AN OVERVIEW OF ELECTROCHEMICAL CARBON BASED SENSORS FOR SENSITIVE MONITORING OF DRUG ACTIVE COMPOUNDS AND THEIR SENSITIVE APPLICATIONS

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ABSTRACT

Nanomaterials are mostly used for creating an electroanalytical biosensor and nanosensor. In the last decades, sensor technology has become very popular in the biomedical and pharmaceutical industry, medical field, food industry, marine sector, etc. with its wide applications. Electroanalytical biosensors are analytical devices that convert a biological response into an electrical signal. New detection technologies need to be more clearly sensitive than the current technologies to be seriously investigated for adoption. Therefore, electroanalytical biomarker studies and strategies for using different nanomaterials are continuously being verified, developed and utilized to increase the sensitivity of biomarkers determination in the cells, body fluids and tissues in the early stages of some diseases. Nowadays, electroanalytical nanosensors have been applied to the wide area, with good advantages. They have very low detection limits and wide linear response range with excellent sensitivity, good stability and reproducibility when compared to other methods. Carbon is one of excellent and the most "multipurpose" elements. Its capability is incredible to create different compounds. Fullerene was the first discovered carbon-based materials. Carbon based nanomaterials provide better stability and sensitivity as compared with the traditional methods. In this conference summary, the properties and contribution of the carbon-based nanomaterials to the electrochemical nanosensor were explained. Moreover, the application of carbon-based nano(bio)sensor and future perspectives of electrochemical sensors were referred to.

INTRODUCTION

Nanotechnology is the study of science, engineering, and technology at the nanoscale, which is measured in several nanometers up to 100 nanometers. Nanosensors are nanotechnologybased sensors that detect a number of analytes by binding with analytes, producing and processing signals. They have many advantages such as sensitivity, selectivity, rapid response, real-time detection, and low cost [1]. In addition, nanosensors have been used in many different applications in biotechnology, drug delivery, agriculture, environmental safety, military, and health diagnostics [2]. Nanomaterials show excellent properties such as chemical and physical stability, lower density, high surface-to-volume ratio, and a high percentage of atoms or molecules on the surface [3]. Especially carbon nanomaterials have attracted considerable interest as a consequence of their electronic and physiochemical aspects that makes them suitable batteries, supercapacitors, for solar cells, photocatalysis, bioimaging, and sensors [4]. They have been used in electrochemical sensor applications owing to increment in electrical conductivity, chemical and physical stability, and high adsorption capacity for a variety of analytes [4]. There are many studies about using carbon materials as nanosensors which are fullerene, carbon nanotubes, graphene nanosheet, carbon nanofibers, and carbon nanohorns for analysis of pharmaceuticals compounds [5-9]. Recently, carbon materials can be used for the detection of different human viruses, and a popular research topic that molecularly imprinted polymers [10,11]. The future of nanosensors and biosensors will rely on lab-on-a-chip systems and point of care testing.

RESULTS AND DISCUSSION

Electrochemical biosensors and nanosensors have significant advantages over other methods such as very low limit of detection values, great sensitivity, good stability, and reproducibility [12,13]. As the demand for smaller, faster, cheaper, and ultrasensitive quantification of samples rapidly increases, these methods provide a viable path toward the next generation of electrochemical

XXIII REUNIÓN DE LA SEQA. OVIEDO, JULIO 2022. CONFERENCIA INVITADA

sensors. Since the first discovery of nano-sized carbon-based materials, i.e., graphene, carbon nanofiber, and carbon nano-onion, they have been widely used in electrochemical nano(bio)sensor applications due to their electrocatalytic features [14,15]. As carbon-based nanomaterials developed and diversified over time, classifications were made according to their molecular models and structures. The most well-known and most frequently used carbon nanomaterials in the as follows: literature are classified Zerodimensional (0D) carbon nanomaterials (i.e., fullerene, carbon quantum dots, carbon nanoonion, nanodiamond, etc.), one-dimensional (1D) carbon nanomaterials (i.e., single and multi-walled carbon nanotubes, nanohorns), two-dimensional (2D) carbon nanomaterials (i.e., graphene, nanoribbons, multilayer graphitic sheets), and three-dimensional (3D) carbon nanomaterials (i.e., nanotube networks, graphite) [16–19]. Classification of 0D, 1D, 2D, and 3D carbon nanomaterials is given in **Figure 1**.



Figure 1. Classification of carbon nanomaterials by dimensionality

When the latest applications of electrochemical nano(bio)sensors are examined in the literature, it is seen that more effective results are obtained with the synergistic effect of the use of multiple nanomaterials. Obtained highly sensitive, more apply, and affordable, easy to portable electrochemical sensors provide a wide range of in environmental applications monitoring, pharmaceutical analysis, biomedical analysis, diagnostics, etc. It is expected that future studies and applications will be more focused on point-ofcare devices and lab-on-a-chip systems that can offer rapid and user-friendly analysis options. Table summarizes the electrochemical sensor 1 applications of selected carbon-based nanomaterials for the determination of various analytes.

CONCLUSION

The integration of nanomaterials with biomolecules and electrochemistry is expected to

produce major advances in the field of electrochemical nano(bio)sensors. Throughout this summary, the carbon nanomaterials are attractive materials for electrochemical sensors applications, because of their several advantages such as lower detection limits, sensitivity, good stability, and reproducibility. Carbon nanomaterials are classified into four dimensions. All of them have different properties. Due to the outstanding physical and electrical properties of fullerene, graphene, and carbon nanotubes, highly selective and sensitive detection of analytes has been shown.

The future of nanomaterials-based sensors has several benefits in sensitivity and specificity over sensors made from traditional materials. They will depend on lab-on-a-chip systems in order to miniaturize biochemical analysis systems and they offer significant advantages in cost, response times, and real-time monitoring, which makes nanosensors suitable for high-throughput applications.

Modifier	Analyte	Metho d	Linear Range	LOD	Real sample	Reference
C ₆₀ @COFs/AuE	Tobramycin	EIS	2.14 nM-10.7 pM	2.95 fM	Milk River	[20]
ND/GCE	Bisphenol A	SWV	0-50 μM	5 nM	NA	[21]
FeC-AuNPs- MWCNT/SPCEs	Serotonin	SWV	0.05-20 μM	17 nM	Urine	
CNHs-CHI@ PtNPs/ GCE	Morphine MDMA	DPV	0.05-25.4 μM 0.05-25.4 μM	0.02 μM 0.018 μM	Serum Urine	[22]
Ti ₃ C ₂ T _x R/CNT/GCE	Hg ²⁺	ASV	0.01-7.0 μΜ	5.2 nM	Lake	[23]
MGO@MIPy/SPCE	Malondialdehyde	DPV	0.01-100 μM	0.01 µM	Serum	[24]
Zn/Zn(OH)₂/GrE	Cu (II)	SWASV	0.6 μM-0.1 nM	0.903 nM	Local source water	[25]

Table 1. Recent applications of electrochemical carbon-based nanosensors on pharmaceuticals.

NA: Not Applicable, MDMA: 3,4-methylenedioxymethamphetamine, COFs: Covalent organic frameworks, FeC: Ferrocene, AuNPs: Gold nanoparticles, MWCNT: multi-walled carbon nanotubes, Ti₃C₂T_xR: Ti₃C₂T_x MXenes nanoribbons, CNT: Carbon nanotube, MGO: Magnetic graphene oxide, MIPy: Molecularly imprinted polypyrrole, ND: Nanodiamond, AuE: Gold electrode, SPCEs: Screen-printed carbon electrodes, GCE: Glassy carbon electrode, GrE: Graphite electrode, EIS: Electrochemical impedance spectroscopy, SWV: Square wave voltammetry, ASV: Anodic stripping voltammetry, SWASV: Square wave anodic stripping voltammetry

REFERENCES

- Z.B.Z. Shawon, M.E. Hoque, S.R. Chowdhury, Nanosensors and nanobiosensors: Agricultural and food technology aspects, Nanofabrication for Smart Nanosensor Applications. (2020) 135– 161. https://doi.org/10.1016/B978-0-12-820702-4.00006-4.
- [2] N. Chauhan, K. Saxena, Nanoscale interface techniques for standardized integration of nanosensors in current devices, Nanosensors for Smart Manufacturing. (2021) 91–114. https://doi.org/10.1016/B978-0-12-823358-0.00005-8.
- [3] R. Keçili, S. Büyüktiryaki, C.M. Hussain, Membrane applications of nanomaterials, Handbook of Nanomaterials in Analytical Chemistry: Modern Trends in Analysis. (2020) 159–182. https://doi.org/10.1016/B978-0-12-816699-4.00007-4.
- [4] E. Asadian, M. Ghalkhani, S. Shahrokhian, Electrochemical sensing based on carbon nanoparticles: A review, Sensors and Actuators
 B: Chemical. 293 (2019) 183–209. https://doi.org/10.1016/J.SNB.2019.04.075.
- [5] B. Thirumalraj, S. Palanisamy, S.M. Chen, B.S. Lou, Preparation of highly stable fullerene C60

decorated graphene oxide nanocomposite and its sensitive electrochemical detection of dopamine in rat brain and pharmaceutical samples, J Colloid Interface Sci. 462 (2016) 375– 381.

https://doi.org/10.1016/J.JCIS.2015.10.009.

- [6] N. Karadas, B. Bozal-Palabiyik, B. Uslu, S.A. Ozkan, Functionalized carbon nanotubes - With silver nanoparticles to fabricate a sensor for the determination of zolmitriptan in its dosage forms and biological samples, Sensors and Actuators, B: Chemical. 186 (2013) 486–494. https://doi.org/10.1016/J.SNB.2013.06.055.
- [7] P.K. Kalambate, M.R. Biradar, S.P. Karna, A.K. Srivastava, Adsorptive stripping differential pulse voltammetry determination of rivastigmine at graphene nanosheet-gold nanoparticle/carbon paste electrode, Journal of Electroanalytical Chemistry. 757 (2015) 150– 158.

https://doi.org/10.1016/J.JELECHEM.2015.09.0 27.

[8] J. Huang, Y. Liu, H. Hou, T. You, Simultaneous electrochemical determination of dopamine, uric acid and ascorbic acid using palladium nanoparticle-loaded carbon nanofibers modified electrode, Biosensors and Bioelectronics. 24 (2008) 632–637. https://doi.org/10.1016/J.BIOS.2008.06.011.

- [9] H. Dai, Y. Li, S. Zhang, L. Gong, X. Li, Y. Lin, Delicate photoelectrochemical sensor for folic acid based on carbon nanohorns supported interwoven titanate nanotubes, Sensors and Actuators B: Chemical. 222 (2016) 120–126. https://doi.org/10.1016/J.SNB.2015.08.065.
- [10] G. Ozcelikay, N. Karadas-Bakirhan, T. Taskin-Tok, S.A. Ozkan, A selective and molecular imaging approach for anticancer drug: Pemetrexed by nanoparticle accelerated molecularly imprinting polymer, Electrochimica Acta. 354 (2020) 136665.

https://doi.org/10.1016/J.ELECTACTA.2020.136 665.

- H. Ehtesabi, Application of carbon nanomaterials in human virus detection, Journal of Science: Advanced Materials and Devices. 5 (2020) 436–450. https://doi.org/10.1016/J.JSAMD.2020.09.005.
- [12] J. Wang, Nanomaterial-based electrochemical biosensors, Analyst. 130 (2005) 421–426. https://doi.org/10.1039/b414248a.
- L. Rassaei, F. Marken, M. Sillanpää, M. Amiri, C.M. Cirtiu, M. Sillanpää, Nanoparticles in electrochemical sensors for environmental monitoring, TrAC Trends in Analytical Chemistry. 30 (2011) 1704–1715. https://doi.org/10.1016/J.TRAC.2011.05.009.
- [14] J. Mittal, S. Osheen, A. Gupta, R. Kumar, Carbon Nanomaterials in Agriculture, Nanoscience for Sustainable Agriculture. (2019) 153–170. https://doi.org/10.1007/978-3-319-97852-9_7.
- [15] B.R. Adhikari, M. Govindhan, A. Chen, Carbon nanomaterials based electrochemical sensors/biosensors for the sensitive detection of pharmaceutical and biological compounds, Sensors (Switzerland). 15 (2015) 22490–22508. https://doi.org/10.3390/s150922490.
- [16] A. Mostofizadeh, Y. Li, B. Song, Y. Huang, Synthesis, properties, and applications of lowdimensional carbon-related nanomaterials, Journal of Nanomaterials. 2011 (2011). https://doi.org/10.1155/2011/685081.
- [17] M. Terrones, A.R. Botello-Méndez, J. Campos-Delgado, F. López-Urías, Y.I. Vega-Cantú, F.J. Rodríguez-Macías, A.L. Elías, E. Muñoz-Sandoval, A.G. Cano-Márquez, J.C. Charlier, H. Terrones, Graphene and graphite nanoribbons: Morphology, properties, synthesis, defects and applications, Nano Today. 5 (2010) 351–372. https://doi.org/10.1016/j.nantod.2010.06.010.
- [18] X. Han, S. Li, Z. Peng, A.O. Al-Yuobi, A.S.O. Bashammakh, M.S. El-Shahawi, R.M. Leblanc, Interactions between carbon nanomaterials and

biomolecules, Journal of Oleo Science. 65 (2016) 1–7. https://doi.org/10.5650/jos.ess15248.

- [19] L. Karadurmus, A. Cetinkaya, S.I. Kaya, S.A. Ozkan, Recent trends on electrochemical carbon-based nanosensors for sensitive assay of pesticides, Trends in Environmental Analytical Chemistry. 34 (2022) e00158. https://doi.org/10.1016/j.teac.2022.e00158.
- [20] R. Yuan, Z. Yan, H. He, Crystal engineering of C60 fullerenes trapped in covalent organic frameworks for enhanced electrochemical impedimetric aptasensing performance, Applied Surface Science. 573 (2022) 151556. https://doi.org/10.1016/j.apsusc.2021.151556.
- [21] L. Jiang, I. Santiago, J. Foord, A comparative study of fouling-free nanodiamond and nanocarbon electrochemical sensors for sensitive bisphenol A detection, Carbon N Y. 174 (2021) 390–395. https://doi.org/10.1016/j.carbon.2020.11.073.
- [22] B. Wu, S. Yeasmin, Y. Liu, L.-J. Cheng, Sensitive and selective electrochemical sensor for serotonin detection based on ferrocene-gold nanoparticles decorated multiwall carbon nanotubes, Sensors and Actuators B: Chemical. 354 (2022) 131216. https://doi.org/10.1016/j.snb.2021.131216.
- [23] Y. Xia, J. Li, G. Zhu, Y. Yi, Innovative strategy based on novel Ti3C2Tx MXenes nanoribbons/carbon nanotubes hybrids for anodic stripping voltammetry sensing of mercury ion, Sensors and Actuators B: Chemical. 355 (2022) 131247. https://doi.org/10.1016/j.snb.2021.131247.
- P. Montoro-Leal, M. Zougagh, A. Sánchez-Ruiz, Á. Ríos, E. Vereda Alonso, Magnetic graphene molecularly imprinted polypyrrole polymer (MGO@MIPy) for electrochemical sensing of malondialdehyde in serum samples, Microchemical Journal. 178 (2022) 107377. https://doi.org/10.1016/j.microc.2022.107377.
- [25] S.E. Berrabah, A. Benchettara, F. Smaili, S. Tabti, A. Benchettara, Electrodeposition of zinc hydroxide on carbon graphite electrode for electrochemical determination of trace copper in water samples using square wave anodic stripping voltammetry, Materials Chemistry and Physics. 278 (2022) 125670. https://doi.org/10.1016/j.matchemphys.2021.1 25670.