I. C. 2009, Sens. Actuators B, 138, 236.
100. Leite, J. D., Fatibello-Filho, O., and Barbosa, A. M. 2003, J. Braz. Chem. Soc., 14, 297.
101. Brondani, D., Scheeren, C. W., Dupont, J., and Vieira I. C. 2009, Sens. Actuators B, 140, 252.
102. Mataveli1, L. R. V., Antunes, N. J., Brigagão, M. R. P. L., De Magalhães, C. S., Wisniewski, C., and Luccas, P. O. 2010, Biosens. Bioelectron., 26, 798.
103. Yan, W., Feng, X., Chen, X., Li, X., and Zhu, J.-J. 2008, Bioelectrochemistry, 72, 21.
104. Sotomayor, M. D. P. T., Tanaka, A. A., and Kubota, L. T. 2002, Anal. Chim. Acta, 455, 215.
105. Sotomayor, M. D. P. T., Tanaka, A. A., and Kubota, L. T. 2003, Electroanalysis, 15, 787.
106. De Oliveira, R. W. Z., Neves, A., and Vieira, I. C. 2008, Sens. Actuators B, 129, 424.
107. Balasoiu, S. C., Van Staden, R. -I. S., Van Staden, J. F., Pruneanu, S., and Radu, G.-L. 2010, Anal. Chim. Acta, 668, 210.
108. Bergquist, J., Ściubisz, A., Kaczor, A., and Silberring, J. 2002, J. Neurosci. Methods, 113, 1.
109. Li, F., Zhang, C., Guo, X., and Feng, W. 2003, Biomed. Chromatogr., 17, 96.
110. Villanueva-Camanas, R. M., Sanchis-Mallols, J. M., Torres-Lapasio, J. R., and Ramis-Ramos, G. 1995, Analyst, 120, 1767.
111. Mishra, A. K., Mishra, A., and Chattopadhyay, P. 2010, Arch. Appl. Sci. Res., 2, 251.
112. Guan, C. L., Ouyang, J., Li, Q. L., Liu, B. H., and Baeyens, W. R. G. 2000, Talanta, 50, 1197.
113. Khuhawar, M. Y., Zardari, L. A., and Laghari, A. J. 2008, Chromatographia, 67, 847.
114. Pharmaceutical analysis by capillary electrophoresis, in Advances in Chromatography, 1995, Brown, P. R. and Grushka, E. (Ed.), N. Y. Marcel Dekker, USA.
115. Morzunova, T. G. 2006, Pharm. Chem. J., 40, 158.
116. Marsh, A., Broderick, M., Altria, K., Rower, J., Donegan, S., and Clark, B. 2008, Methods in Molecular Biology, 384, 202.
117. De Griend, C. E. S., Anders, G. Ek., Widahl-Nasman, M. E., and Andersson, E. K. M. 2006, J. Pharm. Biomed. Anal., 41, 77.
118. Hu, Y., Li, X., and Pang, Z. 2005, J. Chromatogr. A, 1091, 194.
119. Zhao, S., Bai, W., Wang, B., and He, M. 2007, Talanta, 73, 142.
120. He, W. W., Zhou, X. W., and Lu, J. Q. 2007, Chin. Chem. Lett., 18, 91.
121. Zhang, J. Y., Chen, X. G., Hu, Z. D., and Ma, X. 2002, Anal. Chim. Acta, 471, 203.
122. Zhang, L., Chen, G., Hu, Q., and Fang, Y. 2001, Anal. Chim. Acta, 431, 287.
123. Tzanavaras, P. D. and Themelis, D. G. 2007, Anal. Chim. Acta, 588, 1.
124. Felix, F. S. and Angnes, L. 2010, J. Pharm. Sci., 99, 4784.
125. Berzas Nevado, J. J., Lemus Gallego, J. M., and Buitrago Laguna, P. 1996, J. Pharm. Biomed. Anal., 14, 571.
126. Berzas Nevado, J. J., Lemus Gallego, J. M., and Buitrago Laguna, P. 1995, Fresenius J. Anal. Chem., 353, 221.
127. Berzas Nevado, J. J., Lemus Gallego, J. M., and Buitrago Laguna, P. 1995, Anal. Chim. Acta, 300, 293.
128. Felix, F. S., Yamashita, M., and Angnes, L. 2006, Biosens. Bioelectron., 21, 2283.
129. Grünhut, M., Centurión, M. E., Fragoso, W. D., Almeida, L. F., De Araújo, M. C. U., and Band, B. S. F. 2008, Talanta, 75, 950.
130. Grünhut, M., Garrido, M., Centurión, M. E., and Band, B. S. F. 2010, Anal. Chim. Acta, 673, 33.

131. Lupetti, K. O., Vieira, I. C., and Fatibello-Filho, O. 2002, Talanta, 57, 135.
132. Abdulrahman, L. K., Al-Abachi, A. M., and Al-Qaissy, M. H. 2005, Anal. Chim. Acta, 538, 331.
133. Tubino, M., Junior, A. R., and Vila, M. M. D. C. 2004, J. Flow Inject. Anal., 21, 132.
134. Solich, P., Polydorou, Ch. K., Koupparis, M. A., and Efstathiou, C. E. 2000, J. Pharm. Biomed. Anal., 22, 781.
135. Vieira, H. J. and Fatibello-Filho, O. 2004, Eclectic Chem., 29, 79.
136. Teixeira, M. F. S., Marcolino, Jr. L. H., and Fatibello-Filho, O. 2002, Il Farmaco, 57, 215.
137. Marcolino, Jr. L. H., Teixeira, M. F. S., Pereira, A. V., and Fatibello-Filho O. 2001, J. Pharm. Biomed. Anal., 25, 393.
138. Georgiou, C. A., Koupparis, M. A., and Hadjiioannou, T. P. 1991, Talanta, 38, 689.
139. Torres, A. C., Romero, A. M., and Calatayud, J. M. 1998, Microchim. Acta, 128, 187.
140. Huang, C., Chen, H., and He, Q. 2004, Canadian J. Anal. Sci. Spectrometry, 49, 296.
141. Kojlo, A. and Calatayud, J. M. 1995, Anal. Lett., 28, 239.
142. Seckin, Z. E. and Volkan, M. 2005, Anal. Chim. Acta, 547, 104.
143. Pérez-Ruiz, T., Lozano, C. M, Tomás, V., and Ruiz, E. 2007, Microchim. Acta, 158, 299.
144. Zhu, L., Li, Y., and Zhu, G. 2002, Anal. Lett., 35, 2527.
145. Bai, J., Shi, H., Znang, Y., Tian, D., Xu, X., and Kang, W. 2009, Chin. J. Chem., 27, 745.
146. Xu, X., Shi, H., Ma, L., Kang, W., and Li, S. 2010, Luminescence, DOI: 10.1002/ bio.1189.
147. Yu, C., Tang, Y., Han, X., and Zheng, X. 2006, Anal. Sci., 22, 25.
148. Yao, H., Sun, Y. Y., Lin, X., Cheng, J., and Huang, L. 2006, Luminescence, 21, 112.
149. Liu, Y., Liu, Z., and Shi, Y. 2009, Luminescence, DOI 10.1002/bio.1186.
150. Nalewajko, E., Ramírez, R. B., and Kojło, A. 2004, J. Pharm. Biomed. Anal., 36, 219.
151. Michałowski, J. and Hałaburda, P. 2001, Talanta, 55, 1165.
152. Wołyniec, E., Niedźwiedzka, U., and Kojło, A. 2007, Instrum. Sci. Technol., 35, 219.
153. Al-Warthan, A. A., Al-Tamrah, S. A., and Al-Akel, A. A. 1994, Anal. Sci., 10, 449.
154. Zhang, L., Teshima, N., Hasebe, T., Kurihara, M., and Kawashima, T. 1999, Talanta, 50, 677.
155. Garrido, E. M., Lima, J. L. F. C., and Delerue-Matos, C. 1997, J. Pharm. Biomed. Anal., 15, 845.
156. Lin, X. and Gong, J. 2004, Anal. Chim. Acta, 507, 255.
157. Bezerra, V. S., De Lima Filho, J. L., Montenegro, M. C. B. S. M., Araújo, A. N., and Da Silva, V. L. 2003, J. Pharm. Biomed. Anal., 33, 1025.
158. Li, L. J., Chen, Q. F., Cheng, H., Yu, L. B., and Wu, J. L. 2008, Chin. Chem. Lett., 19, 703.
159. Agüí, L., González-Cortés, A., Yáñez-Sedeño, P., and Pingarrón, J. M. 1999, Anal. Chim. Acta, 401, 145.
160. Montenegro, M. C., and Sales, M. G. 2000, J. Pharm. Sci., 89, 876.
161. Mo, Z., Long, X., and Zhang, M. 1999, Talanta, 48, 643.