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Carbon-based Electrochemical Nanosensors for the Determination of PDE5 Enzyme Inhibitors

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ABSTRACT

Sildenafil (SILC), Verdanafil (VRL) and Tadalafil (TAD), which exhibit phosphodiesterase type 5 (PDE5) properties, are active pharmaceutical ingredients that play an important role in the treatment of erectile dysfunction (ED). Traditional analytical methods such as chromatographic and spectrophotometric methods have been widely used for the determination of PDE5 enzyme inhibitors. Nanosensors that will compete with classical analytical methods have been developed for PDE5 enzyme inhibitors using electrochemical methods. The most preferred carbon nanosensors in these studies are; glassy carbon electrode (GCE), screen-printed glassy carbon electrode (SPGCE), graphite paste electrode (GPE), multi-walled carbon nanotube paste electrode (MWCNTPE), boron-doped diamond electrode (BDDE), and pencil graphite electrode (PGE). In addition, new generation carbon-based composite nanosensors have been preferred. In the production of these hybrid sensors, metal or metal oxide nanoparticles, polymers, bioindicators, and carbon materials have been used on the carbon main electrode surface. This review examines the important validation parameters such as sensitivity, selectivity, and detection limits of carbon nanosensors used for PDE5 inhibitors. In addition, the sensitivities between electrochemical methods were compared. The analytical performances of carbon nanosensors were also examined in detail. As a result, the superior performances of carbon nanomaterials developed in the determination of SILC, TAD, and VRL drug active ingredients were definited.

KEYWORDS
PDE5, Sildenafil, Verdanafil, Tadalafil, Carbon and Nanosensors

1. INTRODUCTION

Phosphodiesterase type 5 (PDE5) is the enzyme responsible for the function of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) species and is found densely in the corpus cavernosum. The PDE5 enzyme was first identified as a cGMP-binding protein in 1976. Phosphodiesterase type 5 (PDE5) inhibitors are the most preferred in the treatment of erectile dysfunction (ED) due to their safe and effective profiles [1]. Erectile dysfunction (ED); is the inability to achieve or maintain an erection sufficient for sexual activity due to neurological, psychogenic, vascular, urogenital and hormonal disorders. Seven active ingredients have been developed for

PDE5 inhibitors so far (avanafil, lodenafil, mirodenafil, sildenafil, tadalafil, udenafil and vardenafil), but four have been approved by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) [1,2]. It is also known to be used in therapeutic applications of pulmonary arterial hypertension [3].

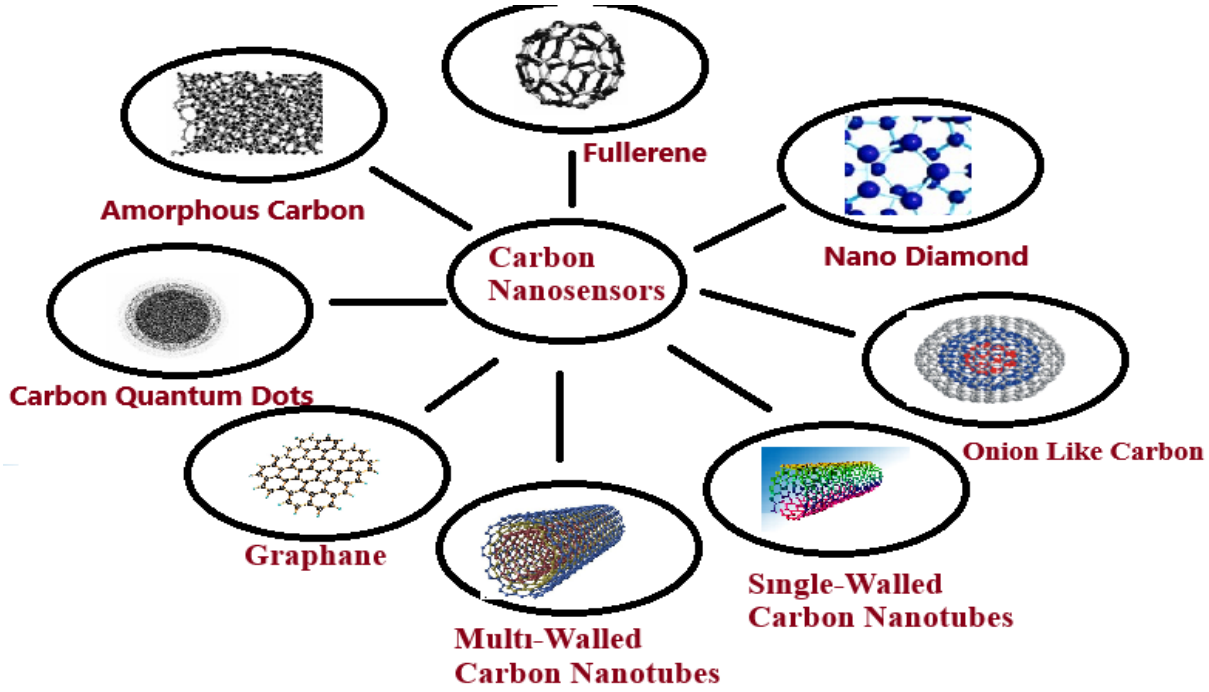
The discovery of sildenafil, the first oral synthetic PDE5 enzyme inhibitor, was found coincidentally during angina and hypertension treatment studies. Later, verdanafil and tadalafil were produced as agents with PDE5 properties. PDE5 enzymes, which play an important role in the treatment of ED, should be used under expert supervision due to their side effects. The most important of these side effects are visual impairment, redness, headache, dyspeptic complaints, congestion and muscle pain. Therefore, the determination of such substances in biological samples is of great importance and these drugs, which have aphrodisiac properties, should be routinely checked. Traditional analytical methods such as chromatographic and spectrophotometric are more prevalent for the determination of PDE5 enzyme inhibitors. However, these methods have many shortcomings such as long pre-treatment, requiring expert personnel, expensive devices and equipment and the need for too many organic solvents. Therefore, scientists have always been in search of an alternative method for many years. Among the alternative analytical methods, electrochemical methods come to the forefront. Electroanalytical methods are fast, simple, cheap, do not require pre-treatment, are portable, flexible and provide on-site analysis and have incredible features. In the last two decades, scientists have successfully determined numerous analytes such as heavy metals from drugs to nucleic acids from pesticides using electrochemical sensors. They have also developed analytical methods and nanosensors that compete with classical analytical methods for PDE5 enzyme inhibitors using electrochemical methods.

2. CARBON-BASED NANOSENSOR TYPES AND ELECTROCHEMICAL SENSITIVITY

Many electrochemical studies have been carried out so far for the active pharmaceutical ingredients sildenafil citrate

(SILC), tadalafil (TAD) and vardenafil hydrochloride (VRL) which are among the PDE5 enzyme inhibitors. Although different nanosensors were used in these studies, carbonaceous nanomaterials were predominantly preferred. The main reason for this can be said to be the extraordinary and unique properties of carbonaceous nanomaterials such as conductivity, stability, large surface area and catalysis. In addition, the other reason for the preference of carbonaceous sensors is that carbon nanomaterials can be easily treated physically and chemically with other materials that exhibit conductivity or catalysis. The most preferred carbonaceous nanosensors in electrochemical studies conducted for the determination of PDE5 enzyme inhibitors are; glassy carbon electrode (GCE), screen-printed glassy carbon electrode (SPGCE), graphite paste electrode (GPE), multi-walled carbon nanotube paste electrode (MWCNTPE), boron-doped diamond electrode (BDDE), and pencil graphite electrode (PGE). Only 4 of these studies used bare electrodes, namely SPGCE, MWCNTPE, CPE and PGE. In other studies, new generation composite nanosensors were preferred. In the production of these hybrid sensors, metal or metal oxide nanoparticles (TiO_2, Ru(II), ZnO, Au and Pt), polymers (chitosan, molecularly imprinted polymer (MIP), nafion, pyrrole) and bioindicators (Cystoseira algae), carbonaceous materials (MWCNTs, NH_2-MWCNTs, reduced graphene oxide (ErGO), 3D Graphene) were treated on the carbonaceous main electrode surface. Electrochemical methods developed for the determination of PDE5 enzyme inhibitors are cylic voltammetry (CV), square wave voltammetry (SWV), Adsorptive cathodic stripping voltammetry (AdCSV), Differential pulse voltammetry (DPV), Potentiometry, amperometry, Adsorptive stripping square wave voltammetry (AdSSWV), Linear sweep adsorptive stripping voltammetry (LSASV), Linear sweep. It was classified as voltammetry (LSV), Batch Injection Analysis with amperometric detection (BIA-AD), Square-wave adsorptive anodic stripping voltammetry (SW-AdASV), Square-wave stripping voltammetry (SWSV) and Differential pulse stripping voltammetry (DPSV). When the sensitivities of these methods are compared, the most sensitive method for SILC was obtained using DPV with

MIP-sol-gel/AuNPs@PHPA-MWCNTs/PGE



nanosensor, and the most sensitive study for TAD was obtained using DPV on GCE/SH/CM-β-CD-Au/SiC nanosensor. Finally, for VRL PDE5 inhibitor, DPV was obtained using OPPy/PtNP/PtE nanosensor. As a general judgment, DPV stands out as the most sensitive technique for PDE5 enzyme inhibitors among electrochemical methods.

3.TECHNICAL DETAILS AND APPLICATION

An important part of electrochemical studies is the support electrolyte, namely the pH value of the medium. The supporting electrolyte seriously affects both the sensitivity of the method and the peak potential. For this reason, the optimum conditions of the developed electrochemical methods should be examined in detail. For the active ingredient of the drug sildenafil citrate (SILC), Britton–Robinson buffer solution (BRS), Acetate buffer solution (ABS), Phosphate buffer solution (PBS), sulfuric acid (H_2SO4) and ammonium sulfate ($(NH_4)_2SO_4$) electrolyte solutions were used. Although optimum conditions were

determined at different pHs between pH 1 and pH 8 for the pH value of the medium, the ideal pH can be said to be a weakly acidic medium. For tadalafil (TAD), only Phosphate buffer solution (PBS) and Britton–Robinson buffer solution (BRS) buffer solutions were used. Optimum support electrolytes were determined at different pHs between pH 3 and pH 7 and ideal electrochemical methods were generally developed in weakly acidic environments. Finally, when looking at the optimum support electrolyte for the active ingredient of the drug vardenafil hydrochloride (VRL), two buffer solutions were used: PBS and BRS. The ideal pH for VRL was more acidic than other PDE5 enzyme inhibitors. In general, no studies were found in very strong acidic regions or very alkaline regions. The reason for this could be that nanosensors are not very stable in very acidic or basic regions or electroactive substances do not give redox reactions.

They have performed analytical application of PDE5 enzyme inhibitors in natural samples with the developed carbon-based nanosensors. For this purpose, they have performed recovery studies in different matrix environments. For this purpose, they have analyzed active pharmaceutical ingredients present or spiked in very different biological, food and environmental samples (human urine, pharmaceutical formulation, water, food samples, two red ginseng drinks and an energy drink, blood plasma and milk, synthetic blood serum and rabbit plasma) very successfully and with high recovery. In addition, another important validation parameter of the developed carbon-based nanosensors is the selectivity of the method. The selectivity of the electrochemical sensors developed for PDE5 inhibitors has been studied in the presence of some organic substances such as ascorbic acid, uric acid, caffeine, folic acid, adenine, epinephrine, thiourea and dopamine in the form of percentage recovery. The interference effect of these organic substances in the determination of PDE5 enzyme inhibitors is enough to be considered as no (less than 5%). Moreover, selectivity studies were carried out in the presence of some anions (SO42-, Cl-, Br- and NO3-) and cations (Na(I), Fe (III), Cu(II), Zn(II), and Ca(II)) and it was determined that ionic species did not significantly affect the determination of inhibitors. As a result, it can be said that the developed nanosensors exhibited extraordinary selectivity performance in the determination of SILC, TAD and VRL active pharmaceutical ingredients. In addition, this is a very promising result for their simultaneous electrochemical determination.

Table 1. Analytical performances of different carbon-based electrodes for Sildenafil citrate (SILC) determination

PDE5 Inhibitors	Electrode	Method	Peak potentials (V)	Optimum pH	Working range	Linear range	LOD	Analytical application	Rpt (RSD);Rpd (RSD) (%)	Recovery (%)	Interferences	Refs.
Sildenafil citrate (SILC) (The active component of viagra®)	SPGCE	CV, SWV	+ 0.43	pH 4.5 (BRS)	1 - 14 µM	1 - 14 µM	55 nM	human urine and pharmaceutical formulation (tablets)	4.8; -	98.5-101.4 (urine) 99.5 (tablets)	UA and AA	[4]
	BiF/GCE	CV, AdCSV	-1.2	pH 4.5 (ABS)	0 .1 – 1 µM	0 .1 - 1 µM	18 nM	Water	1.5; -	---	---	[5]
	LBL RGO-MIES/GCE	DPV	---	pH 5.6 (PBS)	0.02 – 50 µM	0.02 – 0.5 µM and 0.5 - 50 µM	6.2 nM	herbal sexual health products	-; 2.7	92.34 – 97.71	TAD and VRL	[6]
	RuQT/GCE	CV, DPV	+ 1.35	pH 1.0 (H_2SO_4)	12.5 – 499 µM	12.5 – 172 µM and 220 - 499 µM	10.7 µM	---	---	---	---	[7]
	AuNPs/SPGCE	CV, SWV	+ 0.11	pH 7.3 (BRS)	1.8 – 33 µM	1.8 - 33 µM	0.52 nM	human urine and pharmaceutical formulation (tablets)	---	99.3-102.2 (urine) 95.7 - 102.6 (tablets)	UA and AA	[8]
	Ppy/Cit/Graphite	Potentiometry	---	pH 4.0 ($(NH_4)_2SO_4$)	34 -1700 µM	34 -1700 µM	30 µM	pharmaceutical formulation (tablets)	1.4; 2.1	99.6 and 102.7	caffeine, sulfate, chloride and nitrate	[9]
	ErGO-CS/SPCEs	CV, amperometry	+0.2	pH 7.5 (PBS)	100 pg mL^{-1} - 300 ng mL^{-1}	100 pg mL^{-1} - 300 ng mL^{-1}	55 pg mL^{-1}	food samples, two red ginseng drinks and an energy drink	-; 7.1	63,71 and 76	VRL	[10]
	BIA-SPCEs and FIA-SPCEs	amperometry	+1.0	pH 2.0 (BRS)	3 – 21 µM (BIA) 2.5 – 20 µM (FIA)	3 – 21 µM (BIA) 2.5 – 20 µM (FIA)	0.052 µM (BIA) 0.215 µM (FIA)	pharmaceutical formulation (tablets)	3; -	---	---	[11]
	SPCEs	DPV	+1.0	pH 5.0 (ABS)	2 – 200 nM	2 – 200 nM	0.59 nM	human serum and pharmaceutical formulation (tablets)	---	100.5 and 100.9 (tablets) 100.7 and 101.3 (human serum)	Cu^{2+}, Ca^{2+}, Fe^{3+}, AA, folic acid, rutin, adenine, Mg^{2+}, UA, epinephrine, Zn^{2+}, Glu and vitamin B_6	[12]
	SILC-PMA[a]	Potentiometry	---	pH 2 - 5 (ABS)	0.01 – 10000 µM	0.1 – 10000 µM	51.16 nM	pharmaceutical formulation (tablets)	---	99.61 (pure drug) 99.49 and 99.52 (tablet)	Na^{+}, NH_4^{+}, Ba^{2+}, Ca^{2+}, Fe^{3+}, fructose, cholesterol, UA, Mg.stearate,methylparaben, propylparaben, talc and Ti^{4+}	[13]
	SILC-PTA[a]											

	MIP-sol-gel/AuNPs@PHPA-MWCNTs /PGE	DPV	+ 0.2	pH 7.0 (PBS)	0.1 – 30 nM	0.1 – 2 nM and 2 - 30 nM	0.033 nM	Tablet, blood plasma and milk	2.4; 2.7	99.2 – 103 (Tablet) 97.7 – 102.5 (Blood plasma) 98 – 102 (Milk)	lactose, Glu, caffeine, urea, guanine, UA, AA, DA, carvedilol, ceftizoxime and fluoxetine, paroxetine and TAD	[14]
	SPCE	SWV	+1.0	pH 8.0 (BRS)	1 - 20 µM	1 - 20 µM	0.2 µM	Pharmaceutical formulations and adulterated tablet	1.4; 7.8	98.2 - 102	phosphate, lactose, PCT and TAD	[15]
	FeNPs-Naf/GCE	CV, DPV	+1.4	pH 4.0 (BRS)	2.8 – 170.04 µM	2.8 – 19.38 µM	2.128 µM	herbal sexual health products	-0.39 to 0.24; 1.93 to 3.15	96 - 101	NaCl, Na_2SO_4, K_2SO_4, $Ca(H_2PO_4)_2$, NH_4Cl, D-glucose, sodium benzoate, PCT, saccharine, AA, urea, glutamic acid, L-cysteine and UA	[16]

Table 2. Analytical performances of different carbon-based electrodes for tadalafil (TAD) determination

PDE5 Inhibitors	Electrode	Method	Peak potentials (V)	Optimum pH	Working range	Linear range	LOD	Analytical application	Rpt (RSD);Rpd (RSD) (%)	Recovery (%)	Interferences	Refs.
Tadalafil (TAD) (The active component of Cialis®)	MWCNTPE	AdSSWV (Low conc.)	+1.02	pH 3.0 (BRS)	3.6–8.1 µM	3.6–8.1 µM	0.11 µM	pharmaceutical dosage forms (tablets) and human serum samples	0.551; 1.54	100.4	Ca^{2+},K^+, Na^+, 2-mercapto benzimidazole, thiourea, and DA	[17]
		AdSSWV (High conc.)	+1.02		12.7–61.1 µM	12.7– 61.1 µM	3.7 µM		0.238; 0.76			
	TiO2-MWCNTPE	AdSSWV	+1.0		0.27–15.2 µM	0.27–15.2 µM	0.08 µM		0.322; 0.9	100.8		
	GCE/SH/CM-β-CD-Au/SiC	DPV	+0.7	pH 6.0 (PBS) containing 40% acetonitrile	0.01–100 µM	0.01–5.0 µM, 5.0–100 µM	2.5 nM	herbal sexual health products and human serum samples	---	98.2 - 106.7	SILC, VRL, citric acid, AA, UA, Fe^{3+}, Zn^{2+}, Br^- and SO_4^{2-}	[18]
	SCX6-RGO/GCE	DPV	+0.7	pH 6.0 (PBS) containing 40% acetonitrile	0.1 – 1000 µM	0.1–50 µM and 50–1000 µM	0.045 µM	herbal sexual health products and human serum samples	-; 1.8	96;1 - 104	SILC, VRL, oxalic acid, citric acid, AA, UA, Fe^{3+}, Zn^{2+}, Br^- and SO_4^2	[19]
	CP-BDDE	SWV	0.905	pH 4.0 (BRS)	0.15 – 1.28 µM	0.15 – 1.28 µM	19.5 nM	pharmaceutical formulations (tablets)	1.08; -	---	starch, povidone, MCC, TiO_2, Fe_2O_3,	[20]

											MgCo3 and magnesium stearate	
	Pt/NPGR-120	DPV	+0.8	pH 6.8 (PBS) containing 40% acetonitrile	1.30-488.9 µM	1.30-488.9 µM	0.268 µM	human serum samples	-; <7.36	96.8 and 97.3	DA, AA and UA	[21]
	3DG/GCE	LSASV	+0.75	pH 7.0 (PBS) containing 40% acetonitrile	0.05 – 35.0 µM	0.05 – 25 µM	10 nM	herbal sexual health products	-; 4.2	97.3 – 103.0	SILC, VRL, citric acid, AA, UA, Cl^-, NO_3^-, Fe^{3+}, Zn^{2+}, Br^- and SO_4^{2}	[22]
	voMWCNT	LSV	+0.89	pH 5.0 (PBS)	0.85 – 8.9 µM	0.85 – 8.9 µM	78 nM	generic and manipulated pharmaceutical drug	3.9; 3.4	---	---	[23]
	CP-BDDE	BIA-AD	+1.0	pH 4.0 (BRS)	1.0 – 150.0 µM	1.0 – 150.0 µM	0.27 µM	Pharmaceutical formulations and adulterated tablet	1.91; -	---	SILC, PCT, dipyrone and caffeine	[24]
	Ru(II)/GCE	DPV	+0.9	pH 4.0 (BRS)	30.0 – 80.0 µM	30.0 – 80.0 µM	3.85 µM	Commercial tablets	---	92 and 111	---	[25]

Table 3. Analytical performances of different carbon-based electrodes for vardenafil hydrochloride (VRL) determination

PDE5 Inhibitors	Electrode	Method	Peak potentials (V)	Optimum pH	Working range	Linear range	LOD	Analytical application	Rpt (RSD); Rpd (RSD) (%)	Recovery (%)	Interferences	Refs.
Vardenafil hydrochloride (VRL) (The active component of Levitra®)	ErGO-CS/SPCEs	CV, amperometry	+0.2	pH 7.5 (PBS)	100 pg mL^{-1} - 300 ng mL^{-1}	100 pg mL^{-1} - 300 ng mL^{-1}	55 pg mL^{-1}	food samples, two red ginseng drinks and an energy drink	-; 7.1	63,71 and 76	SILC	[7]
	CPE	SW-AdASV	+1.4	pH 3.0 (BRS)	1 – 100 nM	1 – 100 nM	0.3 nM	Pharmaceutical formulations and human serum	0.7-0.8; 0.4-1.0	99.7–101.2	Vitamins A, C and E, Aspirin, ketoprofen, ketorolac, ibuprofen, gabapentin, oxalic acid, UA, Glu, sucrose, starch, gelatin, lactose, Na^+, K^+, Ac^-, PO_4^{3-}, Cl^-, Ca^{+2}, Mg^{+2},	[26]

										Zn^{+2}, Cu^{+2}, Al^{3+}, Se^{4+}, Fe^{3+}, Zn^{2+}, Br^{-} and SO_4^{2}	
	PGE	SW-AdASV	+1.32	pH 3.5 (BRS)	0.3- 100 nM	0.3-100 nM	0.1 nM	Pharmaceutical formulations and human serum	0.312; 0.312 – 7.15	99.0 – 105.5	Na^{+}, K^{+}, Ac^{-}, PO_4^{2-}, Cl^{-}, Ca^{+2}, Mg^{+2}, Zn^{+2}, Cu^{+2}, $NO3^{-}$, $SO4^{2-}$, aspirin, EDTA, PCT, flurbiprofen, Glu, sucrose, starch and AA	[27]
	NH2-MWCNT/ ZnO/GPE	SWSV	+1.375	pH 3.0 (PBS)	0.02 – 1.0 mgL^{-1}	0.02 – 1.0 mgL^{-1}	13.6 μgL^{-1}	pharmaceutical tablets and synthetic blood serum	1.81; 3.44	100.8	AA, UA, DA and Glu	[28]
		DPSV	+1.28		0.01 – 0.5 mgL^{-1}	0.01 – 0.5 mgL^{-1}	4.38 μgL^{-1}		0.96; 1.76	104.4		
	X.O./PGE	SWV	+1.4	pH 2.2 (BRS)	0.1 – 0.6 µM	0.1 – 0.6 µM	0.06 µM	rabbit plasma samples	2.66; 2.68	---	DAC	[29]
	Cystoseira algae-MWCNT/ GCE	DPV	+1.34	pH 1.0 (BRS)	0.1 – 1000 nM	0.1 – 1000 nM	0.0963 nM	tablet, synthetic human serum and urine	0.94; 0.72	100.004 (tablet) 98.56 (serum) 97.98 (urine)	AA and DA	[30]
	OPPy/PtNP/PtE	DPV	+0.2	pH 9.6 (BRS)	0.001 – 50 nM	0.001 – 50 nM	0.0002 nM	pharmaceutical formulations, spiked urine and serum samples	1.18; 0.28-1.31	98.9 and 102.2	SILC, TAD, DPX, urea and DA	[31]

4. Conclusions

Sildenafil, Verdanafil and Tadalafil are organic agents that exhibit PDE5 properties of the drug active ingredients. These substances, which have an important role in the treatment of ED, should be used in a controlled manner due to their side effects. Therefore, the determination of such substances in biological samples is of great importance. Although traditional analytical methods such as chromatographic and spectrophotometric are widely used for the determination of PDE5 enzyme inhibitors, these methods have shortcomings such as long pre-treatment, requiring expert personnel, expensive devices and equipment, and the need for too many organic solvents. However, electroanalytical is an alternative analysis method due to its fast, simple, cheap, non-pre-treatment, portable, flexible and on-site analysis and extraordinary features. Nanosensors have been developed to compete with classical analytical methods using electrochemical methods for PDE5 enzyme inhibitors. These

nanosensors are classified as carbonaceous materials. The most preferred carbonaceous nanosensors in these studies are; glassy carbon electrode (GCE), screen-printed glassy carbon electrode (SPGCE), graphite paste electrode (GPE), multi-walled carbon nanotube paste electrode (MWCNTPE), boron-doped diamond electrode (BDDE), and pencil graphite electrode (PGE). Only 4 studies used bare electrodes, namely SPGCE, MWCNTPE, CPE and PGE. In other studies, new generation composite nanosensors were preferred. In the production of these hybrid sensors, metal or metal oxide nanoparticles (TiO2, Ru(II), ZnO, Au and Pt), polymers (chitosan, molecularly imprinted polymer (MIP), nafion, pyrrole) and bioindicators (Cystoseira algae), carbonaceous materials (MWCNTs, NH2-MWCNTs, reduced graphene oxide (ErGO), 3D Graphene) were treated on the carbonaceous main electrode surface. The most sensitive nanosensors for SILC are MIP-sol-gel/AuNPs@PHPA-MWCNTs/PGE, for TAD are GCE/SH/CM-β-CD-Au/SiC and for VRL inhibitors are OPPy/PtNP/PtE. In addition, DPV stands out as the most sensitive electrochemical method among electrochemical methods. With the developed carbon-based nanosensors, analytical applications of PDE5 enzyme inhibitors in natural samples were performed. In different biological, food and environmental samples (human urine, pharmaceutical formulation, water, food samples, two red ginseng drinks and an energy drink, blood plasma and milk, synthetic blood serum and rabbit plasma), active pharmaceutical ingredients present or spiked were analyzed very successfully and with high recovery. In addition, another important validation parameter of the developed carbon-based nanosensors is the selectivity of the method. Selectivity studies of electrochemical sensors developed for PDE5 inhibitors were also carried out in the presence of some organic anions and cations and it was determined that the types of interference did not have a significant effect on the determination of inhibitors. As a result, the nanosensors developed in the determination of SILC, TAD and VRL drug active ingredients exhibited extraordinary selectivity performance. All these extraordinary analytical performances created wonders in the determination of PDE5 enzyme inhibitors.

5. Ethics approval and consent to participate

This study does not need any Ethics report.

6. Consent for publication

The Authors give consent for publication.

7. Availability of data and materials

All data and materials of the paper are available to the public.

8. Authors' contributions

Jihen AbIDI: Methodology, writing—original draft preparation, supervisor, Nuran KOKENER: Experimental, writing—review and editing, Conceptualization, Investigation, review and editing,

Murat MISIR: Experimental, writing—review and editing.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Abbreviations

AA Ascorbic acid
AdCSV Adsorptive cathodic stripping voltammetry
ABS Acetate buffer solution
AuNPs Gold nanoparticles
AdSSWV Adsorptive stripping square wave voltammetry
BiF Bismuth film
BRS Britton–Robinson buffer solution
BIA Batch Injection Analysis
BIA-AD Batch Injection Analysis with amperometric detection
CV Cyclic voltammetry
Cit Citrate
Cystoseira algae-MWCNT/ GCE Carbon based biosensor materials from algal biomass
CP-BDDE Cathodically pretreated boron-doped diamond electrode
CPE Carbon paste electrode
Carboxymethyl-β-cyclodextrin (CM-β-CD)
DPV Differential pulse voltammetry
DA Dopamine
DAC Daclatasvir dihydro- chloride
DPX Dapoxtine hy- drochloride
DPSV Differential pulse stripping voltammetry
ErGO-CS Electrochemically reduced graphene oxide-chitosan composite layers
EIS Electrochemical impedance spectroscopy
FIA Flow Injection Analysis
FeNPs Ferromagnetic nanoparticles
GCE Glassy carbon electrode
GPE Pencil graphite electrode
Glu Glucose
GCE/SH/CM-β-CD-Au/SiC Carboxymethyl-β-cyclodextrin and thiol- β-cyclodextrin functionalized Au@SiC (β-CD-Au@SiC) modified GCE
LOD Limit of detection
LBL layer-by-layer
LSASV Linear sweep adsorptive stripping voltammetry
LSV Linear sweep voltammetry
MIES Molecularly imprinted electrochemical sensor
MIP-sol-gel molecularly imprinted sol-gel
MWCNT Multiwalled carbon nanotube
MWCNTPE Multiwalled carbon nanotube paste electrode
MCC Microcrystalline cellulose
$(NH_4)_2SO_4$ Ammonium sulfate solution
Naf Nafion

NH_2-MWCNT NH_2 –functionalized multi-walled carbon nanotubes
OPPy Overoxidized polypyrrole
PBS Phosphate buffer solution
Ppy polypyrrole films
PHPA Preyssler heteropolyacid
PGE Pencil graphite electrode
PCT Paracetamol
Pt/NPGR-120 Platinum nanoparticles supported on nitrogen-doped porous graphene (120: SiO2 particles sizes)
PtE Platinum electrode modified with electrodeposited platinum nanoparticles (PtNPs)
Rpt Repeatability
Rpd Reproducibility
RSD Relative standard deviation
RGO Reduced graphene oxide
RuQT Chitosan-Supported Ruthenium
Ru(II) Ruthenium (II)
SWV Square wave voltammetry
SILC Sildenafil citrate
SPGCE Screen-printed glassy carbon electrode
SPCEs Screen-printed carbon electrodes
SPE Screen-printed electrodes
SPCE Disposable stencil-printed carbon electrodes
SILC-PMA and SILC-PTA Ion-pair for (SILC) with phosphotungstic acid (PTA) or phosphomolybdic (PMA) acid: Coated carbon electrodes
SCX6 p-sulfonated calix[6]arene functionalized RGO
SW-AdASV Square-wave adsorptive anodic stripping voltammetry
SWSV Square wave stripping voltammetry
SiC Silicon carbide
TAD Tadalafil
TiO_2- MWCNTPE Titanium dioxide modified MWCNTPE
UA Uric acid
VRL Vardenafil hydrochloride
voMWCNT Vertically oriented multi-walled carbon nanotube
X.O./PGE Pencil Graphite Electrode Decorated with Xylenol Orange Flakes
ZnO Zinc oxide
3DG Three dimensional graphene

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