DICLOFENAC ANALYSIS IN NATURAL WATERS USING THE UV-VISIBLE ABSORPTION METHOD

**Jean Marie Diéne Bakhoum[1,2], Olivier Maurice Aly Mbaye[1,2], Jean Pierre Bakhoum[1],
Mame Diabou Gaye-Seye[1,2], Clément Trellu[2], Atanasse Coly[1], Jean-Jacques Aaron[2*]**

[1]*Laboratoire de Photochimie et d'Analyse, Faculté des Sciences et Techniques,
Université Cheikh Anta Diop, Dakar, Sénégal*
[2]*Laboratoire Géomatériaux et Environnement (EA 4508), Université Gustave Eiffel,
5 boulevard Descartes, Champs-sur-Marne, 77454 Marne-la-Vallée cedex 2, France*

*jeanjacquesaaron@yahoo.fr

In this work, we developed a UV-Visible (UV-Vis) absorption method for the quantification of diclofenac sodium in natural waters. Several UV-Vis absorption method parameters were optimized. The maximum absorption wavelength varied between 276 and 292 nm, depending on the solvent, and the molar absorption coefficients were greater than 10^4 l mol^{-1} cm^{-1}. The linearity of calibration curves extended over one to three orders of magnitude, with good accuracy, the correlation coefficients (R^2) being close to unity. The limit of detection (LOD) and of quantification (LOQ) values of diclofenac sodium obtained by photo-induced UV-Vis method were respectively 20 ng·ml^{-1} and 68 ng·ml^{-1} in water. These values were two times lower than those obtained without irradiation. The low relative standard deviation (RSD) (0.28 by the photo-induced UV-Vis method) values indicated a satisfactory reproducibility of our measurements. Analytical applications to natural waters yielded satisfactory results with average recovery rates ranging from 94.68 to 99.09 %.

Keywords: non-steroidal anti-inflammatory drugs (NSAIDs); diclofenac sodium;
UV-Vis absorption spectrometry; environment

АНАЛИЗА НА ДИКЛОФЕНАК ВО ПРИРОДНИ ВОДИ СО ПРИМЕНА НА UV-Vis АПСОРПЦИОНЕН МЕТОД

Во овој труд беше развиен UV-Vis-апсорпционен метод за квантификација на натриум диклофенак во природни води. Беа оптимизирани повеќе параметри на овој апсорпционен метод. Максималната апсорпциона бранова должина се движеше од 276 и 292 nm во зависност од растворувачот, додека моларните апсорпциони коефициенти беа повисоки од 10^4 1 mol^{-1} cm^{-1}. Линеарноста на калибрационите криви се движеше над еден до три реда на големина, со добра точност, при што коефициентите на корелација (R^2) беа блиску до еден. Вредностите на прагот на детекција (LOD) и на квантифиакција (LOQ) за натриум диклофенак добиени со фотоиндуцираниот UV-Vis-метод соодветно изнесуваа 20 ng·ml^{-1} и 68 ng·ml^{-1} во вода. Овие вредности се два пати помали од оние добиени без ирадијација. Ниските вредности на релативната стандардна девијација (RSD) (0,28 со фотоиндуцираниот UV-Vis-метод) укажуваат на задоволителна репродуцибилност на овие мерења. Аналитичката примена на природни води даде задоволителни резултати со просечни аналитички приноси од 94,68 до 99,09 %.

Клучни изрази: нестероидни антивоспалителни лекови (NSAIDs); натриум диклофенак;
UV-Vis апсорпциона спектрометрија; животна средина

1. INTRODUCTION

Global population growth requires increasing drug use to meet therapeutic needs. This overuse of pharmaceutical products is responsible for the growing presence of pharmaceutical substances in the various compartments (air, water, soil) with potential environmental and health impacts. Drugs in the environment have therefore become a topical issue.[1–3]

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a group of widely used pharmaceuticals for humans and animals possessing antipyretic, analgesic and anti-inflammatory activities, and most of them are available without medical prescription.[4,5] More than 30 million people use NSAIDs every day.[6] It is reported that NSAIDs are only partially removed by sewage treatment plants.[7,8] The combination of widespread use and incomplete disposal in sewage treatment plants results in a significant presence of NSAIDs in surface waters. A number of monitoring surveys have detected the presence of different NSAIDs in freshwater ecosystems in the ng·l^{−1} to µg·l^{−1} concentration range. Although the concentrations of NSAIDs in surface waters are low, the high biological activity of these molecules may give them potential toxicity towards non-target aquatic organisms.[9,10]

In effluents, one of the most frequently detected pharmaceutical compounds is diclofenac.[11,12] This molecule seems to have the highest level of acute toxicity among NSAIDs.[13,14] For example, diclofenac has been shown to exert a potential genotoxic effect on DNA integrity in zebrafish.[15] Due to the continuous input from sewage treatment plants, a pseudo-constant concentration exists in surface waters. This is one of the reasons diclofenac has been included in the EU Water Framework Directive watch list.[16,17]
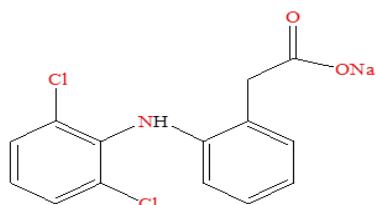

Fig. 1. Chemical structure of diclofenac sodium (NaDCF)

Therefore, there is a need to develop a sensitive, accurate and efficient method to monitor diclofenac residues in the environment.[18] Obviously, the chromatographic methods mainly used for the determination of NSAIDs are very expensive for developing countries. Therefore, they turn to spectroscopic methods which are more accessible, simple, rapid, versatile and economical for the determination of NSAID drugs.[19] Thus, in this present work, we have developed a UV-Vis absorption spectrometry method for the quantification of diclofenac sodium (Fig. 1) in natural waters.

2. MATERIALS AND METHODS

2.1. *Materials*

Diclofenac sodium was supplied by Alfa Aesar as a white powder (analytical grade, purity > 99%). Its physicochemical properties are presented in Table 1.

T a b l e 1

Physicochemical properties of diclofenac sodium[20]

Parameter	Diclofenac sodium salt
Formula	$C_{14}H_{10}Cl_2NO_2Na$
Molecular weight (g·mol^{-1})	318.14
Water solubility (mg l^{-1})	32.40 g l^{-1} at 37 °C

We used seven solvents: ultra-pure water produced by a Milli-Q system (resistivity > 18.2 MΩ cm at 25 °C), methanol (Honeywell, France), ethanol (Honeywell), isopropanol (Honeywell), acetonitrile (Honeywell), DMSO (Prolabo) and butyl acetate (Sigma Aldrich).

2.2. *Instrumentation*

2.2.1. *UV-Vis absorption spectrometry*

UV-Vis absorption spectra were recorded at room temperature, using a Shimadzu-1800 spectrophotometer controlled by the "UV Probe" software. Parallelepiped quartz cells with 1-cm optical path and two polished faces were used for the measurements.

2.2.2. *Irradiation system for the photo-induced UV-Vis absorption method*

In the case of the PIF method, photolysis reactions were carried out in stationary phase, by using an Oriel 8000 power box equipped with a mercury lamp (HBO 200W/ 4 L1 OSRAM). The diclofenac sodium solutions were irradiated over a fixed time interval at room temperature. A 3-ml working solution was placed in an Hellma quartz cell positioned on an optical bench at 30 cm from the mercury lamp.

2.2.3. *Preparation of solutions*

10^{-3} M diclofenac sodium stock solutions were prepared in 10 ml flasks with the appropriate solvent for UV-Vis absorption studies. In most cases, the diclofenac sodium dissolution was performed by ultrasound. Working solutions were obtained by successive dilutions of the stock solutions in order to obtain the desired concentration. All solutions were placed in amber glass bottles covered with aluminum foil to protect them from light and were kept in the refrigerator until use.

2.2.4. *Standard addition procedure*

Natural water samples from wells in Senegal and tap water in France (Marne-la-Vallée) were collected in amber glass bottles of 0.5 l during August 2020. All samples were filtered through 25-mm diameter PTFE filters with 0.45-μm pores from Sigma-Aldrich, in order to remove the suspended organic matter, and stored at 4 °C.

3. RESULTS AND DISCUSSION

3.1. *Optimization of analytical conditions*

3.1.1. *Solvent effect*

The presence of heteroatoms N, O, Cl and Na in the diclofenac sodium chemical structure produced a high polarizability of the molecule, and, therefore, specific interactions occurred with the solvent molecules, which strongly affected its solubility. Due to the presence of the NH group, which can function as electron donor or proton acceptor, and of the carboxylic group, the drug presented a Lewis acid-base character. However, the occurrence of sodium in the diclofenac molecule reduced the Lewis acid properties of the drug.[21]

The UV-visible absorption spectra of $6 \cdot 10^{-5}$ M diclofenac sodium (NaDCF) in different organic and aqueous media without UV irradiation are given in Figure 2. It can be seen that the shape of the absorption spectra was similar in all solvents under study. However, the absorbance as well as the absorption maximum wavelength values of NaDCF varied considerably with the solvent. For protic and aprotic polar solvents, the maximum absorption wavelength increased when the solvent polarity decreased. A bathochromic shift of 16 nm was observed when passing from water to DMSO (Table 2). This indicates that the corresponding electronic transitions are n → π* type. In addition, the absorbance value was the highest in isopropanol and the lowest in water.
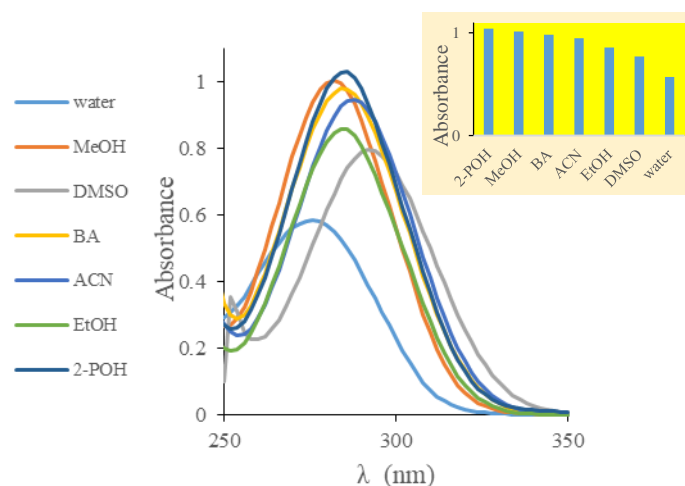

Fig. 2. UV-Vis absorption spectra of diclofenac sodium ($6 \cdot 10^{-5}$ M) in various solvents (MeOH : Methanol; DMSO : Dimethyl sulfoxide; BA : Butyl acetate; ACN : Acetontrile; EtOH : Ethanol; 2-POH : Isopropanol)

T a b l e 2

UV-Vis absorption spectral characteristics of NaDCF in different solvents

Parameter	Polar protic solvents				Polar aprotic solvents		Aprotic apolar solvent
Solvent	Pure water	Methanol	Ethanol	Isopropanol	Acetonitrile	DMSO	Butyl acetate
λ_{abs} (nm) [a]	276	282	284	286	286	292	282
A [b]	0.57	1.01	0.86	1.04	0.95	0.77	0.98

[a] λ_{abs} (nm) = maximum absorption wavelength. [b] A = absorbance

3.1.2. *Effect of the UV irradiation time*

The effect of the UV irradiation time in different media (water, isopropanol, water-isopropanol mixture 90:10 v/v) produced rapid changes in the shape of the NaDCF absorption spectra, which indicated that NaDCF was very sensitive to UV light (Fig. 3). For instance, in ultrapure water, the spectra of the NaDCF photoproduct(s), after a 5-min irradiation time, was characterized by a single band, narrower than that of the parent molecule and localized at about 238 nm.
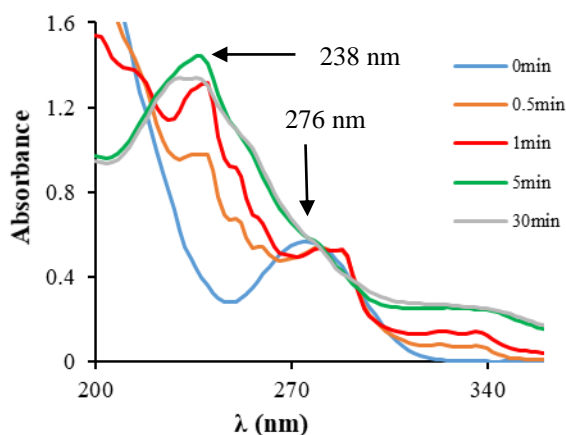
Fig. 3. Effect of the irradiation time on the UV-Vis absorption spectra of NaDCF ($6 \cdot 10^{-5}$ M) in water

Fig. 5. Evolution of the NaDCF ($6 \cdot 10^{-5}$ M) absorbance as a function of the irradiation time at room temperature in:
a) water-isopropanol mixture 90:10 v/v ($\lambda_{abs} = 236$ nm);
b) isopropanol ($\lambda_{abs} = 224$ nm); **c)** ultrapure water ($\lambda_{abs} = 238$ nm)

Also, in isopropanol and in 90:10 v/v water-isopropanol mixture, the NaDCF absorption spectra after irradiation times of, respectively 40 min and 7 min, were characterized by several peaks located at 224, 286, 292, and 376 nm for isopropanol and at 214, 236, 258, 292, 324, 338 nm for the 90:10 v/v water-isopropanol mixture (Fig. 4).
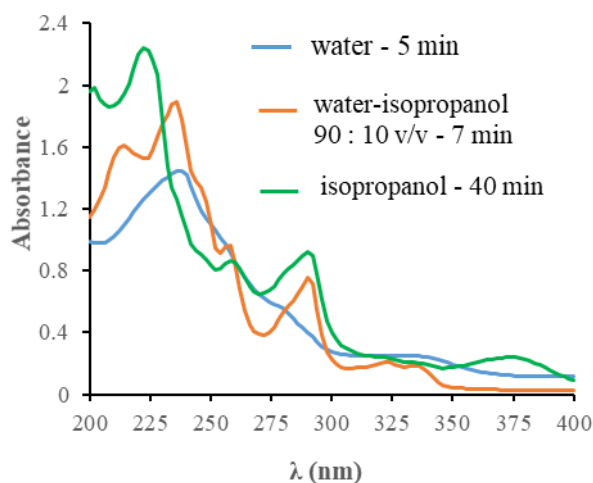
3.2. *Characterization of the color observed after UV irradiation of NaDCF*

After a few minutes of UV irradiation of an aqueous solution of NaDCF, we found that our solution contained in a 3 ml tank was colored. We recorded the UV-Vis absorption spectrum of NaDCF in water between 190 and 800 nm after an optimal irradiation time. As can be seen in Figure 6, the spectrum obtained has an absorption band admitting a maximum at 430 nm corresponding to the yellow coloration observed. It can be concluded that irradiation leads to the formation of an absorbent photo-product in the blue spectrum.

Fig. 4. Photo-induced UV-Vis absorption spectra of NaDCF in water, water-isopropanol mixture 90:10 v/v and isopropanol, at optimal UV irradiation times of 5 min, 7 min and 40 min, respectively

Finally, the evolution of the absorbance intensity was plotted as a function of the irradiation time (Fig. 5). The different forms of obtained curves suggested that the NaDCF photodegradation mechanism varied with the medium at room temperature.
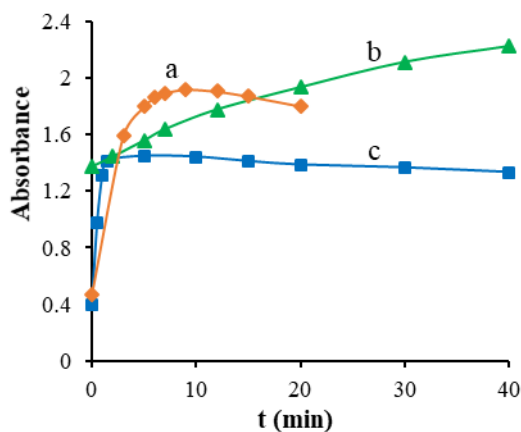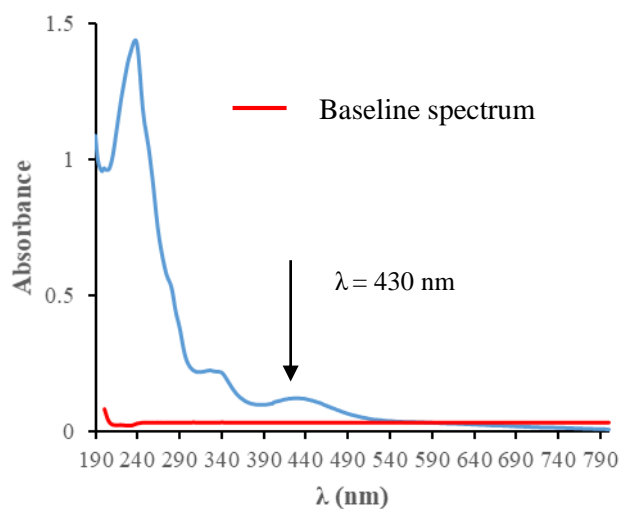

Fig. 6. UV-Vis absorption spectra of NaDCF ($5 \cdot 10^{-5}$ M) between 190 and 800 nm in water after an optimal UV irradiation time of 5-min

3.3. *Analytical performance of the diclofenac sodium UV-Vis absorption method*

Using the Beer-Lambert law, we calculated the molar absorption coefficient (ε_{max}) values of diclofenac, which ranged from 10,037 to 18,885 l mol^{-1} cm^{-1}, according to the solvent (Table 3). These ε_{max} values greater than 10^4 l mol^{-1} cm^{-1} for the main absorption bands indicated that the corresponding electronic transitions were of π–π* type.

Moreover, several literature studies agreed with our results on the NaDCF UV-Vis absorption spectral properties in organic and aqueous media. For example, Packer *et al.*[22] found a maximum absorp-tion at 276 nm in water, with a molar absorption co-efficient ε_{276nm} = 1.04 ($\pm$ 0.02)$\cdot 10^4$ l mol^{-1} cm^{-1}, and a verification of the UV-Vis absorption Beer-Lambert law in a concentration range of about 4 – 40 µg ml^{-1} ($R^2 \geq 0.999$). The same authors also indicated that NaDCF was soluble in ethanol with a maximum ab-sorption wavelength value of 283 nm.

In order to show the analytical interest of the UV-Vis absorption method, we calculated the ana-lytical performances of this method for NaDCF in the different media under study (Table 3). All spectral measurements were performed three times for each concentration and in each medium.
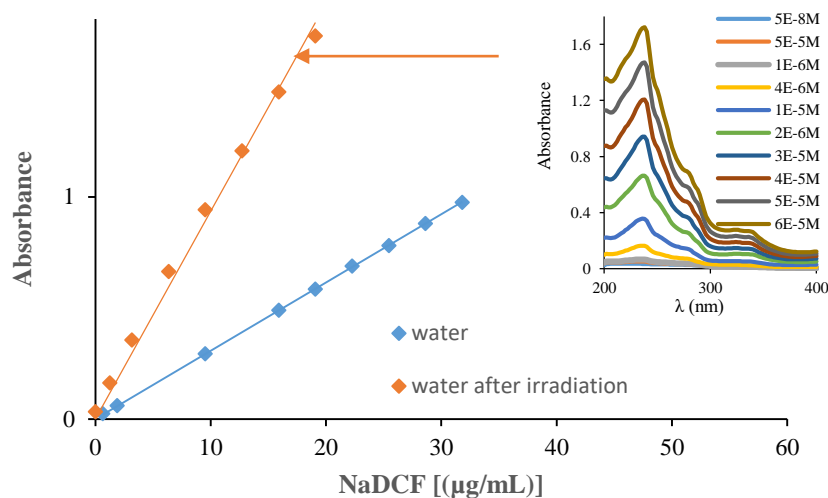

Fig. 7. NaDCF calibration lines in: (♦)water without irradiation, (♦) water after an optimal UV irradiation time of 5 min

Table 3

UV-Vis absorption properties, photo-induced UV-Vis absorption properties and analytical performances for NaDCF in organic and aqueous media

Solvent	λ_{abs} [a] (nm)	ε [b] (l·mol^{-1}·cm^{-1})	R^2 [c]	LOD [d] (ng·ml^{-1})	LOQ [e] (ng.ml^{-1})	RSD (%) [f] (*n* =10)	LDR [g] (ng·ml^{-1})
Butyl acetate	282	14896	0.9994	34	113	0.94	318–25451
Isopropanol	286	17757	0.9988	39	131	0.38	159–19088
Ethanol	284	15651	0.9999	35	117	0.44	159–25451
Methanol	282	16685	0.9994	39	130	0.87	159–19088
Water	276	10037	0.9999	41	137	0.54	636–31814
Acetonitrile	286	18885	0.9984	29	98	0.75	159–31814
DMSO	292	12672	0.9995	23	76	0.99	318–31814
Photo-induced UV-Vis absorption							
Water	238	32735	0.9978	20	68	0.28	159–19088

[a]λabs: Maximum absorption wavelength, [b]ε: Molar absorption coefficient, [c] R^2: Correlation coefficient, [d]LOD: Limit of detection defined as the concentration of analyte giving a signal-to-noise ratio (S/N) of 3 (IUPAC criterion), [e]L-OQ: Limit of quantification defined as the concentration of analyte giving a S/N ratio of 10 (IUPAC criterion), [f]RSD: Relative standard deviation, [g]LDR: Linear dynamic range

The obtained UV-Vis absorption analytical parameters were satisfactory. Indeed, the calibration lines displayed good accuracy with correlation coefficient (R^2) values close to unity (0.998 – 0.999). The low relative standard deviation (RSD) values indicated the good reproducibility of our measurements. Moreover, the detection and quantification limits were relatively low, comprised, respectively, between 23 – 41 ng mL^{-1} and 76 – 137 ng mL^{-1} (Table 3).

In the case of photo-induced UV-Vis absorption, we find a much lower detection and quantification limit, for example two times lower than the detection limits found in water without irradiation, (shown in Fig. 7), respectively equal to 20 and 68 ng mL^{-1}. Therefore, we used this photo-induced UV-Vis absorption method which proves to be remarkably simple, fast and sensitive for ana-

lytical applications in order to quantify diclofenac in natural waters.

3.4. *Analytical applications*

In order to perform analytical applications in tap water and natural water samples collected from wells in Senegal, we used the above-described standard addition procedure. Tap and well water samples were, respectively, fortified with 1 μg mL^{-1} and 2.5 μg mL^{-1} of NaDCF (Table 4). For all samples under study, linear standard addition curves were obtained. Their slope values were close to those measured for the calibration curves, as shown in Figure 8. Our results suggested that there was no significant matrix effect in these tap water and natural water samples. Satisfactory average recovery percentage values ranged between 94.68 and 99.09 % (Table 4).
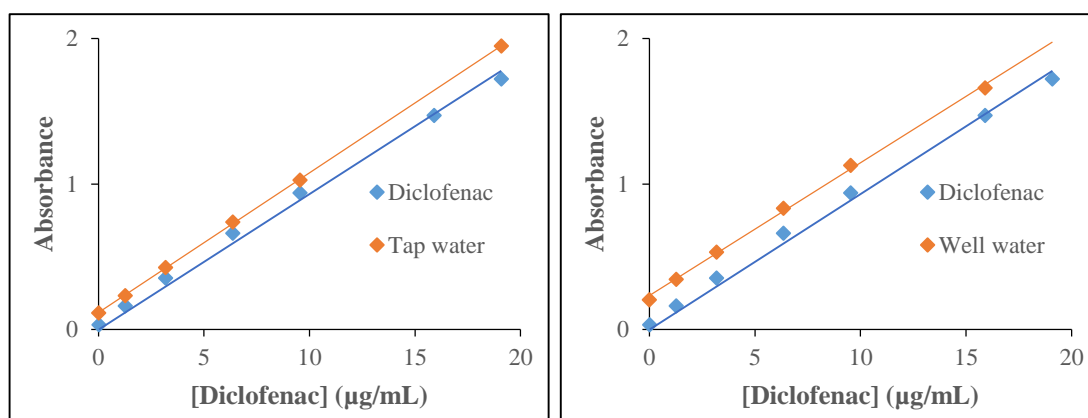

Fig. 8. Calibration curves (◆) and standard addition curves
(◆) of NaDCF in fortified samples of tap water and well water

T a b l e 4

Analytical application of the UV-Vis spectral absorption method
to the NaDCF determination in fortified tap and well water samples,
and evaluation of the recovery rates obtained by the standard addition procedure

Sample	Added (μg·ml^{-1})	Found (μg·ml^{-1})	Recovery (%)[c]	Mean recovery (%)	RSD[d] (%)
Tap water [a]	2.27	1.91	84.14		
	4.18	4.10	98.09		
	7.36	7.64	103.80	99.09	1.73
	10.54	10.89	103.32		
	20.09	21.32	106.12		
Well water [b]	3.77	3.17	84.084		
	5.68	5.28	92.96		
	8.86	8.71	98.31	94.68	3.03
	12.04	12.04	100		
	18.41	18.05	98.04		

[a]Sample initially spiked with 1 μg ml^{-1}. [b]Sample initially spiked with 2.5 μg ml^{-1}.
[c]Triplicate measurements for each concentration. [d]RSD: Relative standard deviation

4. CONCLUSION

In this work, we have developed a simple, inexpensive, accurate and quite sensitive UV-Vis absorption method for the determination of a non-steroidal anti-inflammatory drug, namely diclofenac sodium, in samples of natural waters of Senegal. We have demonstrated the analytical utility of the photo-induced UV-Vis absorption method. The analytical parameters confirmed the good sensitivity and precision of the photo-induced UV-Vis absorption method for the determination of diclofenac sodium. We have also shown the applicability of the photo-induced UV-Vis absorption method to the determination of diclofenac residues in natural water samples with satisfactory recovery values. In addition, the photo-induced UV-Vis absorption method thus developed will serve as a reference in our future work.

REFERENCES

(1) Der Beek, T.; Weber, F.-A.; Bergmann, A.; Hickmann, S.; Ebert, I.; Hein, A.; Küster, A., Pharmaceuticals in the Environment — Global Occurrences and Perspectives. *Environmental Toxicology and Chemistry* **2016**, *35* (4), 823–835. https://doi.org/10.1002/etc.3339

(2) Noguera-Oviedo, K.; Aga, D. S., Lessons Learned from More than Two Decades of Research on Emerging Contaminants in the Environment. *Journal of Hazardous Materials* **2016**, *316*, 242–251. https://doi.org/10.1016/j.jhazmat.2016.04.058

(3) Fekadu, S.; Alemayehu, E.; Dewil, R.; Van der Bruggen, B., Pharmaceuticals in Freshwater Aquatic Environments: A Comparison of the African and European Challenge. *Science of The Total Environment* **2019**, *654*, 324–337. https://doi.org/10.1016/j.scitotenv.2018.11.072

(4) Laine, L., Approaches to Nonsteroidal Anti-Inflammatory Drug Use in the High-Risk Patient. *Gastroenterology* **2001**, *120* (3), 594–606. https://doi.org/10.1053/gast.2001.21907

(5) Méndez-Arriaga, F.; Esplugas, S.; Giménez, J., Photo-catalytic Degradation of Non-Steroidal Anti-Inflammatory Drugs with TiO_2 and Simulated Solar Irradiation. *Water Research* **2008**, *42* (3), 585–594. https://doi.org/10.1016/j.watres.2007.08.002

(6) Singh, G., Gastrointestinal Complications of Prescription and Over-the-Counter Nonsteroidal Anti-Inflammatory Drugs: A View from the ARAMIS Database. *American Journal of Therapeutics* **2000**, *7* (2), 115–122. https://doi.org/10.1097/00045391-200007020-00008

(7) Yu, T.-H.; Lin, A. Y.-C.; Lateef, S. K.; Lin, C.-F.; Yang, P.-Y., Removal of Antibiotics and Non-Steroidal Anti-Inflammatory Drugs by Extended Sludge Age Biological Process. *Chemosphere* **2009**, *77* (2), 175–181. https://doi.org/10.1016/j.chemosphere.2009.07.049

(8) Nebot, C.; Falcon, R.; Boyd, K. G.; Gibb, S. W., Introduction of Human Pharmaceuticals from Wastewater Treatment Plants into the Aquatic Environment: A Rural Perspective. *Environ Sci Pollut Res* **2015**, *22* (14), 10559–10568. https://doi.org/10.1007/s11356-015-4234-z

(9) Parolini, M., Toxicity of the Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) Acetylsalicylic Acid, Paracetamol, Diclofenac, Ibuprofen and Naproxen towards Freshwater Invertebrates: A Review. *Science of The Total Environment* **2020**, *740*, 140043. https://doi.org/10.1016/j.scitotenv.2020.140043

(10) Tyumina, E. A.; Bazhutin, G. A.; Cartagena Gómez, A. D. P.; Ivshina, I., B. Nonsteroidal Anti-Inflammatory Drugs as Emerging Contaminants. *Microbiology* **2020**, *89* (2), 148–163. https://doi.org/10.1134/S0026261720020125

(11) Verlicchi, P.; Al Aukidy, M.; Zambello, E., Occurrence of Pharmaceutical Compounds in Urban Wastewater: Removal, Mass Load and Environmental Risk after a Secondary Treatment — A Review. *Science of The Total Environment* **2012**, *429*, 123–155. https://doi.org/10.1016/j.scitotenv.2012.04.028

(12) Kruglova, A.; Ahlgren, P.; Korhonen, N.; Rantanen, P.; Mikola, A.; Vahala, R., Biodegradation of Ibuprofen, Diclofenac and Carbamazepine in Nitrifying Activated Sludge under 12°C Temperature Conditions. *Science of the Total Environment* **2014**, *499*, 394–401. https://doi.org/10.1016/j.scitotenv.2014.08.069

(13) Fent, K.; Weston, A.; Caminada, D., Ecotoxicology of Human Pharmaceuticals. *Aquatic Toxicology* **2006**, *76* (2), 122–159. https://doi.org/10.1016/j.aquatox.2005.09.009

(14) Chen, G.; Den Braver, M. W.; Van Gestel, C. A. M.; Van Straalen, N. M.; Roelofs, D., Ecotoxicogenomic Assessment of Diclofenac Toxicity in Soil. *Environmental Pollution* **2015**, *199*, 253–260. https://doi.org/10.1016/j.envpol.2015.01.032

(15) Rocco, L.; Izzo, A.; Zito, G.; Peluso, C., Genotoxicity in Zebrafish (Danio Rerio) Exposed to Two Pharmacological Products from an Impacted Italian River. *J Environment Analytic Toxicol* **2011**, *01* (02). https://doi.org/10.4172/2161-0525.1000103

(16) Schmidt, S.; Hoffmann, H.; Garbe, L.-A.; Schneider, R. J., Liquid Chromatography–Tandem Mass Spectrometry Detection of Diclofenac and Related Compounds in Water Samples. *Journal of Chromatography A* **2018**, *1538*, 112–116. https://doi.org/10.1016/j.chroma.2018.01.037

(17) Kern, K., New Standards for the Chemical Quality of Water in Europe under the New Directive 2013/39/EU. *Journal for European Environmental & Planning Law* **2014**, *11* (1), 31–48. https://doi.org/10.1163/18760104-01101002

(18) Zhou, Y.; Xu, J.; Lu, N.; Wu, X.; Zhang, Y.; Hou, X., Development and Application of Metal-Organic framework@GA Based on Solid-Phase Extraction Coupling with UPLC-MS/MS for the Determination of Five NSAIDs in Water. *Talanta* **2021**, *225*, 121846. https://doi.org/10.1016/j.talanta.2020.121846

(19) Gouda, A. A.; Kotb El-Sayed, M. I.; Amin, A. S.; El Sheikh, R., Spectrophotometric and Spectrofluorometric Methods for the Determination of Non-Steroidal Anti-Inflammatory Drugs: A Review. *Arabian Journal of Chemistry* **2013**, *6* (2), 145–163. https://doi.org/10.1016/j.arabjc.2010.12.006

(20) Okumura, M.; Sugibayashi, K.; Ogawa, K.; Morimoto, Y., Skin Permeability of Water-Soluble Drugs. *Chem. Pharm. Bull.* **1989**, *37* (5), 1404–1406. https://doi.org/10.1248/cpb.37.1404

(21) Žilnik, L. F.; Jazbinšek, A.; Hvala, A.; Vrečer, F.; Klamt, A., Solubility of Sodium Diclofenac in Different Solvents. *Fluid Phase Equilibria* **2007**, *261* (1), 140–145. https://doi.org/10.1016/j.fluid.2007.07.020

(22) Packer, J. L.; Werner, J. J.; Latch, D. E.; McNeill, K.; Arnold, W. A., Photochemical Fate of Pharmaceuticals in the Environment: Naproxen, Diclofenac, Clofibric Acid, and Ibuprofen. *Aquat. Sci.* **2003**, *65* (4), 342–351. https://doi.org/10.1007/s00027-003-0671-8