Amanda Natalina de Faria
(Organizadora)

Princípios Físico - Químicos em Farmácia

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APRESENTAÇÃO

O e-book “Princípios Físico-Químicos em Farmácia” é uma obra composta por 16 capítulos onde foram abordados trabalhos, pesquisas e revisões de literatura acerca de diferentes aspectos da aplicação de propriedades físico químicas de produtos e atividades farmacêuticas.

O objetivo principal desta publicação foi dar visibilidade a estudos desenvolvidos em diversas Instituições de Ensino Superior e Pesquisa do Brasil, com o foco voltado aos processos físico químicos no desenvolvimento de metodologias inovadoras, qualidade, validação, análise de plantas medicinais do país, suas moléculas ativas, entre outros.

A riqueza da diversidade de plantas brasileiras e suas análises tornam-se um atrativo à parte neste livro, onde espécies como a *Morus nigra*, *Helianthus annuus, Platonia insignis* Mart, *Theobroma cacao* L., *Theobroma grandiflorum*, *Astrocaryum murumuru* Mart e óleos essenciais são mostrados e enaltecem os conhecimentos regionais.

Assim, diversos assuntos foram discutidos e aprofundados nos capítulos deste e-book, com a finalidade de divulgar o conhecimento científico aos pesquisadores nacionais com o respaldo e incentivo da Editora Atena, cujo empenho para a divulgação científica torna-se cada vez mais notável.

Amanda Natalina de Faria

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OCORRÊNCIA DO FÁRMACO DICLOFENACO SÓDICO EM ÁGUAS SUPERFICIAIS DE UM RIO NO OESTE DO ESTADO DO PARANÁ

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RESUMO: Contaminantes emergentes vêm se destacando em pesquisas devido ao impacto que podem causar ao meio ambiente e à saúde humana. Os medicamentos farmacêuticos têm participado de alguns contaminantes emergentes, cujas características proporcionam acumulação no meio ambiente. As principais fontes de contaminação estão associadas à liberação de excreções humanas e animais, bem como à eliminação de efluentes e drogas nos recursos hídricos. Assim, este trabalho teve como objetivo desenvolver um método analítico para determinação do fármaco diclofenaco sódico, validar a metodologia aplicada e quantificar tal composto em amostras de águas superficiais da cidade de Cascavel. Amostras de água foram coletadas no rio Cascavel e após ajuste de pH, foram filtradas e extraídas por cartuchos de extração em fase sólida. Após a eluição, o analito foi analisado por Cromatografia Líquida de Alta Eficiência, utilizando detector UV-Vis e coluna C18. O método foi submetido a um estudo de validação e registrou um coeficiente de correlação de 0,9996, cujos limites de detecção e quantificação foram de 0,04 e 0,1 $mg.L^{-1}$, respectivamente. Para repetibilidade e precisão intermediária foram obtidos valores de 5,03 e 5,31%, respectivamente, e 82,28% para recuperação analítica. As concentrações obtidas nas amostras reais coletadas no rio Cascavel variaram de 0,70 a 1,06 $\mu g.L^{-1}$. Por outro lado, este estudo demonstrou a otimização deste método para determinar o diclofenaco sódico em amostras de água coletadas no rio Cascavel.

PALAVRAS-CHAVE: contaminantes emergentes; amostras ambientais; diclofenaco; cromatografia líquida; validação analítica.

OCCURRENCE OF DICLOFENAC SODIUM DRUG IN SURFACE WATERS OF A RIVER IN WESTERN PARANÁ STATE

ABSTRACT: Emerging contaminants have been prominent in researches due to their effective impact on the environment and human

health. Pharmaceutical drugs have taken part of some emerging contaminants, whose characteristics provide cumulation in the environment. The main sources of contamination are associated to the release of human and animal excretions, as well as effluents and drugs disposal into water resources. Thus, this study aimed at developping an analytical method to determine diclofenac sodium drug, at validating the applied methodology and at quantifying such compound in surface water samples in Cascavel city. Water samples were collected in Cascavel river and after pH adjusted, were filtrated and extracted by solid phase extraction cartridges. After elution, the analyte was analyzed by High Performance Liquid Chromatography, using UV-Vis detector and C18 column. The method underwent a validation study and registered a 0.9996 correlation coefficient, whose limits of detection and quantification were 0.04 and 0.1 $mg.L^{-1}$, respectively. For repeatability and intermediate precision were obtained values of 5.03 and 5.31%, respectively, and 82.28% for analytical recovery. The obtained concentrations in the actual samples collected in Cascavel river ranged from 0.70 to 1.06 $\mu g.L^{-1}$. On the other hand, this trial has shown this method optimization to determine diclofenac sodium in water samples, collected in Cascavel river.
KEYWORDS: emerging contaminants; environmental samples; diclofenac; liquid chromatography; analytical validation.

1 I INTRODUCTION

Emerging contaminants are defined as compounds of natural or synthetic origin, which are present in products consumed by the population. They can also reach ecosystems through treated or untreated effluents. And, although they have been the subject of recent studies, the presence of such compounds in the environment has been happening for a long time (SOUSA and VASCONCELOS, 2005; BARREIRO and PINTO, 2013). In addition to studies regarding persistent compounds in the environment such as pesticides, pharmacological compounds are highlighted since they are considered as emerging contaminants in environmental samples (AMÉRICO et al., 2013).

Pharmaceutical drugs are meant to be environmental contaminants, because their molecules are biologically active. Most of them have lipophilic characteristics and low biodegradability, which provide high potential for bioaccumulation and persistence in the environment (AMÉRICO et al., 2012). The presence of these substances into the environment are due to their use to treat human and animal diseases, released by excretion and from the outflow by effluents into water resources that receive supplying water (AMÉRICO et al., 2013).

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used therapeutic agents and often prescribed for reports of musculoskeletal pain. An important issue to be stated is that they are taken without prescription for minor pain. Acetylsalicylic acid, paracetamol, diclofenac, ibuprofen and ketoprofen are examples of this class of drugs (RANG, DALE and RITTER, 2001).

As diclofenac sodium is an anti-inflammatory drug and taken worldwide, along the last decades. It has been studied in several kinds of environmental samples, since its occurrence in the environment and its possible toxicity is related to several organisms, such as fish and mussels, which makes it an emerging environmental contaminant. According to the conventional water treatment system, its main removal ranges from about 30 to 70%. And, once it is in the environment, it can interact with other inorganic contaminants, mainly in wastewater treatment plants such as metals, organic contaminants and even with their own metabolites (LONAPPAN et al., 2016).

Studies have shown that these compounds can be detected in environmental samples by chromatographic technique, and high performance liquid chromatography can be used. Among the analytical steps, the extraction phase is a relevant moment. The solid phase extraction (SPE) method has been widely used due to some favorable characteristics such as low solvent consumption and high concentration of the analyte of interest (SOUZA and FALQUETO, 2015; BISCEGLIA et al., 2010). However, monitoring these contaminants has become relevant, since they are not part of water quality control by Brazilian legislation yet.

Thus, this study aimed at developping and validating a method to determine diclofenac sodium as well as its presence in surface water samples from Cascavel River. Hence, it contributes to the indicators survey concerning water quality, which will be treated and consumed again by its population.

2 I MATERIALS AND METHODS

2.1 Studied area

Cascavel River (24º32' and 25º17'S, 53º05 'and 53º50'W) is placed in Cascavel, a city from Paraná state, Brazil. It has a total flow of 973 $m^3.h^{-1}$, and 345 $m^3.h^{-1}$ are captured by SANEPAR Company – Companhia de Saneamento do Paraná – which is a publicly traded joint stock corporation controlled by Paraná State. The company provides treated water supply, sewage collection and treatment and solid waste management services of nearly 100% inhabitancies, in urban area of this city (AQUINO, BUENO and MENEZES, 2014).

2.2 Sample Collection and Preparation

The samples were collected at Cascavel River, in an upstream point from the Water Treatment Station, in southern city, from August to December 2017.

After samples collection, pH was adjusted to 3.0 with an addition of 6 $mol.L^{-1}$ HCl and filtration occurred using a 0.45 µm cellulose nitrate membrane (Sartorius Stedim®) in a vacuum system to remove particulate matter in suspension. Filtered samples were stored in an amber glass vial and kept under refrigeration (4°C) for further analyses.

2.3 Extraction and quantification of analytes

The samples were submmited to an extraction process in solid phase using Chromabond® C18 polypropylene SPE cartridges (6 mL/500 mg) with a vacuum Manifold equipment. Then, 5 mL methanol were used plus 5 mL ultrapurified water for cartridges conditioning. Then, each sample was percolated through the cartridges with a flow adjusted to 6 $mL.min^{-1}$. After percolating the whole sample, cartridges were dried at room temperature for 24 hours. After the drying phase, analytes were eluted with 5 mL methanol, concentrated in a rotavaporator equipment and transferred to vials for further chromatographic analysis.

Therefore, in order to determine diclofenac sodium concentrations in water samples, a chromatographic method was developed using standard solutions its compound (diclofenac sodium salt - USP, PHR1144-1G - Sigma Aldrich®) at the following concentrations: 0.1; 0.2; 0.4; 0.6; 0.8 and 1.0 $mg.L^{-1}$.

The standard solutions were analyzed by High Performance Liquid Chromatography (HPLC) using Shimadzu® equipment with UV-VIS detector (SPD-20A) and C18 column (Akzo Nobel®, Kromasil®, 4.6 mm x 150 mm x 5 µm). Five analytical conditions were tested, as shown in Table 1.

Parameters	Method 1	Method 2	Method 3	Method 4	Method 5
Mobile phase	Methanol: 0.1% Water acidified with formic acid (75:25 v/v)	Methanol: 0.1% Water acidified with formic acid (75:25 v/v)	Methanol	0.1% Water acidified with formic acid	Methanol: 0.1% Water acidified with formic acid (50:50 v/v)
Temperature	25 °C	25 °C	25 °C	25 °C	25 °C
Flow	1 $mL.min^{-1}$	1 $mL.min^{-1}$	1 $mL.min^{-1}$	1 $mL.min^{-1}$	1 $mL.min^{-1}$
Injection volume	20 μL	20 μL	20 μL	20 μL	20 μL
UV Wavelength	280 nm	300 nm	280 nm	280 nm	280 nm

Table 1: Analytical conditions tested for diclofenac method in surface water samples.

After optimizing chromatographic conditions, the method validation was carried out based on parameters such as linearity, selectivity, limits of detection and quantification, precision and recovery. Vials containing water samples were then sent to quantify the analysis of the studied compound.

3 I RESULTS AND DISCUSSION

3.1 Optimization of chromatographic conditions

The chromatographic conditions that showed the best results to quantify and

validate diclofenac sodium determination method were from method 1: mobile phase composed of methanol: 0.1% water acidified with formic acid (75:25), isocratic, storage temperature at 25 °C, 1 mL.min^{-1} flow, 20 µL injection volume, with retention time of 10 minutes.

3.2 Validation of Method

According to the Inmetro's guidance document - DOQ-CGCRE nº. 008/2016 (INMETRO, 2016) and Anvisa Resolution nº.166/2017 (ANVISA, 2017), some parameters must be analyzed in order to assure that the methods are appropriate for their purposes, such as linearity, sensitivity, limit of detection, limit of quantification, precision and accuracy.

a) Linearity

The linearity analysis of method took into account the square linear regressions of the lines of analytical curves in solvent, considering the summit areas and respective concentrations of standard solutions of diclofenac sodium (0.1; 0.2; 0.4; 0.6; 0.8 and 1.0 mg.L^{-1}). It was used an Excel® software to obtain the following linear regression equation: *y = 46524x+817.13*, with a coefficient of determination (R^2) and correlation coefficient (r) equal to 0.9993 and 0.9996, respectively (Fig. 1).

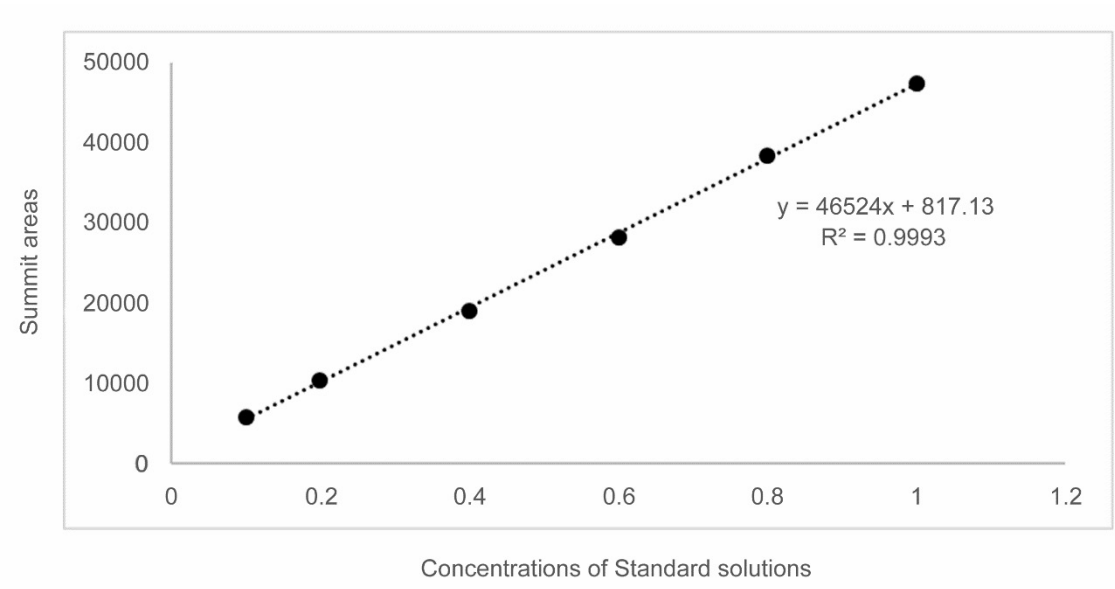

Figure 1: Analytical curve of diclofenac sodium compound.

According to the Resolution nº.166/2017 (ANVISA, 2017), the linearity of a method must be demonstrated by its ability on obtaining analytical responses directly proportional to the analyte concentration in a sample; and correlation coefficient should be superior to 0.990, while angular coefficient should be significantly different from zero. The results were satisfactory for linearity since they were in accordance with the enacted legislation.

b) Selectivity

Selectivity was carried out by comparing a matrix with an analyte addition and a matrix without the addition of analyzed analyte, according to the determined methodology.

The results of these measurements were evaluated considering the characteristic peak retention times. There was no analyte signal in the matrix without addition of diclofenac sodium compound, since the studied compound shows a retention time of approximately 6.205 minutes (Fig. 2).

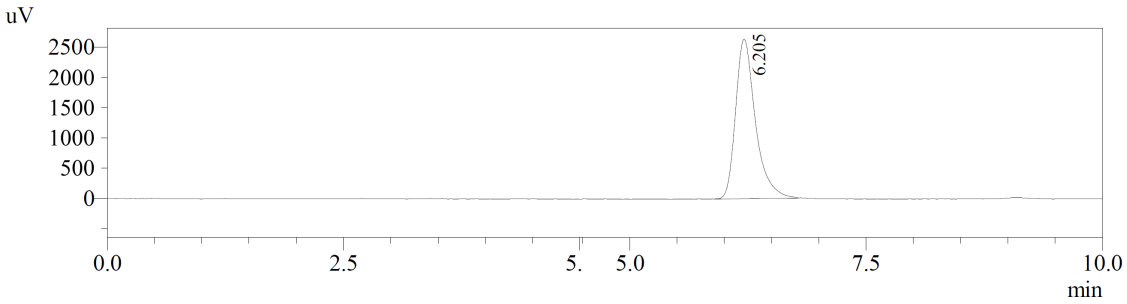

Figure 2: Chromatogram of retention time of diclofenac sodium compound.

Selectivity is the ability of the method to measure a compound in the presence of other components such as impurities, degradation products and matrix components (INMETRO, 2016). It is crutial to be aware when undergoing with chromatographic analysis to ensure purity of the chromatographic peaks.

Selectivity refers to the analytical signal free of interference, its proof, knowing the formulation components (ANVISA, 2017). For selectivity, retention time average of the sample plus the standard diclofenac sodium solution was 6.205 minutes. No chromatographic peak was recorded in the sample without the analyte addition, and the baseline was kept. This shows that under the proposed method conditions, the studied compound is identified in a known sample according to its characteristic retention time.

c) Limits of detection and quantification

The visual method was applied for detection limit, so, based on tested concentrations that ranged from 0.001 to 0.05 $mg.L^{-1}$, answers of the peak area were registered, related to diclofenac sodium.

It was observed that 0.04 $mg.L^{-1}$ was the lowest concentration detected according to the method conditions for diclofenac sodium, since when concentration was inferior to this one, there was no response of the chromatographic peak signal. And for the limit of quantification, 0.1 $mg.L^{-1}$ was considered the first point of analytical curve, excluding the zero point.

The Limit of Detection (LOD) is applied when measuring a sample with low

analyte level or trace analysis, and it is important to know the lowest concentration of analyte or of property that can be detected by this method. There are several ways of calculating it. But, it is usually evaluated by the signal-to-noise ratio with value 3 or by testing analyte standard solutions at concentrations lower than the first point on calibration curve, observing the first concentration to be detected (visual method).

On the other hand, the Limit of Quantification (LOQ) is usually the standard calibration curve with the lowest concentration, excluding the white one. And, it can also be calculated by both signal-to-noise ratio with value 10, and visual method (INMETRO, 2016; ANVISA, 2017; RIBANI et al., 2004).

Limits of detection and quantification are essential to establish an analytical capacity and determine traces of chemical substances. Although, in order to validate these parameters, a certain number of fortified samples with the studied compounds should be analyzed near to the desired concentration level (usually near the smallest point of calibration curve) in which it will be possible to detect and/or quantify the analytes (IMOTO and FREITAS, 2008).

d) Precision

Precision was determined based on repeatability and intermediate precision of the standard diclofenac sodium solution at 0.1 $mg.L^{-1}$ concentration. While, repeatability was evaluated by the same analyst on the same day, intermediate precision was evaluated by the standard solution analysis on different days and by a different analyst. So, in this study, a 5.03% variation was registered for repeatability and 5.31% for intermediate precision.

The obtained results regarding the precision study are in accordance with what cited legislations have recommended, which is up to 20%. It also showed that the greatest range occurred when different analysts ran the test on different days.

e) Accuracy

The accuracy assay was carried out by comparing the analytical results of the standard diclofenac sodium solution with the lowest concentration of the analytical curve, submitted to the extraction process in solid phase, whose obtained results showed the same non-extracted standard solutions.

The processes, frequently used to evaluate the trend of a method, are, among others, by the use of certified reference materials (CRM), participation in interlaboratory comparisons and recovery trials achievement. The trend implies a combination of random and systematic error components. It is important to determine the trend with respect to appropriate reference values and establish traceability to recognized standards (INMETRO, 2016; ANVISA, 2017). It was observed that 82.28% of analytical recovery were recorded for diclofenac sodium compound. Percentages of analyte recovery, close to 100%, are desirable, however, smaller values are allowed. So, it can be inferred that the obtained value in this study is satisfactory.

3.3 Analysis of surface water samples

The results for Cascavel River regarding the analyzed surface water samples, as well as retention time, peak chromatographic area and statistical data are presented in Table 2. The obtained results ranged from 0.70 to 1.06 μg.L^{-1}, with 0.03 as maximum standard deviation and showing low dispersion of data.

Collect	Average retention time (min)	Average Area (μV)	Results±SD* (μg.L^{-1})
1	6.23	19,634.5	1.11 ± 0.03
2	6.18	50,041.1	1.06 ± 0.01
3	6.23	33,608.2	0.70 ± 0.01

Table 2 Occurrence of diclofenac sodium in the samples of surface water of Cascavel River.

*SD = Standard Deviation

Studies also report the presence of drugs as contaminants in river samples, as in a study that was carried out in Spain (VALCÁRCEL et al.,2011). It reported that the second most detected drug into a river was diclofenac, with a concentration range from 0.212 to 0.5 μg.L^{-1} (IBÁÑEZ et al., 2013).

In 2016, results such as 0.22 μg.L^{-1} and 0.051 μg.L^{-1} were obtained (LOPES et al., 2016; ELLIS, 2016), confirming not only the occurrence of drugs as contaminants in urban receiving waters, but also that this fact usually follows trace levels and low flow conditions. While in 2017, diclofenac was detected in water bodies, in Elbe basin in Czech Republic at 1.08 μg.L^{-1} concentration (MARSIK et al., 2017).

Water treatment and distribution in the studied municipality are carried out by the conventional method and they followed these steps: coagulation, flocculation, decantation, filtration, disinfection and fluoridation.

The conventional treatment system, including wastewater treatment plants, shows from moderate to high degradation efficiency of diclofenac, whose average ranges from 30 to 70% (LONAPPAN et al., 2016). The presence of these compounds in the environment represents one of the worldwide problems that impair water quality and there is a causative impact in the aquatic environments.

There are few studies in Brazil addressing the occurrence of drugs in the environment and their effects. Most of them are carried out in developed countries (TORRES et al., 2012). Improvements in wastewater treatment field and the search for new treatment methods have been carried out, such as ozonation and osmosis, in order to effectively remove organic contaminants (PISARENKO et al., 2012; SHEN

et al., 2014; DANG, NGHIEM and PRICE, 2014).

However, most treatment plants do not have these processes in their routine due to the high cost, consequently, some residues of these harmful organic molecules can be recorded (PEDROUZO et al., 2011).

4 I CONCLUSION

So, the proposed method to determine diclofenac sodium was validated according to the legislation enacted in this trial for analyses at trace levels. The SPE process was appropriate for the studied compound with satisfactory recovery rate. The analysis, according to the proposed method of the water samples collected in Cascavel River, registered the presence of diclofenac sodium compound.

REFERENCES

AMÉRICO, J. H. P.; ISIQUE, W. D.; MINILLO, A.; CARVALHO, S. L.; TORRES, N. H. Fármacos em uma estação de tratamento de esgoto na região centro-oeste do Brasil e os riscos aos recursos hídricos. Revista Brasileira de Recursos Hídricos, n. 17, p. 61-67, 2012.

AMÉRICO, J. H. P.; TORRES, N. H.; AMÉRICO, G. H. P.; CARVALHO, S. L. Ocorrência, destino e potenciais impactos dos fármacos no ambiente. SaBios: Revista Saúde e Biologia, n. 8, p. 59-72, 2013.

AQUINO, C. A. N.; BUENO, N. C.; MENEZES, V. C. Desmidioflórula (Zygnemaphyceae, Desmidiales) do rio Cascavel, oeste do estado do Paraná, Brasil. Hoehnea. n. 41, 2014.

BARREIRO, E. J.; PINTO, A. C. Oportunidades e desafios para a inovação em fármacos: agora ou nunca! Revista Virtual de Química, n. 5, p. 1059-1067, 2013.

BISCEGLIA, K. J.; ROBERTS, A. L.; SCHANTZ, M. M.; LIPPA, K. A. Quantification of drugs of abuse in municipal wastewater via SPE and direct injection liquid chromatography mass spectrometry. Analytical and Bioanalytical Chemistry, n. 398, p. 2701-2712, 2010.

BRASIL. Agência Nacional de Vigilância Sanitária. Resolução N° 166, de 24 de julho de 2017: ”Dispõe sobre a validação de métodos analíticos e dá outras providências”. **Diário Oficial da União,** Brasil, 2017.

DANG, H. Q.; NGHIEM, L. D.; PRICE, W. E. Factors governing the rejection of trace organic contaminants by nanofiltration and reverse osmosis membranes. Desalination and Water Treatment, n. 52, p. 4-6, 2014.

ELLIS, J. B. Pharmaceutical and personal care products (PPCPs) in urban receiving Waters. Environmental Pollution, n. 144, p. 184-189, 2016.

IBÁÑEZ, M.; GRACIA-LO, E.; BIJLSMA, L.; MORALES, E.; PASTOR, L.; HERNÁNDEZ, F. Removal of emerging contaminants in sewage water subjected to advanced oxidation with ozone. Journal of Hazardous Materials, n. 260, p. 389–398, 2013.

IMOTO, M. N.; FREITAS, R. J. S. Determinação dos limites de detecção e quantificação em análise de resíduos de pesticidas organohalogenados por cromatografia em fase gasosa. Pesticidas: Revista Ecotoxicologia e meio ambiente, n. 18, p. 35-44, 2008.

INMETRO. Instituto Nacional de Metrologia, Qualidade e Tecnologia. DOQ-CGCRE-008 – Orientação sobre validação de métodos analíticos. Revisão 04 – agosto, 2016.

LONAPPAN, L.; BRAR, S. K.; DAS, R. K.; VERMA, M.; SURAMPALL, R. Y. Diclofenac and its transformation products: Environmental occurrence and toxicity - A review. Environment International, n. 96, p. 127–138, 2016.

LOPES, V. S. A.; RIENTE, R. R.; SILVA, A. A.; TORQUILHO, D. F.; CARREIRA, R. S.; MARQUES, M. R. C. Development of a solid-phase extraction system modified for preconcentration of emerging contaminants in large sample volumes from rivers of the lagoon system in the city of Rio de Janeiro, Brazil. Marine Pollution Bulletin, n. 110, p. 572–577, 2016.

MARSIK, P.; REZEK, J.; ZIDKOV, M.; KRAMULOVA, B.; TAUCHEN, J.; VANEK, T. Non-steroidal anti-inflammatory drugs in the watercourses of Elbe basin in Czech Republic. Chemosphere, n. 171, p. 97-105, 2017.

PEDROUZO, M.; BORRUL, F.; POCURULL, E.; MARCE, M. R. Drugs of abuse and their metabolites in waste and surface waters by liquid chromatography-tandem mass spectrometry. Journal of Separation Science, n. 34, p. 1091–1101, 2011.

PISARENKO, A. N.; STANFORD, B. D.; YAN, D.; GERRITY, D.; SNYDER, S. A. Effects of ozone and ozone/peroxide on trace organic contaminants and NDMA in drinking water and water reuse applications. Water Research, n. 46, p. 316-326, 2012.

RANG, H. P.; DALE, M. M.; RITTER, J. M. Farmacologia. 4ª ed. Rio de Janeiro: Guanabara Koogan,2001.

RIBANI, M.; BOTTOLI, C. B. G.; COLLINS, C. H.; JARDIM, I. C. S. F.; MELO, L. F. C. Validação em métodos cromatográficos e eletroforeticos. Química Nova, n. 27, p. 771-780, 2004.

SHEN, J.; HUANG, J.; RUAN, H.; WANG, J.; VAN DER BRUGGEN, B. Techno-economic analysis of resource recovery of glyphosate liquor by membrane technology. Desalination, n. 342, p. 118–125, 2014.

SOUSA, M. V. N.; VASCONCELOS, T. A. Fármacos no combate à tuberculose: passado, presente e futuro. Química Nova, n. 28, p. 678-686, 2005.

SOUZA, C. P. F. A.; FALQUETO, E. Descarte de Medicamentos no Meio Ambiente no Brasil. Revista Brasileira de Farmácia, n. 96, p. 1142–1158, 2015.

TORRES, N. H.; AMÉRICO, J. H. P.; FERREIRA, L. F. R. F.; NAZATO, C.; MARANHO, L. A.; VILCA, F. Z. V.; TORNISIELO, V. L. Fármacos no ambiente-revisão. Revista de Estudos ambientais, n. 14, p. 67-75, 2012.

VALCÁRCEL, Y.; ALONSO, S. G.; RODRÍGUEZ-GIL, J. L.; MAROTO, R. R.; GIL, A.; CATALÁ, M. Analysis of the presence of cardiovascular and analgesic/anti-inflammatory/antipyretic pharmaceuticals in river- and drinking-water of the Madrid Region in Spain. Chemosphere, n. 82, p. 1062-1071, 2011.

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