

Conference Paper

A Bibliographic Review of Diclofenac Sodium Determination with Electrochemically Modified Sensors in Different Biological, Pharmaceutical, and water Sources

Revisión Bibliográfica De La Determinación De Diclofenaco De Sodio Utilizando Sensores Modificados Por Procesos Electroquímicos Para Muestras Biológicas, Farmacéuticas Y Agua

X CONGRESO
INTERNACIONAL DE
CIENCIA TECNOLOGÍA
EMPENDIMIENTO E
INNOVACIÓN SECTEI 2023

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Published: 25 September 2024

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Abstract

Diclofenac sodium (DS) attracts the interest of researchers because it is one of the most prevalent pharmaceuticals in aqueous matrices and has the potential to harm aquatic life. However, most of the techniques used to analyze it are expensive and require a highly trained professional to perform them. On the other hand, there is the possibility of testing DS with electrochemical sensors. They are currently available for determining contaminants in different samples (tablets, blood, urine), but only a few articles analyze DS in wastewater. This is how the selection of articles for the review was organized by the type of modifier used in the working electrode. In addition, recent improvements in DS detection using electrochemical techniques in pharmaceutical formulations, biological fluids, and environmental materials were provided and discussed, along with a brief description of the results and methods used in the development publications.

Keywords: diclofenac sodium, wastewater, modifier, electrochemical detection..

Resumen

El diclofenaco sódico (DS) atrae el interés de los investigadores porque es uno de los productos farmacéuticos más presentes en matrices acuosas y tiene el potencial de dañar la vida acuática. Sin embargo, la mayoría de las técnicas utilizadas para analizarlo son costosas y requieren de un profesional altamente capacitado para realizarlas. Por otro lado, existe la posibilidad de probar DS con sensores electroquímicos. Actualmente están disponibles para la determinación del contaminante en diferentes muestras (tabletas, sangre, orina), pero sólo unos pocos artículos analizan el DS en aguas residuales. Es así como la selección de los artículos para la revisión se organizó por el tipo de modificador utilizado en el electrodo de trabajo. Además,

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se brindaron y discutieron mejoras recientes en la detección de DS mediante técnicas electroquímicas en formulaciones farmacéuticas, fluidos biológicos y materiales ambientales, junto con una breve descripción de los resultados y métodos empleados en las publicaciones de desarrollo.

Palabras Clave: *Diclofenaco Sódico, Aguas Residuales, Modificador, Detección Electroquímica.*

1. Introduction

In recent decades, industry and population have been growing at a rapid rate, leading to the growth of anthropogenic pollutant emissions to the environment, especially to water sources, which have increased enormously in recent years [1]. As a result, different types of contaminants in water sources are becoming more and more common. Even if it is only at trace level, it is not safe for the environment, animals, or human health [2]. This can cause toxic side effects, such as behavioral change, inhibition of cell proliferation, and reproductive damage in animals and humans. Furthermore, studies show that, with a high concentration of antibiotics, there are several changes in the bacterial structure that generate resistance to bacteria and affect the food chain, which can threaten drinking water sources [3].

Among these antibiotics is diclofenac sodium (DS), which is a commonly used human and veterinary drug that attracts the interest of researchers since it is one of the most frequently presented pharmaceutical products in water matrices and has the potential to harm aquatic life [4]. It enters water bodies through wastewater treatment facilities (WWTPs), while most animal waste from DS is released directly into the ecosystem [5]. Consequently, several analytical methods have been developed for the quantification of DS concentrations in pharmaceutical and biological samples. Methods such as chromatography (liquid chromatography (LC), gas chromatography-mass spectrometry (GC-MS), tandem mass spectrometry, capillary zone electrophoresis (CZE), spectrophotometry [6, 7], and spectrofluorimetry [8]. These are very sensitive with low detection limits but require the use of organic solvents, expensive apparatus, and highly qualified specialists. Furthermore, sample preparation is a mandatory step before analysis, which makes them unsuitable for field work [9].

In comparison, potentiometric sensors have the advantage of being environmentally friendly, with a simple design, portable for in situ monitoring, using small amounts of samples, and providing sensitive and reliable results at a low cost [9]. Furthermore, one of the most important advances is the increase in the detection of contaminants produced by waste from the pharmaceutical industry. This is achieved with the modification of working electrodes, thus increasing the speed at the electrode surface in



the electrode modification, the active detection area, the bonding surface, stability, electroconductivity, and excellent catalytic activity. [10]

However, the latest determination techniques have not been widely studied to analyze the concentration of DS in wastewater sources. As a result, they can be expanded and applied to improve measurement accuracy and save costs. In this study, we brought together the most promising and feasible ways to create electrochemically modified sensors to assess DS in various sources (blood, urine, wastewater, and groundwater). The methodology chosen was based on performance characteristics such as price, detection limit, preparation technology, linear range, and selectivity/interfering chemicals (Fig. 1). These are detailed in the tables and graphs that follow. Finally, in the future, we would like to expand the information collection to prepare electrochemically modified sensors to determine DS in groundwater, wastewater, and municipal water. Thus, providing an easy, fast, and economical way to determine this contaminant worldwide, particularly in places such as South America and Africa, where the technology to carry out the aforementioned analytical methods is insufficient.

2. Methodology

2.1. Literature exploration and selection

This analysis included publications from Scopus, Science Direct, and the Web of Science database. The literature was searched using the three databases and Google Scholar. Except for some additional publications due to their academic value, preference in the selection of content was given to articles published between 2015 and 2022. For the survey and selection of the literature, at least two key phrases from the search strings were evaluated. The first word refers to the working electrode material (glassy electrodes, glassy carbon electrodes, multi-walled carbon electrodes, carbon nanotubes, single-walled carbon nanotubes, and metals). The second refers to surface modification techniques (printing, coating, and cyclovoltammetry techniques). Literature was only evaluated if it was published in English for an indefinite period until October 10, 2022. A systematic review and meta-analysis using author-reported simulation data [11] was used to evaluate the manual review of selected published studies.

2.2. Quality analysis of selected literature

The considered publications were downloaded into a separate folder by the initial author and titled below the electrode material in operation and the method used to manufacture



it. The titles and abstracts of these publications were scanned for eligibility based on their main content. Finally, the central idea of each study was evaluated, and the key findings were extracted and compared with the other published articles.

2.3. Extraction and analysis of results

Data from published studies were separated into two groups. Literature was prioritized based on characteristics such as technology accessible in the electrochemical laboratory of Babes Bolyai University, year of publication, place of origin, nature of the study, type of article, area of study, and design of the study. Following this, information was selected according to the type of working electrode used. The type of electrochemical surface modification techniques, category of modification, and in-depth discussion on surface characterization techniques (Electron Force Microscopy (EFM), Energy Dispersive X-ray Analysis (EDX), Infrared Spectrometry (FTIR)). Analysis of cyclic voltammograms (CV), electrochemical impedance spectroscopy (EIS), and a real sample. The selected articles were originally organized in an Excel table for clear and statistical examination. IBM-SPSS static software, version 17.0 (IBM Corp., TX, USA, 2021), was used to analyze the collected information.

3. Results and discussion

3.1. Statistical analysis of the results

The comprehensive static review analysis found 100 valuable published records, most of which came from journals indexed in the Web of Science. 40 records were eliminated due to duplicate downloads, reducing the number of records considered to 60. 20 publications were removed from a total of 60 records due to a lack of relevance of in-depth research and analysis. Additionally, 12 records were temporarily omitted due to minor information retrieval and the year of publication, resulting in a final considered record count of 28 articles. Through a comprehensive static review analysis, 28 published articles were included in the process. The research importance retrieved from the publications was briefly reviewed in the following parts, and the classification results according to the region of development and year of publication are summarized in Figure 1.

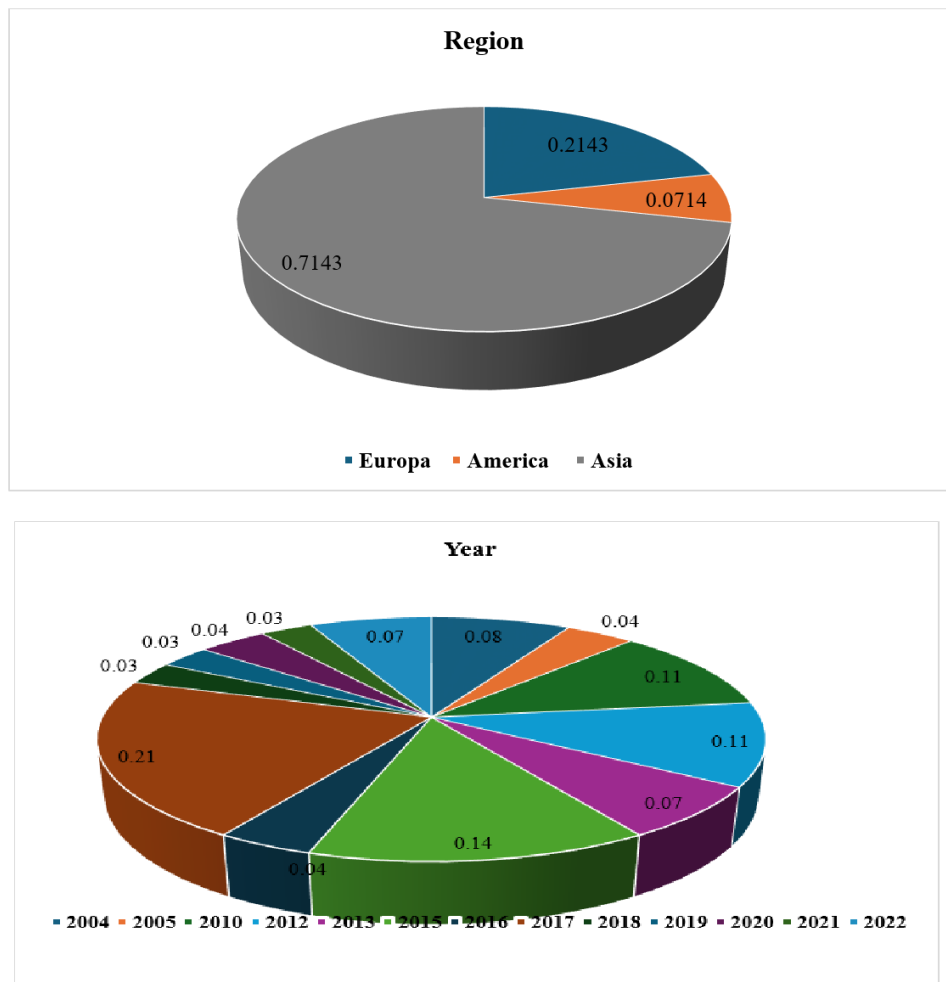


Figura 1

Static examination of the year and location of the creation of the electrochemically modified sensors for measuring DS concentration.

3.2. Electrochemical Sensors for the determination of DS

Electrochemical sensors are by far the most widely used type of sensor due to their advantages, which include detection limits as low as picomoles, rapidity, and low-cost equipment used for determination. The analytical information in electrochemical sensors is derived from the electrical signal produced by the interaction of the target analyte and the recognition layer [12]. The information in the following paragraph was compiled with a focus on potentiometric sensors that base their analysis on specific parameters such as sensor-analyte interaction. This occurs when no current is allowed to flow in the system which produces a Nernstian equilibrium formed at the sensor interface, providing information on the concentration of the analyte.



In this sense, it is essential to understand the chemical reaction that will occur on the electrode surface. to detect DS. The author [13] explains the oxidation mechanism of the drug (see Figure 2), in which the oxidation peak that occurs between 0.65 and 0.70 V is clearly observed, which is sensitive to the change in the pH of the electronic system. Furthermore, in the presented mechanism, DS is irreversibly oxidized to 5-hydroxydiclofenac through a $2e^-$, $2H^+$ loss process that gives rise to an oxidation peak at ~ 662 mV when the scan is initiated in the positive direction. The 5-OH, diclofenac is reduced in the successive cathodic scans, becoming 3% 3% 3% 4% 4% 4% 7% 11% 21% 4% 7% 11% 14% Year 2004 2005 2010 2012 2013 2015 2016 2017 2018 2019 2020 2021 2022 diclofenac-2,5-quinone imine. During the second anodic scan, a new oxidation peak is observed and is related to the oxidation of diclofenac-2,5-quinone imine, involving $2e^-$ y $2H^+$ [14].

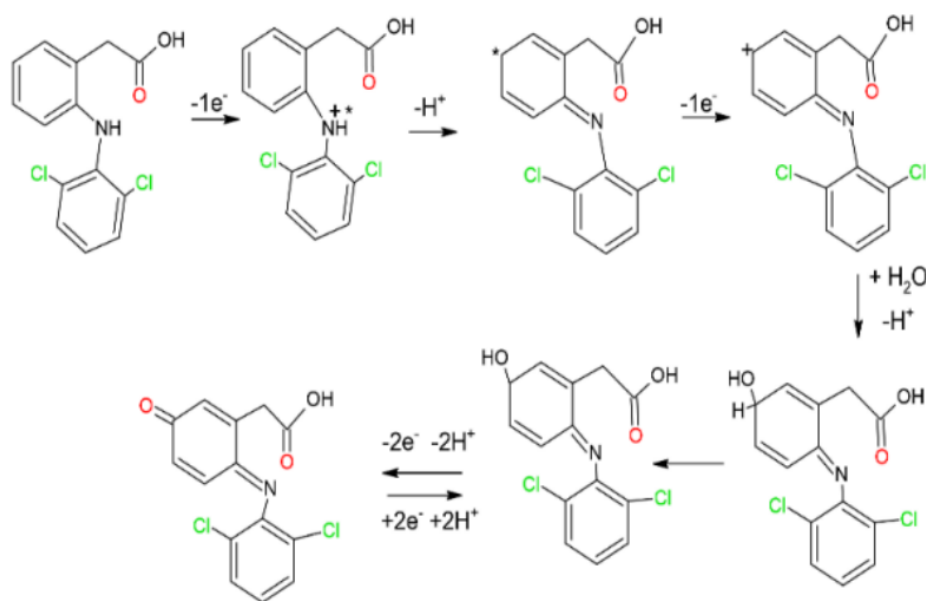


Figura 2

Oxidation mechanisms of the DS proposed by the author [14] at a pH equal to 7.0 on the surface of a glassy carbon electrode (GCE) modified using multi-walled carbon nanotubes (MWCNTs).

Therefore, it is necessary to create a surface that allows the production of the aforementioned reaction mechanism. It is also necessary to evaluate what the surface and range characteristics should be to influence the maximum potential to change the detection characteristics. As a result, the information compiled in the following sections is divided according to the type of modification that the electrode surface experiences and the characteristics of the sensors (see Figure 3).



3.3. Detection of diclofenac using carbon nanotubes (CNTS) as a surface modifier

Several studies were conducted using GCE modified with carbon nanotube composites as a working agent. Furthermore, the possibility of modifying the working electrode with the incorporation of MWCNTs is now being explored, which provides a greater surface area, high mechanical resistance, and improvements in electrical conductivity [15-25]. It is due to the low cost, easy manufacturing, and techniques available for manufacturing sensors that this type of electrode is the most commonly used. Furthermore, the wide pH range, from acidic to basic (4–8), allows its use in different applications, ensuring its robustness.

The reaction mechanism mentioned in Section 3.1 can occur on the surface of the modified electrochemical sensor using GCE/CNTs sensors, ensuring the quality of the determination of the drug present in the different samples. For example, the GCE modification using nanocellulose/MWCNT was prepared by the drop-casting method, and the DS concentration was tested using differential pulse voltammetry (DPV) [26]. This sensor reported a working concentration in the range of 0.1–0.5 μM with a limit of detection (LOD) of 0.0012 μM . The applicability of the sensor was tested in blood and urine obtained from different patients. In contrast, unmodified GCE sensors reported a low detection limit when samples were tested with a linearity range equal to 0.01–0.05 μM and a LOD equal to 0.0053 – 1.6 μM [24]. The DS concentration was determined using the same technology (DPV) in all tests, but the pH varied, allowing us to see how pH affects the extent of the reaction. Furthermore, the modified GCE electrodes have a large electrical surface area, which ensures that reactions can occur in the sensor. Likewise, MWCNT-modified working electrodes have attracted the interest of researchers due to their unique properties. Such as larger surface area, sharp electrochemical response, good adsorption capacity, improved chemical stability, significant electrical conductivity, and higher mechanical strength.

Table 1 summarizes most of the current trends in the preparation of MWCNT-modifying sensors. Additionally, the type of modifier, the electrochemical technique used for the determination, the linearity, the LOD, and the source of the analysis are shown. These are the main parameters used to describe the difference between the different sensors manufactured. Furthermore, the realized modified sensors are remarkably simple to manufacture, hence the possibility of large-scale production, the use of relatively low-cost materials, and the potential for use in wide DS concentration ranges.

Furthermore, this type of sensor can guarantee accurate analysis in a short time (on the order of seconds for a quick scan). They can be used without the need for



expensive and bulky equipment, solvents, or special gases. Finally, the modified sensors demonstrate remarkable electrocatalytic activity in the DS electro-oxidation process by drastically reducing the oxidation overpotential and increasing the peak current. For the detection of DS concentrations, the modified electrodes demonstrated high LOD, a wide linear concentration range, high stability, strong repeatability, and fast response. [18]

Tabla 1

Main results in the determination using carbon nanotubes (CNTs) as modifiers of the working electrode.

Modifier	Determination method	Linearity (μM)	LOD (μM)	Reference
NC-fMWCNTsCuN/GCE	SWV	0.05-80	0.00048	[27]
MWCNTs	DPV	0.047-12.95	0.017	[28]
NC/fMWCNTs/CuN	SWV	0.05 - 80	0.00014 0.00048	[19]
MWCNTs/ Chitosan	SWV	0.3 - 200	0.021	[22]
Nanocellulose /f-MWCNTs	CV	0.05 -50.00	0.2	[23]
Cellulose/f-MWCNT	DPV	0.05-1.00	0.0012	[26]
No Modifier	DPV	0.01 –0.05	0.053 - 1.6	[24]

Square wave voltammetry (SWV) technique,
Differential pulse voltammetry (DPV),
Linear Scan Voltammetry (LSV),
Chronoamperometry (CP)
Gold nanoparticles (AuNPs),
Copper nanoparticles (CuN),
Nanocellulose (NC),
Ethylene glycol dimethacrylate (EGDMA),
Ionic liquid (IL),
Graphite Electrode (PGE)

3.4. DS detection using graphite oxide (GO) as a modifier.

Researchers have become interested in graphene and its derivative, graphite, because of their remarkable electrical properties. These characteristics are a result of the arrangement of carbon atoms in a perfect honeycomb lattice. The backbone is formed by hybridized sp^2 orbitals. These orbitals are important in sensing applications because they allow graphene-based materials to interact with their environment and convert these interactions into a readable electrical signal [14]. Furthermore, in the internal structure of graphene and its derivatives, the phenomenon known as ballistic transport occurs, in which electrons travel submicrometer lengths without dispersion. As a result, graphene-based sensors are extremely electrically robust [29]. However, under ambient conditions, the mobility of charge carriers is still limited by the dispersion of impurities,

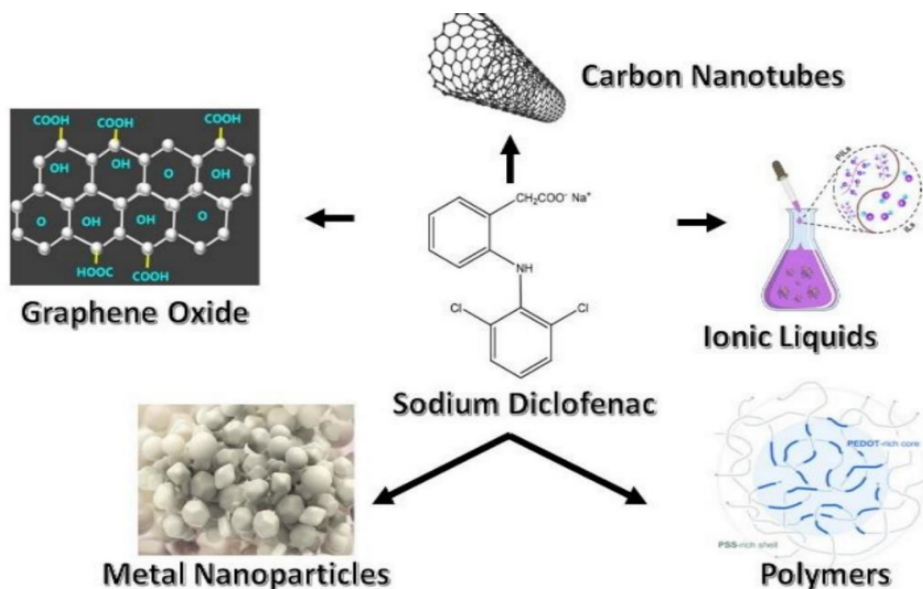


Figura 3

Various modified electrodes for the electrochemical determination of diclofenac sodium in different sources.

which decreases the detection capacity of wastewater samples [29]. On the other hand, thanks to a strong ambipolar electric current due to the field effect, graphene can be electrically doped by tuning the charge carriers between electrons and holes. This is critical in the field of water quality sensing, as selectivity toward the desired analyte is essential and graphene can be easily doped with a wide variety of compounds [30].

As proof of the above, [20] improved the performance of the sensor by adding graphene oxide functionalized with carboxyl ions to it. Under normal conditions, the sensors reported a low limit of detection (LOD) equal to $0.09 \mu\text{M}$ when tested in urine, which was 10 times lower than sensors prepared without modifier [31]. Furthermore, its active surface area was 0.2165 cm^2 , which was almost seven times larger than the geometric area of PGE, ensuring a linear relationship between DS and DPV concentrations in the range of $0.047\text{--}12.95 \text{ mM}$. As a result of their ability to withstand large concentrations of interfering species, sensors prepared with this modification can be used as selective DS sensor in the presence of interference [31].

3.5. Determination of DS using metal nanoparticles or metal oxides as modifiers

Metals and alloys have been widely studied in the construction of sensors to determine different contaminants in water. Gold and titanium metals have a wide range of

**Tabla 2**

General determination results using graphene oxide (GO) as a modifier of the working electrode.

Modifier	Determination method	Linearity (μM)	LOD (μM)	Reference
GO/COOH	CV, LSV	1.2- 400	0.09	[20]
No modifier	DPV	0.80 – 9.5	0.76	[31]
GO/ZnO	SWV	01 - 1	5.06	[32]
GO/Co (OH) ₂ /CHNF	CV, SWV	3.7-140	0.05	[33]
GO/Ag/ZnO	DPV	0.025-20	0.02	[34]
GO/Cu	CV	20-400	0.08	[35]

applications due to their high electrocatalytic activity and mechanical properties (see Table 3). Accordingly, the author [36] fabricated a new electrochemical sensor based on bimetallic Au-Pt nanoparticles decorated with multi-walled carbon nanotubes. Those have a large specific surface area and high electrical conductivity and can significantly facilitate the electron transfer process of the redox probe on the electrode surface. Furthermore, a linear calibration curve was obtained in the concentration range of 0.5–1000 μM . The detection limit of the prepared sensor was 0.3 μM . Finally, the presence of interfering species in the solution has no significant effect on the current response of the DS, and the maximum current changes were less than 5%.

Furthermore, the author [37] used iron oxide nanoparticles functionalized with an anaphoric polymer (β -CD) to test the presence of diclofenac in wastewater. The sensor achieved an LOD equal to 0.11 μM and exhibits the highest selectivity toward the DS anion when present with organic compounds. Also, some inorganic anions may exist in pharmaceutical forms and are expected to be present in wastewater. Finally, the results of the analyses of pharmaceutical forms and wastewater showed the applicability of the sensors both in quality control and in environmental studies, without the need for prior treatment before analysis. The application of metal-decorated particles in the detection of contaminants arises as a consequence of the high performance of the electrode, which is determined by its electronic conductivity and accessible surface areas. As a result, the practical technique to improve the electrochemical performance of sensors is to construct composites by mixing highly electrocatalytic active materials with substances of excellent conductivity to change the electrode surface. Also, the modification of metallic electrodes is one of the most important technological advances to increase drug detection and electron transfer rates on the electrode surface [30].

**Tabla 3**

Main results in the determination using nanoparticles and metal oxides as a working electrode modifier.

Modifier	Determination method	Linearity (μM)	LOD (μM)	Reference
CeO ₂ Au-	DPV	0.4 – 1.6	0.4	[17]
AuNPs/MWCNT	CV	0.03 – 200	0.02	[18]
GO/Cu/ Zeolite	DPV	3.01 - 15	0.3	[38]
MoS ₂	CV	0.05 - 600	0.03	[39]
Ru/TiO ₂	CV	0.291	11.48	[40]
Au/MWCNTs/GO	CV	0.4 – 1000	0.09	[41]
Hg/GO	CV	0.002 - 5	0.32	[42]
Pt/MWCNTs	CV	0.5 – 1000	0.3	[36]
Fe ₃ O ₄ / polymer	CV	0.001 - 0.1	0.11	[37]
C ₃ N ₄ /CuAl	DPV	0.5-60	0.38	[43]

3.6. DS detection using polymers as a modifier

One of the most successful potentiometric sensors used today, mainly in clinical analysis and quality control, is based on conductive polymeric membranes with ionophores incorporated directly into the polymeric matrix [44]. In addition, some polymers can modify the internal structure of the working electrodes. For example, the author [45] prepared a printed electrochemical sensor based on a polyaniline nanocomposite. Electrochemical studies of the prepared sensor demonstrated a change in peak-to-peak separation equal to 0.248 V. This is due to a more reversible charge transfer process in the polyamide relative to that of the PGE electrode that can be attributed to a possible catalytic effect of the nanocomposite added to the carbon paste [29]. Likewise, the surfaces of the evaluated electrodes (GPE and polyamide-GPE) were 0.013 ± 0.001 and 0.019 ± 0.002 cm², respectively. This showed an improvement in the active surface area of approximately 46% of the modified electrode relative to the unmodified one. Furthermore, the calculated average concentration (22.7 ± 2.0 mg·L⁻¹ DS) demonstrated adequate reproducibility of the proposed sensor. Finally, the tolerance limit was determined as the concentrations of foreign substances, which gave an error of less than $\pm 5\%$. The results of peak height variation observed for DCF in the presence of tested species (ascorbic acid, glucose, and urea) in the proportions of 1:1–1:1000 (DCF to interferences, in mol L⁻¹) confirm that the presence of different interferences did not significantly affect the efficiency of the sensor even at a level 1000 times higher than the analyte [45].

**Tabla 4**

Main results in the determination using polymers as a modifier of the working electrode.

Modifier	Determination method	Linearity (μM)	LOD (μM)	Reference
MAA/EGDMA	CV	Not reported	5	[21]
TiO ₂ /PEDOT	CV	0.715 - 1.62	0.02-0.03	[25]
GO/ Polyamide	CV	1.61	1.2	[45]
GO/ Polypyrrol	CP	0.011 - 0.310	19	[44]
PDMS / PC	CV	1.01 - 5.01	5	[46]
PVC	CV	0.005 - 0.5	0.32	[47]
MIP	CV	No Reportado	0.077	[48]

Polipyrrol PC: Polycarbonate

PVC: Polyvinyl Chloride

PDMS: Poly(dimethylsiloxane)

PEDOT: Poly (3,4-ethylene dioxythiophene)

MIP: Molecularly Imprinted Polymer

3.7. Detection of DS using ionic liquids as a modifier

Potentiometric methods using liquid ion electrodes (ILE) are an attractive alternative in drug determination because they offer simple procedures and low-cost electrodes, as well as good selectivity and sensitivity [13]. Recently, ILEs have been used as paste binders to fabricate carbon composites, which provide an obvious increase in the electrochemical response of electroactive substrates and reduce the overpotentials of some organic substances [49]. In this sense, the author [13] prepared a sensor based on the combination of MWCNTs and butylimidazole. The realized sensor reaches a detection limit equal to $0.018 \mu\text{M}$ and a linear range equal to $0.05 - 50 \mu\text{M}$. Furthermore, the stability of the proposed electrode was evaluated by measuring the decrease in DS current after one month of storage. The current response decreased by only 5%, indicating that the MWCNTs-IL modifier is sufficiently stable. The author concluded that the main advantage of using the MWCNT-IL is easy and rapid renewal of the surface after each use, and the GO-modified MWCNT-IL exhibits high electrocatalytic activity for the oxidation of DS.

4. Conclusions

This bibliographic study includes the most economical technologies to prepare electrochemically modified sensors for the determination of diclofenac sodium in different

**Tabla 5**

Main results using ionic liquids as a working electrode modifier.

Modifier	Determination method	Linearity (μM)	LOD (μM)	Reference
MWCNTs-IL	DPV	0.05 – 50	0.018	[13]
GO/[bpim,dfc]	DPV	3.18 - 0.318	0.015	[49]
MWCNTs/Cu(OH) ₂ nanoparticles/IL nanocomposites	DPV	0.18-119	0.04	[50]

[bpim,dfc]: Butylimidazole, propargyl bromide

samples (urine, blood, and tablets). The differentiation between the different technologies was established by the type of modifier that the authors used to build the sensors. Comparing the performance in terms of LOD and linearity of the different sensors, it can be concluded that a significant advance occurred when graphene was used as a working electrode modifier. This type of sensor can be doped by p or n dopants. As a result, in the sensor matrix, we can add different types of chemicals. In this sense, the most selective sensors were prepared with GCE and MWCNTs using printed modification technologies. This type of sensor reported an LOD equal to 0.017 μM . The other sensor types did not reach this LOD. On the other hand, there were not too many sensors prepared with metal electrodes. This occurs because the prices of the selected electrodes are high. It is expected that with the advancement of methods for obtaining nanoparticles in the future, this price will fit within the estimated budget selected for different projects.

Furthermore, continuous monitoring of DS in real-time samples will be more useful than batch monitoring. Detection and efforts to build continuous systems are encouraging. Most of the sensors were evaluated using real samples, obtained from pharmaceutical products, biological fluids and environmental samples. Furthermore, the examples discussed are represented in a variety of modifiers and different electrochemical determination methods. They are mostly based on voltammetric methods (CV, DPV and SWV) and to a lesser extent amperometry techniques (AMP and CAMP).

Finally, the present literature study provides a comprehensive picture of the scope and complexity of the preparation of various electrochemical sensors. We can also ensure the selectivity and sensitivity of electrochemically modified sensors by adjusting their various characteristics. Although there was not much information on wastewater sensors, we should adapt various technologies in the laboratory to develop sensitive and low-cost sensors that can be used for continuous monitoring of the river or different water sources.



Acknowledgement

Juan Hidalgo Viteri appreciates the support for the research that was funded by the scholarship offered by the Tempus Foundation within the framework of the Stipendium Hungaricum Scholarship Program, funded by Decision 285/2013 of the Government of Hungary (07.26).

References

- [1] Starling VM, Amorim CC, Leão Occurrence MM. Legacy and emerging pollutants in Latin America: A critical review of occurrence and levels in environmental and food samples. *J Hazard Mater.* 2019;372:17–36.
- [2] Khanmohammadi A, Jalili Ghazizade A, Hashemi P, Afkhami A, Arduini F, Bagheri HJ. An electrochemical impedance spectroscopy-based aptasensor for the determination of SARS-CoV-2-RBD using a carbon nanofiber–gold nanocomposite modified screen-printed electrode. *Iran Chem Soc.* 2020;17:2429–2447.
- [3] Meijer D, Wilting J. Removal and tracing of cephalosporins in industrial wastewater by SPE-HPLC: Optimization of adsorption kinetics on mesoporous silica nanoparticles. *Eur J Pharm Biopharm.* 1997;43:243–252.
- [4] Mehinto AC, Hill EM, Tyler CR. Occurrence of pharmaceuticals in municipal wastewater treatment plants and receiving surface waters in central and southern Finland. *Environ Sci Technol.* 2010;44:2176–2182.
- [5] Zhang Y, Geissen SU, Gal C. Carbamazepine and diclofenac: Removal in wastewater treatment plants and occurrence in water bodies. *Chemosphere.* 2008 Nov;73(8):1151–1161.
- [6] de Souza RL, Tubino M. Spectrophotometric determination of diclofenac sodium in pharmaceutical tablets via oxidative coupling reaction with 2,4-dinitrophenyl hydrazine in the presence of potassium periodate. *J Braz Chem Soc.* 2005;16:1068.
- [7] El-Didamony AM, Amin AS. Adaptation of a color reaction for spectrophotometric determination of diclofenac sodium and piroxicam in pure form and in pharmaceutical formulations. *Anal Lett.* 2004;37(6):1151–1162.
- [8] Carreira LA, Rizk M, El-Shabrawy Y, Zakhari NA, Toubar SS. Quantitative determination of diclofenac sodium in solid dosage forms by FT-Raman spectroscopy. *J Pharm Biomed Anal.* 1995;13(11):1331–1337.
- [9] Yilmaz B, Ciltas U. Determination of diclofenac in pharmaceutical preparations by voltammetry and gas chromatography methods. *J Pharm Anal.* 2015 Jun;5(3):153–160.



- [10] Lalwani G, Henslee AM, Farshid B, Lin L, Kasper FK, Qin YX, et al. Two-dimensional nanostructure-reinforced biodegradable polymeric nanocomposites for bone tissue engineering. *Biomacromolecules*. 2013 Mar;14(3):900–909.
- [11] Tawfik GM, Dila KA, Mohamed MY, Tam DN, Kien ND, Ahmed AM, et al. A step by step guide for conducting a systematic review and meta-analysis with simulation data. *Trop Med Health*. 2019 Aug;47(1):46.
- [12] Baranwal J, Barse B, Gatto G, Broncova G, Kumar A. Electrochemical sensors and their applications: A review. *Chemosensors (Basel)*. 2022;10(9):363.
- [13] Sarhangzadeh K, Khatami A, Jabbari M, Bahari S. Simultaneous determination of diclofenac and indomethacin using a sensitive electrochemical sensor based on multiwalled carbon nanotube and ionic liquid nanocomposite. *J Appl Electrochem*. 2013;43:1217–1224.
- [14] Zubiarrain-Laserna A, Kruse P. Review—Graphene-Based Water Quality Sensors. *J Electrochem Soc* 37:167.
- [15] Honaker NC, Malode SJ, Kulkarni RM, Shetti NP. Electrochemical behavior of diclofenac sodium at core-shell nanostructure modified electrode and its analysis in human urine and pharmaceutical samples. *Sensors (Basel)*. 2020;1:100002.
- [16] Nguyen D, Quang-Hai L, Tuan-Linh N, Van-Tuan D, Hoai N, Hong-Nam P, et al. Nanostructured mixed layers of organic materials obtained by nanosphere lithography and electrochemical reduction of aryldiazonium salts. *J Electroanal Chem (Lausanne)*. 2022;921:116709.
- [17] de Carvalho R, Bettsa AJ, Cassidy JF. Metal nanoparticles and carbon-based nanomaterials for improved performances of electrochemical (bio)sensors with biomedical applications. *Micro J*. 2020;158.
- [18] Afkhami A, Bahiraei A, Madrakian T. Amperometric detection of diclofenac at a nanostructured multi-wall carbon nanotubes sensing films. *Mater Sci Eng*. 2016;59:168–176.
- [19] Salahuddin M, Akhter S, Basirun W, Alhaji Mohammed M, Abd Rahman N, Salleh N. Synthesis of novel nano-sulfonamide metal-based corrosion inhibitor surfactants. *Surf Interfaces*. 2022.
- [20] Karuppiah C, Cheemalapati S, Chen S, Palanisamy S. Carboxyl-functionalized graphene oxide-modified electrode for the electrochemical determination of nonsteroidal anti-inflammatory drug diclofenac. *Ionics*. 2015;21(1):231–238.
- [21] Blanco-López MC, Lobo-Castañón MJ, Miranda-Ordieres AJ, Tuñón-Blanco P. Voltammetric response of diclofenac-molecularly imprinted film modified carbon electrodes. *Anal Bioanal Chem*. 2003 Sep;377(2):257–261.



- [22] Shalauddin M, Akhter S, Bagheri S, Sayuti M, Adib N, Basirun W. Immobilized copper ions on MWCNTS-Chitosan thin film: an enhanced amperometric sensor for electrochemical determination of diclofenac sodium in aqueous solution. *Int J Hydrogen Energy*. 2017;42(31):19951–19960.
- [23] Shalauddin Md, Shamima Akhter A, Jeffre W, Basirun, Bagheri S, Nadzirah S, Rafie M. Hybrid nanocellulose/f-MWCNTs nanocomposite for the electrochemical sensing of diclofenac sodium in pharmaceutical drugs and biological fluids. *Ele Acta*. 2019;304.
- [24] Berto S, Cagno E, Prenesti E, Aragona E, Bertinetti G, Giacomino S, et al. Voltametric study for the determination of diclofenac in aqueous solutions using electro-activated carbon electrodes. *Appl Sci (Basel)*. 2022;12(16):7983.
- [25] Thiagarajan S, Rajkumar M, Chen S. Nano TiO₂ -PEDOT film for the simultaneous detection of ascorbic acid and diclofenac. *Int J Electrochem Sci*. 2012;7(3):2109–2122.
- [26] Shalauddin M, Akhter S, Wan J, Akhtaruzzaman M, Alhaji M, Abd Rahman M, et al. Hybrid nanocellulose/f-MWCNTs nanocomposite for the electrochemical sensing of diclofenac sodium in pharmaceutical drugs and biological fluids. *Electrochim Acta*. 2019;304:323–333.
- [27] Shalauddin M, Akhter S, Wan J, Akhtaruzzaman M, Alhaji M, Abd Rahman M, et al. Bio-synthesized copper nanoparticle decorated multiwall carbon nanotube-nano cellulose nanocomposite: An electrochemical sensor for the simultaneous detection of acetaminophen and diclofenac sodium. *Surf Interfaces*. 2022;34(102385).
- [28] Parvizi G, Alipour E, Ali Sabzi R. Modification of a disposable pencil graphite electrode with multiwalled carbon nanotubes: Application to the electrochemical determination of diclofenac sodium in some pharmaceutical and biological samples. *Anal Methods*. 2016.
- [29] Geim AK, MacDonald AH. Graphene: exploring carbon flatland. *Phys Today*. 2020;60:35. (2007).
- [30] Brennan E, Futvoie P, Cassidy J, Schazmann B. *Int J Environ An Ch*. 2017;97:588–596.
- [31] Aguilar-Liraa G, Álvarez GA, Zamora A, Palomar M, Rojas A, Rodríguez JA, et al. New insights on diclofenac electrochemistry using graphite as working electrode. *J Electroanal Chem (Lausanne)*. 2017;794:182–188.
- [32] Kokab T, Shah A, Abdullah M, Arshad M, Nisar J, Naeem M, et al. Simultaneous femtomolar detection of paracetamol, diclofenac, and orphenadrine using a carbon nanotube/zinc oxide nanoparticle-based electrochemical sensor. *ACS Appl Nano Mater*. 2021;4(5):4699–4712.
- [33] El-Wekil M, Alkahtani A, Hassan Refat A, Ashraf MM. Advanced sensing nanomaterials-based carbon paste electrode for simultaneous electrochemical



- measurement of esomeprazole and diclofenac sodium in human serum and urine samples. *J Mol Liq.* 2018;262:495–503.
- [34] Naz S. “Graphene oxide functionalized with silver nanoparticles and ZnO synergic nanocomposite as an efficient electrochemical sensor for diclofenac sodium.” *NANO: Brief Reports and Reviews.* 16(12):1-13. <https://doi.org/10.1142/S1793292021501393>
- [35] Haichi Y, Jianhang J, Qiuju L, Yingzhi L. Electrochemical determination of diclofenac sodium in pharmaceutical sample using copper nanoparticles/reduced graphene oxide modified glassy carbon electrode. *Int J Electrochem Sci.* 2021;:16.
- [36] Eteya M, Rounaghi H, Deiminiat B. Fabrication of a new electrochemical sensor based on AuPt bimetallic nanoparticles decorated multi-walled carbon nanotubes for determination of diclofenac. *Microchem J.* 2019;144:254–260.
- [37] Elbalkiny HT, Yehia AM, Riad SM, Elsharty YS. A. M. YehiaSaf, M. RiadYasser, S. Elshart. 2019. Potentiometric diclofenac detection in wastewater using functionalized nanoparticles. *Microchem J.* 2019;145:90–95.
- [38] Manea F, Ihos M, Remes A, Burtica G, Schoonmanc J. Electrochemical determination of diclofenac sodium in aqueous solution on Cu-Doped zeolite-expanded graphite-epoxy electrode. *Electroanalysis.* 2010;22(17-18):2058–2063.
- [39] Reza Baezzat M, Tavakkoli N, Zamani H. Synthesis of novel nano-sulfonamide metal-based corrosion inhibitor surfactants. *Anal Bioanal Chem Res.* 2022;9:153–162.
- [40] Killedar L, Ilager D, Shetti NP, Aminabhavi TM, Reddy K. Construction of a new electrochemical sensor based on MoS₂ nanosheets modified graphite screen printed electrode for simultaneous determination of diclofenac and morphine. *J Mol Liq.* 2021;340:116891.
- [41] Nasiri F, Hossein Rounaghi G, Ashraf N, Deiminiat B. A new electrochemical sensing platform for quantitative determination of diclofenac based on gold nanoparticles decorated multiwalled carbon nanotubes/graphene oxide nanocomposite film. *Int J Environ An Ch.* 2019.
- [42] Santini AO, Pezza HR, Pezza L. Determination of diclofenac in pharmaceutical preparations using a potentiometric sensor immobilized in a graphite matrix. *Talanta.* 2006 Jan;68(3):636–42.
- [43] Ankit K, Ravindra K, Shreanshi A, Tiwari I. Oxidized g-C₃N₄ decorated with Cu–Al layered double hydroxide as a sustainable electrochemical sensing material for quantification of diclofenac. *Mater Chem Phys.* 2023;:294.
- [44] Oliveira MC, Bindewald EH, Marcolino LH Jr, Bergamini MF. Potentiometric determination of Diclofenac using an ion-selective electrode prepared from polypyrrole films. *J Electroanal Chem (Lausanne).* 2017;732:11–16.



- [45] Mostafavi M, Yaftian M, Piri F, Shayani-Jam H. A new diclofenac molecularly imprinted electrochemical sensor based upon a polyaniline/reduced graphene oxide nanocomposite. *Biosens. Bioelectron.* 2018;122:160-167.
- [46] Schirmer C, Posseckardt J, Schröder M, Gläser M, Howitz S, Scharff W, et al. Portable and low-cost biosensor towards on-site detection of diclofenac in wastewater. *Talanta.* 2019 Oct;203:242–247.
- [47] Kormosha Z, Hunkaa I, Bazel Y. A potentiometric sensor for the determination of diclofenac. *J Anal Chem.* 2009;64(8):853–858.
- [48] Dinh-Hai-Ngan N, Quang-Hai L, Tuan-Linh N, Van-Tuan D, Hoai-Nam N, Hong-Nam P, et al. Electrosynthesized nanostructured molecularly imprinted polymer for detecting diclofenac molecule. *J Electroanal Chem (Lausanne).* 2022;:921.
- [49] Brennan E, Futvoie P, Cassidy J, Schazmann B. An ionic liquid-based sensor for diclofenac determination in water. *Int J Environ An Ch.* 2017. <https://doi.org/10.1080/03067319.2017.1333607>
- [50] Arvand M, Gholizadeh TM, Zanjanchi MA. MWCNTs/Cu(OH)₂ nanoparticles/IL nanocomposite modified glassy carbon electrode as a voltammetric sensor for determination of the non-steroidal anti-inflammatory drug diclofenac. *Mater Sci Eng C.* 2012 Aug;32(6):1682–1689.