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Article

Trace-level detection of pharmaceutical residues in River Water of Hull, United Kingdom

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Abstract
A comprehensive trace analysis method was developed in this study for the quantification of four commonly used pharmaceuticals, namely diclofenac, cetirizine, triclosan, and phenylephrine, in Winestead drain river water from the Humber Region United Kingdom. The method involved a combination of (SPE) solid phase extraction (SPE) and liquid chromatography mass spectrometry (LC-MS/MS), offering a sensitive and selective approach for the detection and quantification of these pharmaceutical compounds. The water samples were collected from three different locations along the Winestead drain and subjected to SPE using a suitable sorbent material. The analytes were retained on the sorbent, The interfering matrix components were washed away while the retained analytes were eluted using an appropriate solvent, the eluted samples were then analysed using a high-performance liquid chromatography (HPLC) system coupled with a tandem mass spectrometer. Multiple reaction monitoring (MRM) was used for selective detection and quantification of the pharmaceuticals. The method exhibited excellent linearity over a wide concentration range for all target analytes, with correlation coefficients (R^2) ≥0.99, indicating the method's capability to detect these compounds at low concentrations. The precision and accuracy were evaluated by analysing spiked multicomponent solvent, and the results demonstrated satisfactory precision (%RSD < 10%) and accuracy (recovery rates ranging from 55% to 80%). The method developed was applied to analyse river water samples collected from Winestead drain. The presence and concentrations of diclofenac, cetirizine, triclosan, and phenylephrine were determined, highlighting the occurrence of these pharmaceutical compounds in the aquatic environment.

Keywords: *pharmaceuticals, river, trace analysis, SPE, LC-MS/MS, LOQ*

INTRODUCTION

In the past years, there has been raising concern around the world regarding the presence of different types of emerging contaminants including pharmaceuticals residues and personal care products in the aquatic environment. The greatest danger posed by these emerging contaminants described is due to lack of knowledge on their toxicological effects on the environment and on humans, also their detection, analysis, and removal techniques that has not received enough attention [1,2]. Due to inadequate knowledge on analytical detection techniques, these emerging contaminants gain access to the environment uncontrolled and unregulated [3,4]. Pharmaceuticals, such as cetirizine, phenylephrine, diclofenac, and triclosan, are extensively used for various medical purposes and personal care products [5,6]. There has been wide sensitization on method development for analysing these pharmaceutical residues in the environment [7,8]. Non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac are among the 10 top persistent pollutants and one of the most widely used medications globally [9]. It represents one of the groups of pharmaceuticals commonly used in human and veterinary care [10,11]. It is mostly used in the treatment of symptoms such as inflammation, pain, and fever and could be obtained over the counter or by prescription [12]. Diclofenac can bioaccumulate in the tissues of aquatic organisms, particularly in fish [13.14]. This means that the drug can accumulate in the food chain, with higher trophic level predators potentially being exposed to higher concentrations of diclofenac [15]. Cetirizine, an antihistamine widely used to treat allergy symptoms, is among the pharmaceuticals that have been detected in water bodies [16].

As its consumption increases, so does its occurrence in rivers, leading to potential ecological implications. Studies have shown that chronic exposure to cetirizine may lead to behavioural changes, reproductive disruptions, and altered physiological processes in aquatic organisms [17,18]. Moreover, its continuous presence in river water can contribute to the development of antibiotic resistance and may have broader implications for the overall ecosystem health [19]. Phenylephrine, a widely used decongestant, has emerged as one of the pharmaceuticals of concern in aquatic environments, including river waters. Triclosan, an antimicrobial agent commonly used in personal care products and consumer goods, has raised significant environmental concerns due to its persistent presence in water bodies, including river waters [20]. This study has become critical as a result of the ecotoxicological risk to humans and aquatic organism attributable to active pharmaceutical residues in the environment [12].

Recent research has demonstrated that complex combinations of pharmaceuticals residues from distinct pharmacological classes may negatively affect the development, growth, reproduction of aquatic organisms [21] and also have harmful effects on biota at environmental concentration level [22÷24]. As a result, there is an increasing need for the advancement of efficient analytical process that facilitate fast, sensitive and selective detection of trace levels of these emerging pollutants in environmental samples [25]. Sensitive and reliable analytical methods are required to account for the presence of contaminants at trace levels, and a validation process is a crucial step when there isn't an official method that incorporates several analytes. an official method that incorporates several analytes.

This study presents the results of a validated analytical technique based upon solid-phase extraction (SPE) step, utilizing Waters Oasis HLB 20cc Extraction Cartridges, followed LC–MS/MS with electrospray ionization (ESI) for the detection and quantification of four commonly used Pharmaceuticals (diclofenac, phenylephrine, triclosan and cetirizine) in river water samples. The identification and quantification of series of targeted pharmaceutical residues at several locations along the Winstead drain river in Hull United Kingdom aided in establishing the method's sensitivity and applicability.

MATERIALS AND METHOD

Reagent, chemical and reference standard

Analytical grade (98%) Formic acid, acetonitrile, methanol and water used for the mobile phase were purchased from Merck Sigma-Aldrich, Poole, United Kingdom. Oasis HLB 20cc (1g) Extraction Cartridges from Waters Corporation (Milford, MA, USA) were used for the solid phase extraction. All of the pharmaceutical reference standards (diclofenac, phenylephrine, triclosan, and cetirizine) were purchased from Merck Sigma Aldrich, Poole, UK and of high purity. Individual stock solutions of the appropriate standard (1mg/ml) were prepared by weighing out approximately 10mg of each pharmaceutical standard and dissolving it in 10mL acetonitrile/water (50:50 v/v) and stored at -20ºC in amber bottles to avoid degradation. Through suitable combining of stock solution, a series of working solution at different concentration were prepared by appropriate serial dilution of the mixture in acetonitrile and water (50:50 v/v).

Solid phase extraction

Because these substances are typically found in the environment at extremely low concentration, a sample pre-concentration procedure was carried out before the analysis [26÷28]. Solid phase extraction was carried out to extract the target pharmaceutical residues, including cetirizine, phenylephrine, diclofenac and triclosan on Waters Oasis HLB 20cc (1g) LP extraction cartridge with the aid of a Varian vacuum extraction device. Conditioning of Oasis HLB 20cc (1g) LP extraction cartridge were consecutively carried out with 20 mL of methanol after which the cartridge was equilibrated with 20 mL of ultrapure water, at a flow rate of 1 mL/min. 20 mL each of the river water samples were loaded on four extraction cartridges at a constant flow rate of 1mL/min followed by a washing step with 10 mL of ultrapure water. The process was repeated three times resulting in 60 mL extracted by each cartridge giving 240 mL extracted in total. The analytes were eluted with 20 mL

methanol at 1ml/min into a test tube. The resulting eluates were evaporated to dryness under a moderate stream of nitrogen and reconstituted with 1ml methanol and preserved at -20 ºC prior to the analysis-by-analysis LC-MS/MS.

Recovery experiment

The SPE method's accuracy and precision were determined through spike and recovery experiments. For these experiments multicomponent solvent comprising acetonitrile and water (50:50 v/v) were spiked with standard solutions of analytes at concentration levels of 100 ng mL^{-1}. In order to calculate recovery rates, the concentration of the analytes detected before undergoing sample preparation (cetirizine, diclofenac, phenylephrine and triclosan) were subtracted from the concentration of the analytes after going through the solid phase extraction process.

Liquid chromatography- mass spectrometry

The LC analysis was performed using a Shimadzu HPLC system Nexera (Kyoto, Japan) equipped with two LC-30AD high pressure pumps, a SIL-20A auto-sampler, a DGU-20A5 degasser, a UV/Vis SPD-M20A detector and a CBM-20A interface was used for the LC analyses. Chromatographic separation was achieved with a Shimadzu C18 end capped column (150 mm × 2.1 mm, 5 um) with a 0.1% aqueous solution of formic acid (v/v) (solvent A) and acetonitrile with 0.1% formic acid (v/v) (solvent B) as mobile phases.

The LC was directly interfaced to the electrospray ionization (ESI) source coupled to a Shimadzu MS 8060 triple quadrupole mass spectrometer. After the chromatographic separation, the pharmaceuticals were ionized using an electrospray ionization source (ESI) operating in the negative ion mode for diclofenac and triclosan, while cetirizine and phenylephrine were ionized in the positive mode [29,30]. The measurement's algorithm is as follows: once the system is switched to the negative mode all transitions in the negative mode are measured. After switching to the positive mode, all transitions in this mode are measured. The following parameters were adjusted to maximize ionization: drying gas flow rate of 10 L min^{-1}, interface temperature of 300°C, nebulizing gas flow 3 L min^{-1}, heating gas flow 10 L min^{-1}, heat block temperature 400°C and oven temperature 40°C. Nitrogen was used as collision gas. The mass spectrometer was run in a multiple reaction monitoring (MRM) mode in which the protonated molecular ion was isolated and the fragment ions were monitored. Multiple reaction monitoring (MRM) transitions were used for verification and quantification of the target compounds. Most of the compounds showed at least two MS/MS transitions, the fragmentation products for each compound were selected based on the transitions with the highest signal intensity.

RESULTS AND DISCUSSION

To achieve LC separation by gradient elution, an aqueous solution containing deionized water and 0.1% formic acid (solvent A) and acetonitrile containing 0.1% formic acid (solvent B) were used as the mobile phase. The mobile phase solvents were chosen based on prior chromatographic separations for multi-class compounds that were published [30]. Conditions for different gradient and isocratic elution were evaluated. To ensure a consistent ESI signal increase during the entire gradient elution, formic acid was added to both solvents. To determine the mass spectrometry conditions and the best mode of ionization, full scan acquisitions were carried out over defined mass ranges for each pharmaceutical. Two fragment ions from the precursor ion were chosen from the target pharmaceuticals MS/MS spectra in order to generate two MRM transitions channels (Table 1). The chromatographic separation is shown in Fig.1. Using the MRM profile obtained for the quantification transition from a 100 ng mL^{-1} standard.

Selected LC electrospray ionization MS/MS experimental parameters for the analysis of trace pharmaceutical residues by multiple reaction monitoring (MRM) in positive and negative ion mode. The Applied standard for quantification and verification of pharmaceutical residues in water samples: LC retention time and MRM transitions. Data correspond to 100ng/ml of each pharmaceutical in ACN/H_2O.

Table 1. LC electrospray ionization MS/MS conditions, established experimentally

Compound	Group	Precursor ion (m/z)	Retention time	ESI Mode	Product ion (m/z)	MRM Transition
Cetirizine	Anti-histamines	389	0.96	+	201[M-H-$C_{13}H_{10}Cl]^+$ 166[M-H-$C_{13}H_{10}$]	389>201[a] 389>166[b]
Phenylephrine	Nasal Decongestants	168	0.79	+	107[M-H-$C_7H_7O]^+$ 134[M-H-$C_9H_{10}O]^+$	168>107[a] 168>134[b]
Diclofenac	Non-steroidal anti-inflammatory	294	3.53	-	250[M-H-$CO2]^-$ 214[M–H–$ClCO2]^–$	294>178[a] 294>214[b]
Triclosan	Antibacterial	287	4.88	-	35[M-H-$C_{12}H_7Cl_2O_2]^-$ 142	287>35[a] 287>142[b]

[a]MRM transitions used for quantification purposes
[b]MRM transitions for verification purpose

Figures 1 to 4 displays a representative chromatogram from LC-ESI-MS/MS for each pharmaceutical at 100 ng/mL in acetonitrile and water at a 50:50 (v/v) ratio. The targeted pharmaceuticals displayed typical fragmentation from the chosen precursor ions and exhibited behaviour that was consistent with that described in earlier studies.

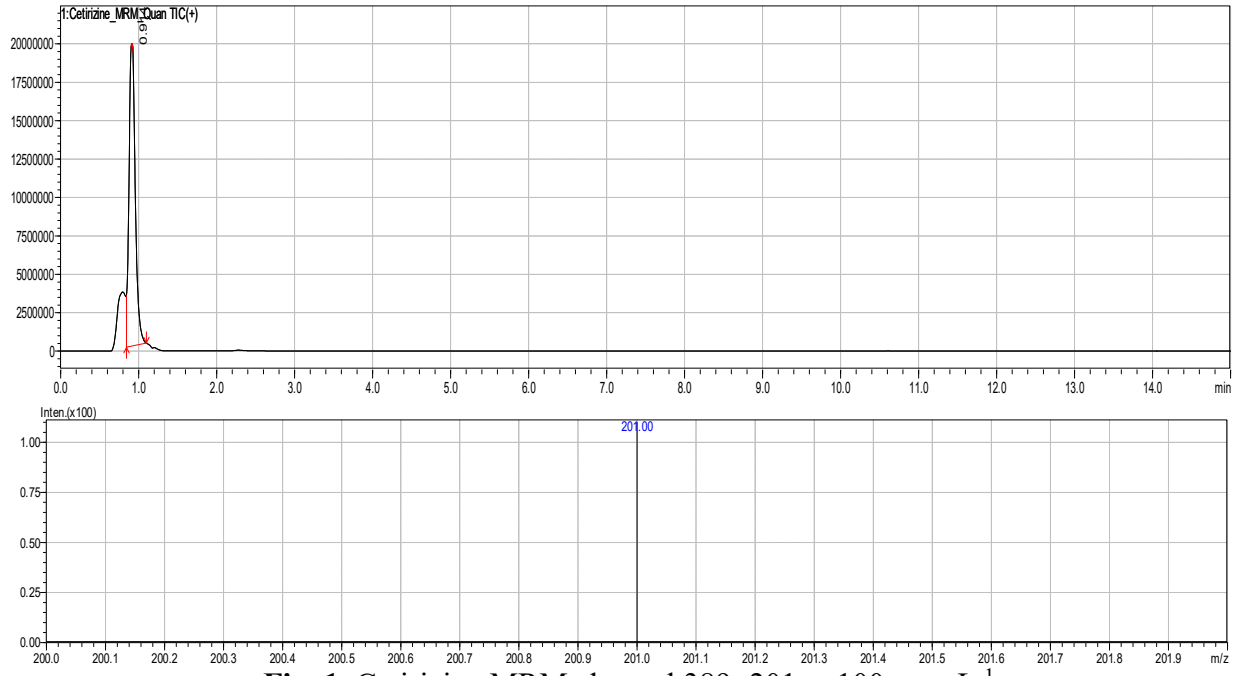

Fig. 1. Cetirizine MRM channel 389>201 at 100 ng mL^{-1}

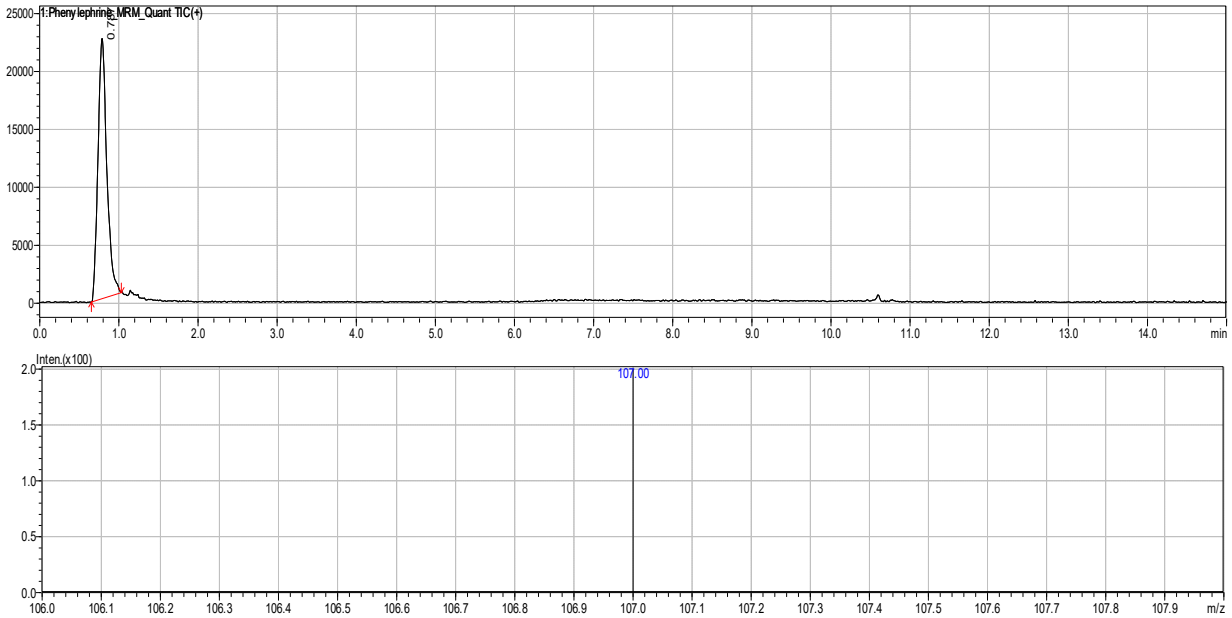

Fig. 2. Phenylephrine MRM 168>134 at 100 ng mL^{-1}

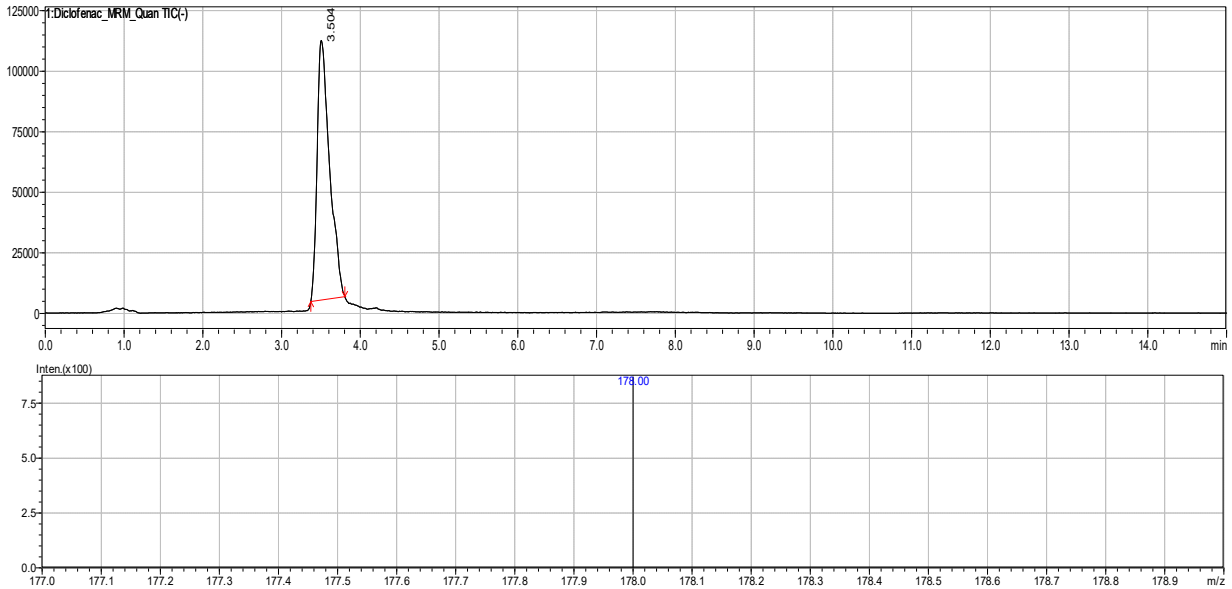

Fig. 3. Diclofenac MRM 294>178 at 100 ng mL^{-1}

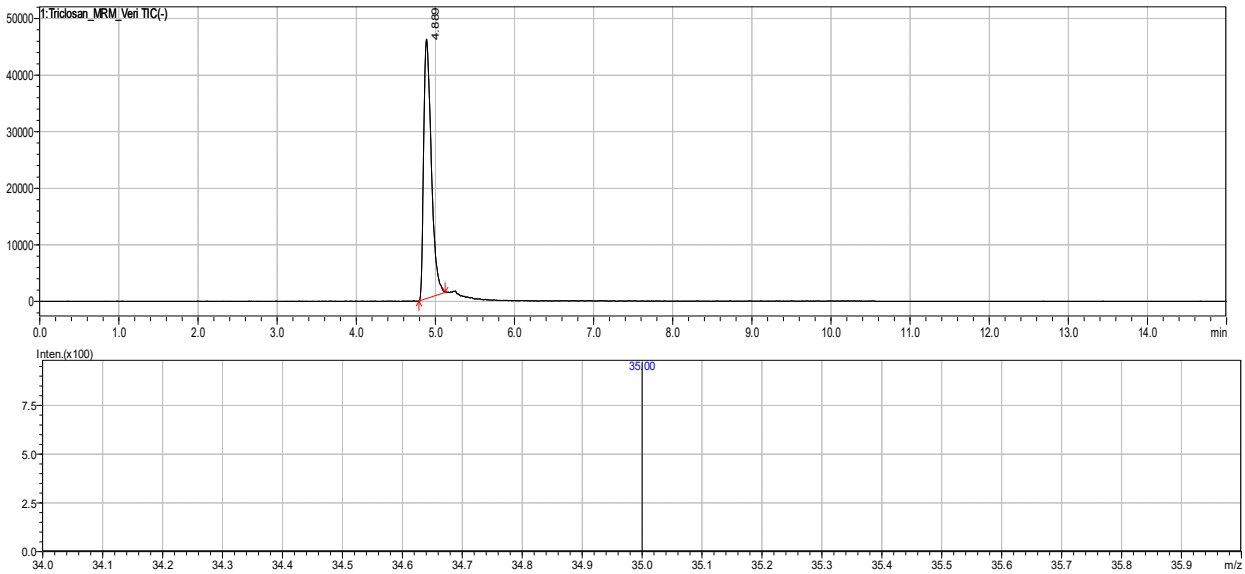

Fig. 4. Triclosan MRM 287>35 at 100 ng mL^{-1}

It was possible to select the most intense MS/MS transitions by infusing individual pharmaceuticals at a concentration level of 100ng/ml in ACN/Water (1:1) in both ESI positive and negative mode. For the pharmaceuticals analysed in the positive mode, an intense protonated molecular ion $[M^{+}H]^{+}$ was obtained in the positive ESI mode while for those analysed in the negative mode the deprotonated molecular ion $[M^{-}H]^{-}$ was obtained. The Product ions were estimated under MS/MS conditions and the fragment ions agree with available data. The main fragments ion for Diclofenac is formed during the collision-induced dissociation are generated by expulsion of CO_2 molecules $[M\text{-}H\text{-}CO2]^{-}$ [m/z =250] for the first transition and $[M–H–ClCO2]^{-}$ [m/z = 214] for the second transition. For Cetirizine m/z = 201 is identified as the first transition at $[M\text{-}H\text{-}C_{13}H_{10}Cl]^{+}$ and[m/z = 166]corresponding to $[M\text{-}H\text{-}C_{13}H_{10}]$ is used for the second transition. Triclosan has a characteristic products ion [m/z = 35] which signifies removal of Cl $[M\text{-}H\text{-}C_{12}H_7Cl_2O_2]^{-}$ which is used for the first transition and [m/z = 142] The major fragmentation pattern detected for Phenylephrine was attributed to $[M\text{-}H\text{-}C_7H_7O]^{+}$ [m/z = 107] was used for the first transition while [m/z = 134] corresponding to $[M\text{-}H\text{-}C_9H_{10}O]^{+}$ was used for the second transition.

Method validation

The calibration curves were linear for the pre-determined calibration ranges for the individual pharmaceutical standard (cetirizine, phenylephrine, diclofenac and triclosan), figures 5 to 8. The calibration curve was evaluated by analysing twelve different concentrations of the standard solutions within the range of 0.0001÷50 ug mL^{-1}. The standard guidelines were used for the determination of detection limit (LOD) and quantification limit (LOQ). The LOD and LOQ obtained were between 0.005 and 0.050 ng mL^{-1} and from 0.10 to 0.50 ng mL^{-1}, respectively (Table 2). The limits achieved were satisfactory for environmental analysis. Accuracy value was 2 (approximately 98%) for the measured calibration concentration and precision value was lower than <10%. The value obtained for accuracy and precision of the measurements are appropriate for analytical analysis.

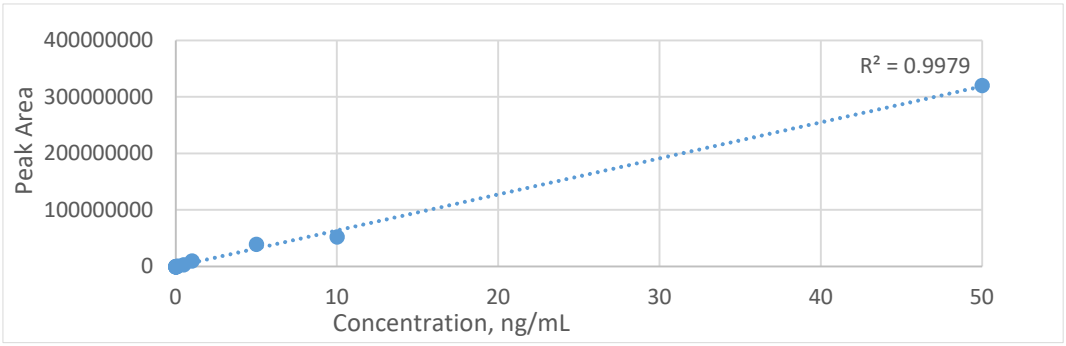

Fig. 5. Calibration curve for cetirizine standard

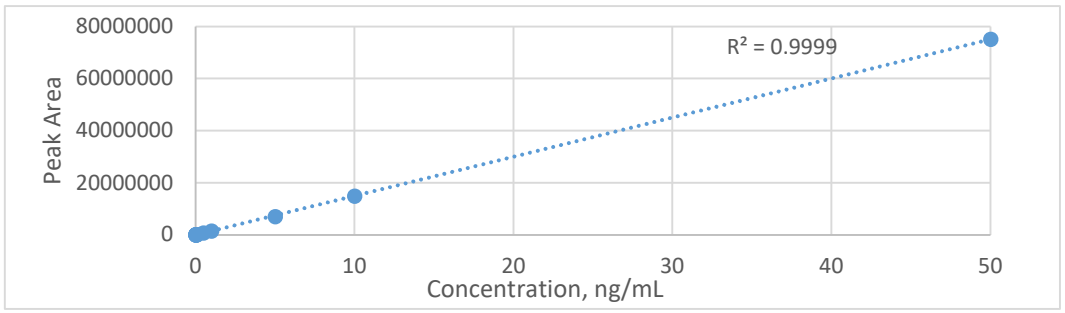

Fig. 6. Calibration curve for phenylephrine standard

The regression equations and the correlation coefficients (r^2 ≥0.997) for all pharmaceutical's standards are shown in Table 2. Extraction recovery of the compounds in multicomponent solvent spiked at 100 ng mL^{-1} ranged from 55.7 to 80.2%. The extraction recovery results for all compounds were determined by comparing the peak areas of the pharmaceutical standard in acetonitrile/water solution at 100 ng mL^{-1} before and after extraction. The Peak Area after extraction is the peak area of the analyte in the standard solution after going through the solid phase extraction process.

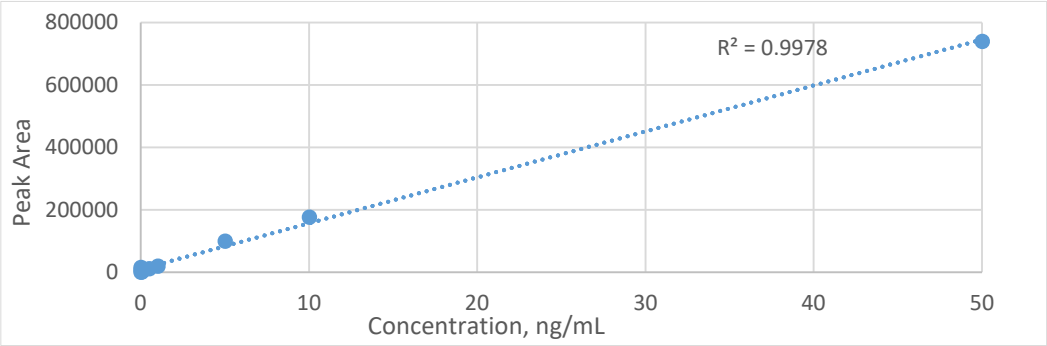

Fig. 7. Calibration curve for diclofenac standard

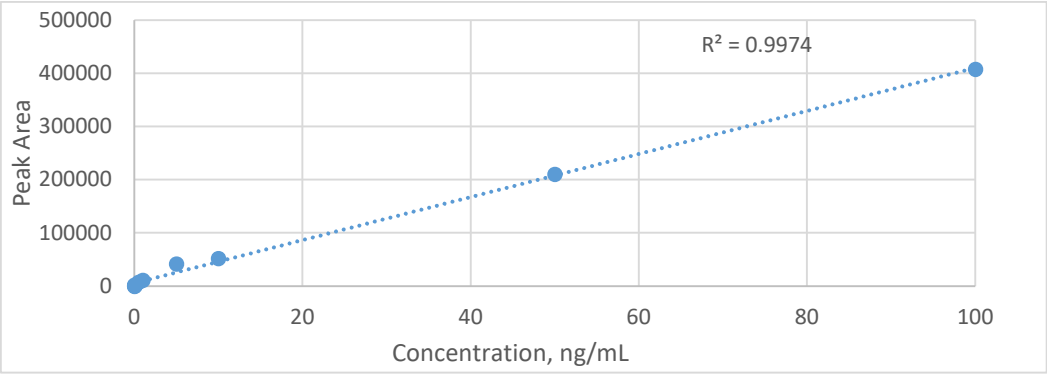

Fig. 8. Calibration curve for triclosan standard

While the peak area before extraction refers to the peak area of the analyte in the unprocessed standard solution (i.e., the standard solution before undergoing any sample preparation). Though the extraction recovery for triclosan was lower compared to another pharmaceutical standard. However, the overall performance of the method was still acceptable with respect to extraction recovery (55.7÷80.2%) and precision (<10%). The LODs and LOQs are in the range of 0.005 to 0.050 ng mL^{-1}, and the method LOQs varied from 0.10 to 0.50 ng mL^{-1}, which are still comparable to those of earlier method reported. Average recovery rates (n=3) from deionized water and river water samples ranged from 87 to 95% for the experiments performed at 100 and 1,000 ng mL^{-1}, and the standard deviation was acceptable (1.2÷5%).

Analytical parameters of the solid-phase extraction liquid chromatography (LC) mass spectrometry (MS/MS) method. Extraction recovery rates (%) from multicomponent solvent spiked at 100 ng/ml, linearity, LOD and LOQ.

Table 2. Analytical parameters for SPE-LC-MS/MS method

Compound	Range (ng/mL)	Calibration equation	R^2	LOD (ng/mL)	LOQ (ng/mL)	Recovery (%)
Cetirizine	0.0001÷50	y=5407364x+2780074	0.9979	0.010	0.10	80.2
Phenylephrine	0.0001÷50	y=1434080x+205953	0.9999	0.005	0.50	78.2
Diclofenac	0.01÷50	y = 12505x + 22846	0.9978	0.005	0.10	58.6
Triclosan	0.005÷100	y = 3963.8x + 6238.6	0.9974	0.050	0.10	55.7

Sample analysis

The positive quantification findings of the pharmaceuticals (Cetirizine, Phenyleprine, Diclofenac and Triclosan) in the three sampling sites along Winestead drain are represented in Fig. 3. All the four pharmaceuticals analysed were detected in the river water with varying concentration ranging from 0.005 to 0.01 ng mL^{-1}. The relative standard deviation (RSDs) of the results (n=3) in the analysed water sample was less than 20%, indicating that the analytical procedure provided precise results. Samples taken from the three separate locations were quantified at concentrations equal to or greater than the LOQ for all the pharmaceuticals under study, Fig. 9.

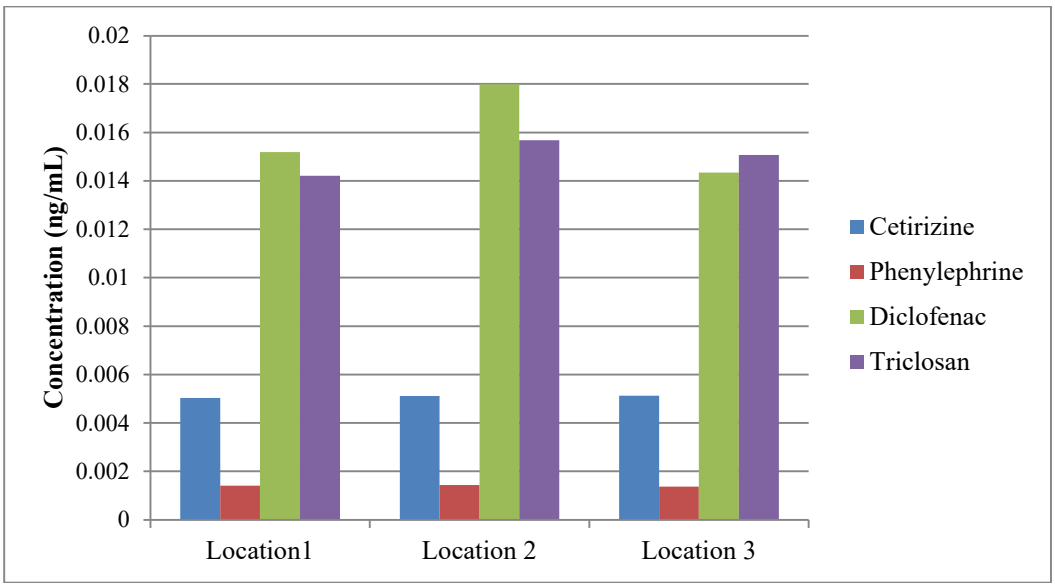

Fig. 9. Distribution of the compounds in the sampled locations (average value, ng/mL)

Diclofenac shows the highest concentration ranging from 0.0143 ng mL^{-1} to 0.0179 ng mL^{-1} at one of the sampled locations. The occurrence of diclofenac residues in river water could be as a result of large amount of it been used as painkillers, and can be gotten over the counter as over the counter (OTC) drugs without prescription. Followed by Triclosan which concentration ranges between 0.0142 ng mL^{-1} to 0.0157 ng mL^{-1}. The presence of triclosan in the water sample could be attributed to it abundance as a result of its bulk usage mainly in personal care products such as soaps, toothpastes and sterilizer. The concentration of Cetirizine is between the range 0.0050 ng/mL to 0.0051 ng/mL. Cetirizine (An antihistamine) usage is mostly based on treating seasonal allergic reactions (high fever), which may be reflected in seasonal fluctuations in pharmaceutical concentrations in river water. Phenylephrine was observed in lower frequency than the rest of pharmaceuticals studied in all the sampled location ranging from 0.0013 ng mL^{-1} to 0.0014 ng mL^{-1}. From the results obtained, it could be established that the conventional treatments plants were not able to remove completely most pharmaceuticals before they are discharged into waterways [31,32]. A significant number of pharmaceuticals are used annually in treating and preventing diseases in both humans and animals. Although the amounts of pharmaceuticals residues found in river waters and the environment are many orders of magnitude lower than those needed to cause effects in humans or animals, their long-term impacts on the environment are typically an issue of concern within the scientific community.

CONCLUSIONS

A quick and effective method based on solid phase extraction and liquid chromatography-tandem mass spectrometry was validated, allowing the determination of four pharmaceuticals (cetirizine, phenylephrine, diclofenac and triclosan) with different physical-chemical properties in river water. The application of SPE as a sample preparation technique plays a fundamental role in the successful detection of trace levels of the pharmaceuticals in the water sample. By selectively extracting target analytes and eliminating interference from matrix components, SPE enhances the sensitivity and accuracy of subsequent LC-MS/MS analysis, allowing for reliable quantification of the pharmaceuticals even at low concentrations. The LC-MS/MS technique, with its high sensitivity, selectivity, and wide dynamic range, proves to be an indispensable tool for the analysis of these pharmaceutical compounds in the river water. The LC-MS/MS determination of the pharmaceutical residues was satisfactory, enabling verification and quantification using the MRM acquisition mode, by monitoring at least two ion transitions for each of the pharmaceuticals under study which is in compliance with EU regulation for confirmation of pharmaceutical residues in aquatic environment. The method achieved satisfactory recoveries and precisions for the four pharmaceuticals which were in line with previously reported studies. The key results of the study showed that the method was able to detect and quantify trace levels of pharmaceuticals in river water with limits of detection

ranging from of (0.005÷0.050 ng/mL) and limit of quantification ranging from (0.10÷0.50 ng/mL) respectively.

REFERENCES

[1] YU, T., LIN, A.Y., PANCHANGAM, S.C., HONG, P.A., YANG P., LIN, C., Chemosphere, **84**, no. 9, 2011, p. 1216, https://doi.org/10.1016/j.chemosphere.2011.05.045.

[2] IZADI, P., IZADI, P., SALEM, R., PAPRY, S.A., MAGDOULI, S., PULICHARLA, R., BRAR, S.K., Environ. Pollut., **267**, 2020, https://doi.org/10.1016/j.envpol.2020.115370.

[3] BARROSO, P.J., SANTOS, J.L., MARTÍN, J., APARICIO, I., ALONSO, E., Crit. Rev. Environ. Sci. Technol., **49**, 2019, p.104, https://doi.org/10.1080/10643389.2018.1540761.

[4] SACHER, F., LANGE, F.T., BRAUCH, H., BLANKENHORN, I., J. Chromatogr. A, **938**, no. 1-2, 2001, p. 199, https://doi.org/10.1016/s0021-9673(01)01266-3.

[5] OLANIYAN, L.W.B., MKWETSHANA, N., OKOH, A.I., SpringerPlus, **5**, 2016, https://doi.org/10.1186/s40064-016-3287-x.

[6] PROSSER, R.S., SIBLEY, P.K., Environ. Int., **75**, 2015, p. 223, https://doi.org/10.1016/j.envint.2014.11.020.

[7] PETROVIC, M., GONZALEZ, S., BARCELÓ, D., TrAC Trends Anal. Chem., **22**, no. 10, 2003, p. 685, https://doi.org/10.1016/S0165-9936(03)01105-1.

[8] FARRÉ, M., GROS, M., HERNÁNDEZ, B., PETROVIC, M., HANCOCK, P., BARCELÓ, D., Rapid Commun. Mass Spectrom., **22**, no. 1, 2008, p. 41, https://doi.org/10.1002/rcm.3324.

[9] GREEN, G.A., Clin. Cornerstone, **5**, no.1, 2001, p. 50, https://doi.org/10.1016/S1098-3597(01)90069-9.

[10] MADUREIRA, T.V., BARREIRO, J.C., ROCHA, M.J., CASS, Q.B., TIRITAN, M.E., J. Chromatogr. A, **1216**, no. 42, 2009, p. 7033, https://doi.org/10.1016/j.chroma.2009.08.060.

[11] MEIJIDE, J., LAMA, G., PAZOS, M., SANROMÁN, M.A., DUNLOP, P.S., J. Environ. Chem. Eng., **10**, no. 3, 2022, https://doi.org/10.1016/j.jece.2022.107630.

[12] HERNANDO, M.D., HEATH, E., PETROVIC, M., BARCELÓ, D., Anal. Bioanal. Chem., **385**, 2006, p. 985, https://doi.org/10.1007/s00216-006-0394-5.

[13] CHOI, K., KIM, Y., PARK, J., PARK, C.K., KIM, M., KIM, H.S., KIM, P., Sci. Total Environ., **405**, no.1-3, 2008, p. 120, https://doi.org/10.1016/j.scitotenv.2008.06.038.

[14] SCHULZE, T., WEISS, S., SCHYMANSKI, E., VON DER OHE, P.C., SCHMITT-JANSEN, M., ALTENBURGER, R., STRECK, G., BRACK, W., Environ. Pollut., **158**, no. 5, 2010, p. 1461, https://doi.org/10.1016/j.envpol.2009.12.032.

[15] LONAPPAN, L., BRAR, S.K., DAS, R.K., VERMA M., SURAMPALLI, R.Y., Environ. Int., **96**, 2016, p. 127, https://doi.org/10.1016/j.envint.2016.09.014.

[16] BISCEGLIA, K.J., YU, J.T., COELHAN, M., BOUWER, E.J., ROBERTS, A.L., J. Chromatogr. A, **1217**, no.4, 2010, p. 558, https://doi.org/10.1016/j.chroma.2009.11.062.

[17] GRABIC, R., FICK, J., LINDBERG, R.H., FEDOROVA, G., TYSKLIND, M., Talanta, **100**, 2012, p. 183, https://doi.org/10.1016/j.talanta.2012.08.032.

[18] VIENO, N.M., TUHKANEN, T., KRONBERG, L., J. Chromatogr. A, **1134**, no. 1-2, 2006, p. 101, https://doi.org/10.1016/j.chroma.2006.08.077.

[19] DAUGHTON, C.G., TERNES, T.A., Environ. Health Perspect., **107**, no. 6, 1999, p. 907, https://doi.org/10.1289/ehp.99107s6907.

[20] STOKER, T.E., GIBSON, E.K., ZORRILLA, L.M., Toxicol. Sci., **117**, no. 1, 2010, p. 45, https://doi.org/10.1093/toxsci/kfq180.

[21] MA, J., GUO, X., Front. Nutr.,**12**, 2025, https://doi.org/10.3389/fnut.2025.1596673.

[22] FRAKER, S.L., SMITH, G.R., Environ. Toxicol., **19**, no.3, 2004, p. 250, https://doi.org/10.1002/tox.20017.

[23] HERNANDO, M.D., FERNÁNDEZ-ALBA, A.R., TAULER, R., BARCELÓ, D., Talanta, **65**, no. 2, 2005, p. 358, https://doi.org/10.1016/j.talanta.2004.07.012.

[24] POMATI, F., CASTIGLIONI, S., ZUCCATO, E., FANELLI, R., VIGETTI, D., ROSSETTI, C., CALAMARI, D., Environ. Sci. Technol., **40**, no. 7, 2006, p. 2442, https://doi.org/10.1021/es051715a.

[25] LOOS, R., LOCORO G., CONTINI, S., Water Res., **44**, no.7, 2010, p. 2325, https://doi.org/10.1016/j.watres.2009.12.035.
[26] PEDROUZO, M.L., Pharmaceuticals and personal care products in environmental waters. Universitat Rovira i Virgili, 2010, http://www.tdx.cat/TDX-0217111-103024.
[27] MUSARURWA, H., CHIMUKA, L., TAVENGWA, N.T., J. Environ. Sci. Health B, **54**, no.9, 2019, p. 770, https://doi.org/10.1080/03601234.2019.1633213.
[28] OSORIO, V., SCHRIKS, M., VUGHS, D., DE VOOGT, P., KOLKMAN, A., Talanta, **186**, 2018, p. 527, 10.1016/j.talanta.2018.04.058.
[29] OMOTOLA, E.O., OLATUNJI, O.S., Heliyon, **6**, no.12, 2020, https://doi.org/10.1016/j.heliyon.2020.e05787.
[30] TSIZIN, S., BOKKA, R., KESHET, U., ALON, T., FIALKOV, A.B., TAL, N., AMIRAV, A., Int. J. Mass Spectrom., **422**, 2017, p. 119, https://doi.org/10.1016/j.ijms.2017.09.006
[31] TERNES, T.A., Water Res., **32**, no.11, 1998, p. 3245, https://doi.org/10.1016/S0043-1354(98)00099-2.
[32] STACKELBERG, P.E, GIBS, J., FURLONG, E.T., MEYER, M.T., ZAUGG, S.D., LIPPINCOTT, R.L., Sci. Total Environ., **377**, no. 2-3, 2007, p. 255, https://doi.org/10.1016/j.scitotenv.2007.01.095.

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