ISSN-1996-918X

Pak. J. Anal. Environ. Chem. Vol. 21, No. 2 (2020) 232 – 246

http://doi.org/10.21743/pjaec/2020.12.25

Determination of Acetylsalicylic acid and Naproxen in waste and Tap Water of the Municipal Area of the Sukkur City by SPE-LC-MS/MS

Waheed Ali Mirbahar[1], Mir Munsif Ali Talpur[*1], Tajnees Pirzada[1] and Syed Ghulam Musharraf[2]

[*1]*Institute of Chemistry, Shah Abdul Latif University, Khairpur, Sindh, Pakistan.*

[2]*International Center for Chemical and Biological Sciences (ICCBS), University of Karachi, Karachi-75270, Pakistan.*

**Corresponding Author Email: mirmunsif_salu@yahoo.com*

Received 24 February 2020, Revised 10 August 2020, Accepted 15 September 2020

Abstract

This study is based on an environmental assessment of acetylsalicylic acid and naproxen in waste and tap water samples of twenty different locations of municipal area of Sukkur city, Sindh, Pakistan. Both drugs belong to the most frequently used Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) group. The specified pharmaceuticals were extracted from the wastewater and tap water samples by Solid Phase Extraction (SPE) method using Waters Oasis hydrophilic lipophilic balance (HLB) cartridges. Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) technique was applied for the detection and quantification of selected drugs. Negative Electron Spray Ionization (ESI) was used along with Multi Reaction Monitoring (MRM) mode. Pharmaceuticals concentration were found 7.38-827 µg/L and 5.47-328.95 µg/L in waste and tap water samples, respectively. The results obtained are comparable with the data reported in literature. Human health risk assessment caused by acetylsalicylic acid and naproxen in aquatic media was observed by applying Risk Quotient (RQ) approach. The calculated RQ values are low enough (order of 10^{-3} to 10^{-5}) to cause a direct risk for consumers, but their presence in water may pose a danger synergistically.

Keywords: Waste water, Tap water, Non-steroidal anti-inflammatory drugs (NSAIDs), Solid phase extraction (SPE), Liquid chromatography-mass spectroscopy (LC-MS/MS), Risk assessment.

Introduction

Water is the vital natural source for health and survival of living things [1]. The availability of pure drinking water for human beings on earth is a great challenge due to industrialization, urbanization and ever increasing population in present time [2]. All unnecessary materials entering into water through various unhealthy activities by mankind causes water pollution [3]. Being a universal solvent, it is directly related to basic need for living creatures, but also a major source to cause diseases. According to World Health Organization (WHO), 80% diseases are waterborne. Globally 3.1% population dies due to the inappropriate quality of water [4]. Major sources of water pollution are: industrial waste full of heavy metals, domestic waste, marine dumping, radioactive waste and atmospheric deposition [5]. Immune suppression, reproductive failure, skin diseases, cholera, vomiting, typhoid, extensively drug resistant (XDR) fever,

including damage of flora and fauna are some horrible episodes of polluted water [6].

Water pollution by pharmaceutically active compounds (PhACs) is one of the modern world health challenging problem which constitute a health risk to humans, animals as well as aquatic ecosystems [7].

Worldwide thousands of tons of pharmaceuticals are manufactured annually, which enter into aquatic media [8]. Hence continuous monitoring of the aquatic environment is essential for the quality status of water because water contamination affects the endocrine system of humans, negative effects on fish, bacteria, algae, plants and a particular risk for pregnant women, their babies as well as children along with aquatic organisms.. Humans and animal health care along with crop production is maintained by bulk use of pharmaceuticals which may enter the environment by hospital effluents, sewage sludge, municipal sewage, landfill leachates, contaminated liquid manure, septic tanks and livestock activities etc. [9]. Many purification techniques are being applied to get pure drinking water like chlorination, ozonation, bank filtration and slow sand filtration etc. But they are not much effective for purification of organic pollutants, especially pharmaceuticals due to their complex and non-biodegradable nature [10]. Work on pollutants have been mostly focused on low concentration contaminants like pharmaceuticals and their metabolites due to the high transformation rate in the environment and ineffective removal processes [11] which causes their presence in drinking water [12]. These drugs taken by humans and animals due to incomplete metabolism are excreted as parental compounds, synthetic precursors or their metabolites through urine and feces or manufacturing [13].

Non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly prescribed or self-medicated, as pain killers and fever reducing drugs in humans as well as at the veterinary side [14]. NSAIDs constitute human health issues like myocardial infarction, gastrointestinal bleeding, renal failure and reproduction system of aquatic organisms [15]. NSAIDs cause different types of ulcers and their chronic use may produce intestinal perforations [16]. Metabolites are by-product derivatives of parent pharmaceutical compounds formed biotically or abiotically [17]. Drug metabolism in the human body involves the conversion of parent pharmaceuticals into more soluble & more polar metabolites through a series of complex reactions for the purpose of physiological action and easy elimination [18]. Drug metabolites, also have ability to revert into their original form of the drug. These bio transformation products undergo further reactions to produce more reactive metabolites. These bio-active metabolites are dangerous to humans, as they can bind to proteins and other cellular parts, to disrupt cellular function, a toxic effect and an immune response or none at all. This may also inhibit the activity of cytochrome enzymes, affecting the metabolism of other drugs; consequently they accumulate inside the body to cause severe toxic effects [19]. Regular intake of drugs for long time, even at sub-therapeutic level cause acute and chronic effects on human health [20].

Materials and Methods

Chemicals Required

Ultra-pure standards of acetylsalicylic acid and naproxen were purchased from Sigma-Aldrich (Germany). Organic solvents (methanol, acetone and ethyl acetate) of analytical grade (Merck, Germany) were used to prepare stock solutions and stored at -18°C.

LC-MS/MS grade formic acid (Thermo Fisher Scientific. Waltham, MA, USA).

Sampling

The tap and waste water samples were collected directly in 3L pre washed polyethylene plastic bottles from twenty different locations of municipal area of Sukkur city, Sindh, Pakistan, they were immediately transferred to the laboratory in a portable icebox and extracted within 48 h to avoid further degradation. For wastewater, scoop-type device was used and then the samples passed through a 2 mm sieve to remove sludge before entering into a collection unit. All glass wares were thoroughly cleaned, oven dried at 300°C for decontamination about 8 h and finally rinsed with Millipore Quality (Milli-Q) water before use. Milli-Q water purification system (Millipore Corporation, Bedford, MA, USA). Samples were collected randomly following the guidelines of Environmental Protection Agency (EPA) [21] from the locations shown in Table 1 Global Positioning System (GPS) was adopted to locate the position of a place properly at latitudes and longitudes.

Solid Phase Extraction (SPE) of Raw Water Samples

Each water sample was filtered through Whatman's filter paper (pore size 1.6 µm). The filtrate was acidified with 3.5 M HCl to pH 2, in order to obtain maximum extraction of acidic compounds and stored at 4°C. Solid phase extraction oasis HLB cartridges (waters, international, USA) were conditioned successively with 3 mL ethyl acetate-acetone (50:50 v/v) mixture, 3 mL methanol and 3 mL ultrapure water (acidified to pH 2). These solutions have good interaction with the selected drugs so they are used to enhance the extraction efficiency [22, 23].

Table 1. **List of sampling stations of waste and tap water of municipal area of Sukkur city.**

Sample Nos.	Sampling Area	Sampling Stations, GPS coordinates	
		Latitude	*Longitude*
1	Al-Madina colony	27°42′ 59. 0"N	68°50′ 50. 6"E
2	Akhuwat Nagar colony	27°42′ 38. 0"N	68°50′ 13. 1"E
3	Bhosa line	27°42′ 15. 9"N	68°51′ 54. 9" E
4	Barrage colony	27°41′ 28. 1"N	68°51′ 0 4. 1" E
5	Bandar road	27°41′ 27. 8"N	68°52′ 05. 5" E
6	Shikarpur phatak	27°42′ 26. 0"N	68°50′ 49. 6" E
7	Shams abad	27°41′ 33. 6"N	68°51′ 22. 8" E
8	Bhutta road	27°41′ 34. 0"N	68°51′ 28. 2" E
9	Canal road	27°43′ 13. 7"N	68°48′ 35. 1" E
10	Goldsmith bazaar	27°41′ 38. 1"N	68°52′ 03. 7" E
11	Golimar	27°42′ 27. 4"N	68°50′ 58. 1" E
12	Gharibabad	27°41′ 43. 1"N	68°51′ 43. 0" E
13	Ghantaghar	27°41′ 40. 2"N	68°51′ 51. 0" E
14	High court road	27°41′ 39. 6"N	68°51′ 01. 9" E
15	Hussaini road	27°42′ 23. 4"N	68°52′ 55. 1" E
16	Local board	27°41′ 51. 2"N	68°52′ 25. 4" E
17	Locus park	27°41′ 42. 9"N	68°51′ 17. 2" E
18	Makrani muhalla	27°41′ 20. 8"N	68°51′ 42. 0" E
19	Miani road	27°41′ 23. 6"N	68°51′ 43. 5" E
20	Mobile market	27°41′ 41. 1"N	68°51′ 49. 4" E

Preconditioned, wet cartridges were loaded with 250 mL of wastewater and 1000 mL of tap water samples under vacuum at a flow rate of 12 to 15 mL/min, then washed with methanol-water (40:60 v/v) and dried under vacuum for 1 h. Then adsorbed analytes were eluted by 10 mL (50:50 v/v) ethyl acetate-acetone mixture.

The eluates were concentrated by rotary vaporizer and subsequently transferred to 1.5 mL glass vials. Ultimately the extracts were evaporated to dryness under a gentle stream of nitrogen and preserved at -18^{o}C for further analysis.

LC-MS/MS Quantitation

Quantification was performed by using Multi Reaction Monitoring (MRM) mode on 6460 Triple Quad, Agilent technologies mass spectrometer (USA) coupled with reverse

phase UPLC (1200 series infinitely Better, Agilent Technologies (USA) with thermostat, binary pump and auto-sampler at following instrumental conditions mentioned in Table 2.

Table 2. **Conditions optimized for LC-MS/MS analysis.**

UPLC conditions		LCMS/MS Conditions	
Column	XDB-C18 (Agilent technologies, 1.8 µm, 2.1 x 50 mm)	Temperature	300 °C
Mobile phase	H_2O (0.1 % acetic acid) (A) +ACN (B)	Nebulizer pressure (N_2)	40 psi
Mode	Isocratic mode, ACN + H_2O (0.1 % acetic acid) (1:1).	Drying gas flow (N_2)	9 L/min
Flow rate	0.2 mL/min	Ion source	ESI
Run time	5 min	Capillary voltage	4500/3500
Column thermostat	40 °C	Scan range (m/z)	50-500
Injection volume	5 µL	MRM mode	Positive/ Negative

Geomorphology of the Sampling Sites

Sukkur formerly Aroar and Bakhar, is the 14th largest city of Pakistan. It is situated on the west bank of the Indus River and is headquarter/capital of Division and District. Modern Sukkur was built by the British general Sir Charles Napier in the 1840s. It covers an area of 5,165 square kilometers while its population is 335,551 people. The city of Sukkur is located at an altitude of 220 feet (67 m) from sea level, having terrestrial coordinates 68°52' east and 27°42' north. The main source of drinking water for peoples is river Indus. The climate of Sukkur is characterized by very hot and hazy summer with dry and cool winter (10-50°C, wind speed at 10 km/h, 19% humidity). Sukkur is a hub of many small and large scale industries including pharmaceuticals. It is also a center of medical activities in upper Sindh. It has a medical college, a civil hospital and many governments as well as private medical centers.

Water Purification Processes Applied

Drinking water in Sukkur was purified by simple conventional methods in two steps. First it was co-agulated by alum and secondly disinfected by chlorine. No any kind of advance technique was applied, whereas ground water taken directly without any treatment [24].

Results and Discussion

Purity Assessment of Standard Drugs by UPLC

Purity assessment of standard drugs was performed by taking their UPLC profile at following conditions. Accurately weighed 1 mg of standards was dissolved in 1 mL methanol for stock solutions then appropriately diluted with mobile phase by following serial dilutions to achieve the desired concentration. Good peak shapes were obtained (Fig. 1-3) at following instrumental conditions (Table 3) showing high purity.

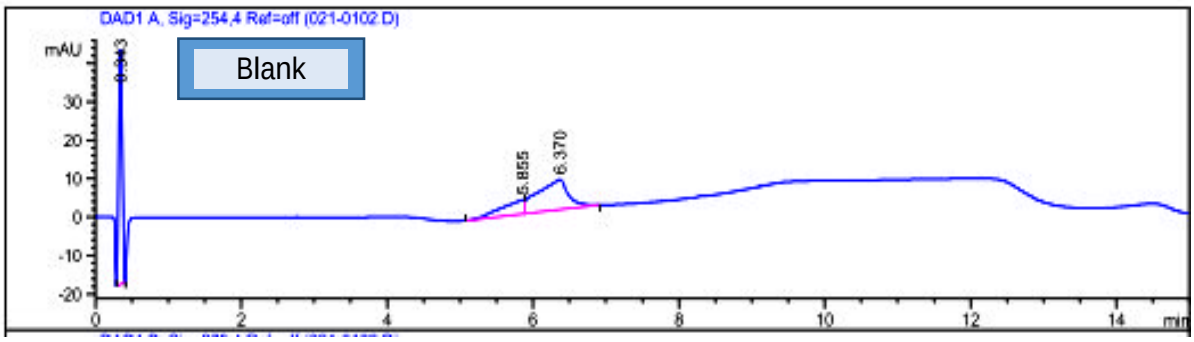


Figure 1. **UPLC profile for blank**

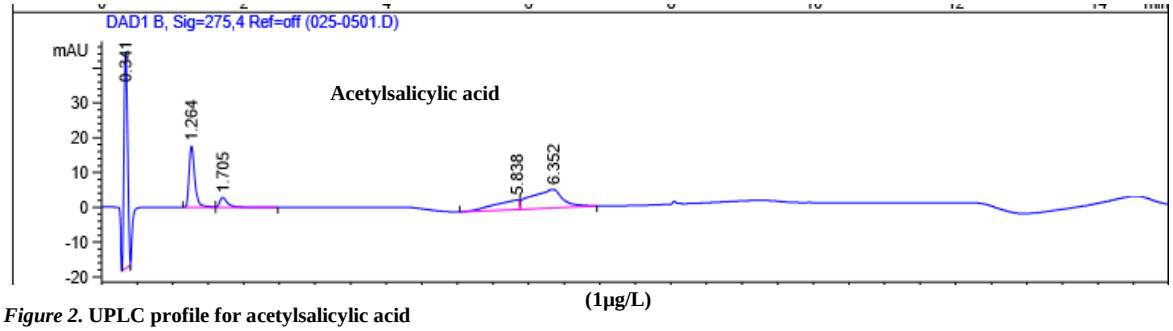


Figure 2. **UPLC profile for acetylsalicylic acid**

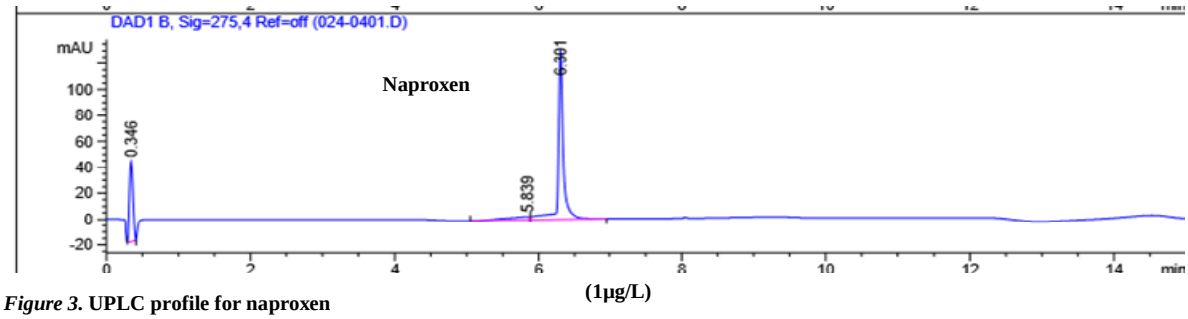


Figure 3. **UPLC profile for naproxen**

Table 3. **Conditions optimized for UPLC analysis.**

HPLC system	UPLC ultimate 3000, Agilent technologies
Wavelength	235 nm, 254 nm, 275 nm
Column	Poroshell 120, EC-18, 2.7 µm, 3.0, 50 mm
Mobile Phase	MeOH + H_2O(0.1% formic acid)
Flow Rate	0.5 mL/min
Injection Volume	5 µL
Run Time	14 min
Gradient Mode	MeOH (10%-90%) Water (90%-10%)

LC-MS/MS Analysis

Method Validation

The method linearity was established by constructing calibration curves at different concentration ns ranges from 0.5-1000 µg/L for each standard (Fig. 4a-4b).

The slope, regression coefficient and intercept were obtained from calibration curves. LOD and LOQ were calculated as the minimum detectable amount of the analyte with a signal-to-noise ratio of 3 and 10, respectively. The obtained results are shown in Table 4. Acetonitrile was used as a blank and for each analyte the value of R^2 was more than 0.99. One calibration standard and blank (ACN) were measured repeatedly throughout the sequence to check the instrumental background and signal stability.

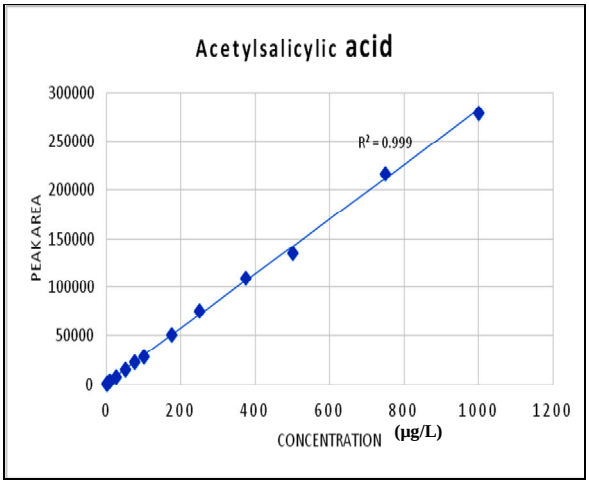


Figure 4a. **Calibration curve for acetylsalicylic acid**

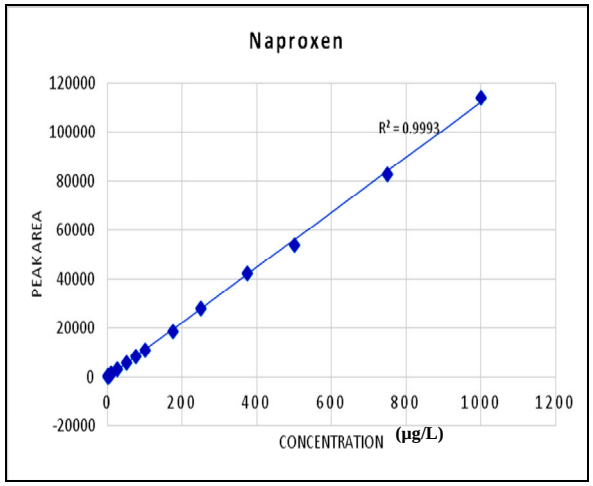


Figure 4b. **Calibration curve for naproxen**

Table 4. **LOD, LOQ, slope, regression equation and regression co-efficient.**

Analyte	Linear calibration range (µg/L)	Regression equations	R^2	LOD = 3×S/N (µg/L)	LOQ =10×S/N (µg/L)
Acetylsalicylic acid	0.5 – 1000	Y=281.2x + 980.21	0.999	0.28	0.84
Naproxen	0.5 – 1000	Y=112.08x– 96.685	0.9993	0.84	2.55

Method Precision

It was determined by intra-day and inter-day repeated analysis and expressed as relative standard deviation percentage (RSD %) and accuracy (%) in Table 5. Three standard mixtures of analytes at concentration of 125, 250 and 500 µg/L and six successive injections in one day and six consecutive days in triplicate were used, respectively. RSD for intra-day analysis was 0.99-2.1% and 1.3-2.3%, whereas inter-day analysis was 1.0-1. 3% and 0.9-3.5% for acetylsalicylic acid and naproxen, respectively.

Table 5. **Inter-day and intra-day precision of acetylsalicylic acid and naproxen .**

Drugs	Concent-rations (µg/L)	Intra-day			Inter-day		
		Found (µg/L)	RSD (%)	Accuracy (%)	Found (µg/L)	RSD (%)	Accuracy (%)
Acetyl-salicylic acid	125	126.4	0.99	101.1	126.9	1.3	101.5
	250	252.1	1.9	100.8	251.7	2.0	100.7
	500	498.3	2.1	99.7	498.6	1.0	99.7
Naproxen	125	127.3	1.6	101,8	126.5	1.1	101.2
	250	251.8	1.3	100.7	251.3	0.9	100.5
	500	496.7	2.3	99.3	495.1	3.5	99.0

LC-MS/MS Optimization

For quantitative analysis Agilent mass hunter software was used to optimize the parameters like collision energy (CE) and fragmentor voltage (FV) etc. mentioned in the Table 6. Multiple Reaction Monitoring (MRM) mode applied was negative ion mode. The most abundant fragment was selected for quantitative analysis (Fig. 6a-8).

Table 6. ***P*****arameters optimized for LC-MS/MS analysis.**

Reference Compounds	Retention time (min)	Precursor Type	Precursor *(m/z)*	MS/MS transitions *(m/z)*	Fragmentor Voltage	Collision Energy	Dwell Time
Acetylsalicylic acid	1.563	$[M-H]^-$ -ve mode	179	179--> 137	60	2	50
Naproxen	2.264	$[M-H]^-$ -ve mode	229	229 ---> 185	80	5	50

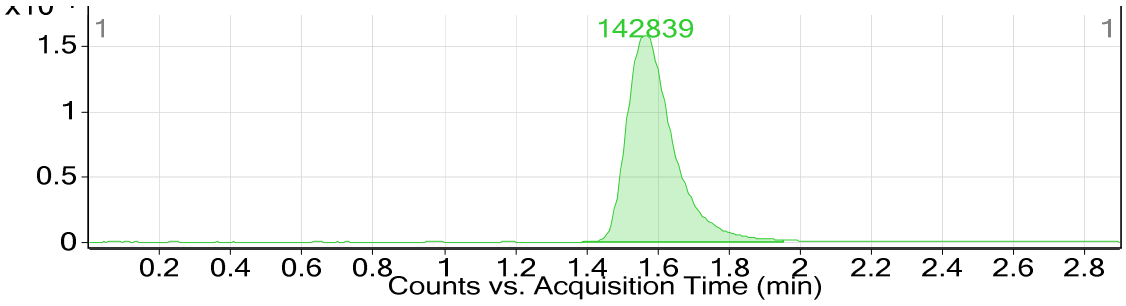


Figure 6a. **MRM chromatogram**

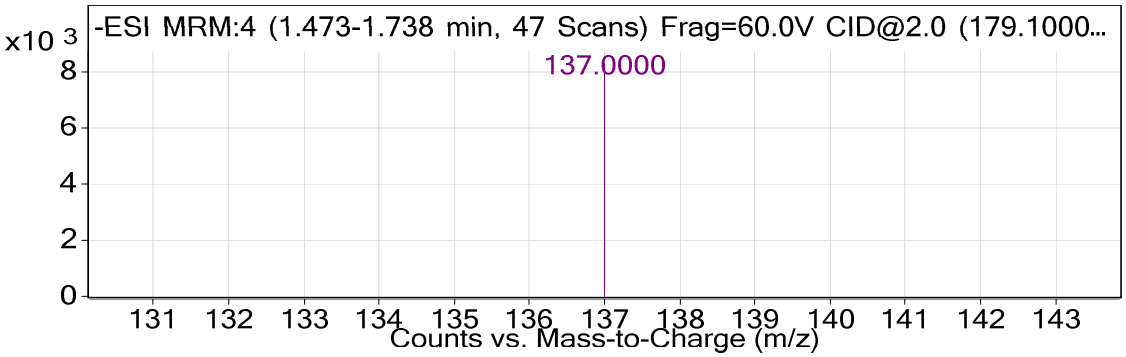


Figure 6b. **LCMS/MS transition for acetylsalicylic acid**

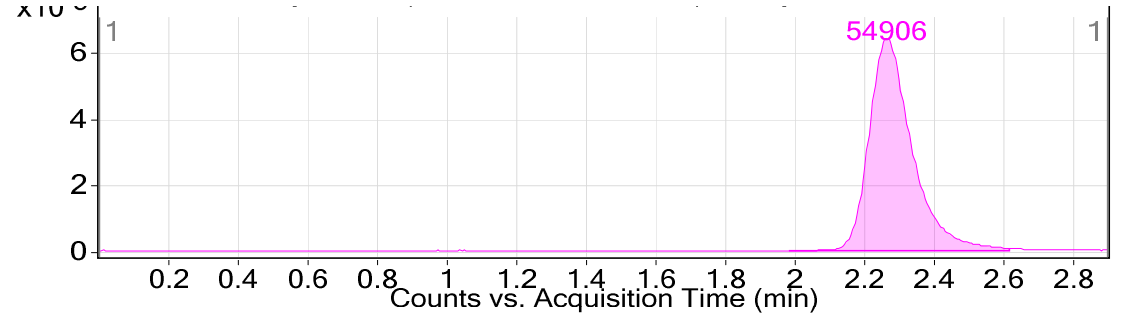


Figure 7a. **MRM chromatogram for naproxen**

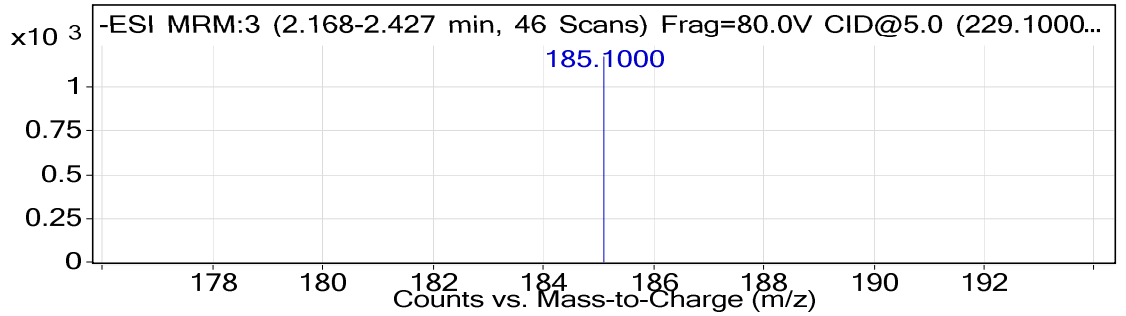


Figure7b. **MS/MS transition for naproxen**

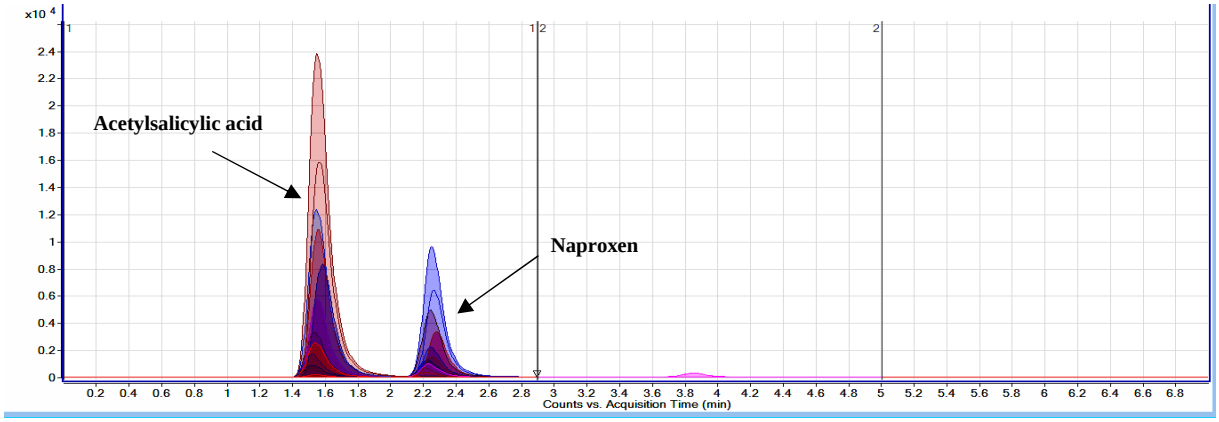


Figure 8. **MRM chromatograms of acetylsalicylic acid and naproxen**

Pharmaceuticals Detection in Waste and Tap Water

The results indicated that both pharmaceuticals naproxen and acetylsalicylic acid were present in waste as well as tap water samples Table 7-8 and Fig. 9-12. The concentration of acetylsalicylic acid ranges between 7.38-190.06 µg/L in waste water while 5.47-62.27 µg/L in tap water. At only one site similar detections were found from not detected 1.3 µg/L for acetylsalicylic acid in the water of the Umgeni river system in South Africa [33]. Among 20 samples it was present in all sites except W4 where it was below detection limit (BDL). In tap water, it was detected in all samples where as it was below detection limit in 6 samples (T3, T4, T5, T14, T17 and T20).

Naproxen has been found comparatively in greater concentration ranging from 26.80-827.61 µg/L and 8.96-328.95 µg/L in waste and tap water, respectively. Concentration of naproxen in waste water mentioned in Table 7 is in accordance with findings in influent and effluent from wastewater treatment plants (WWTPs) at France from 0.26-23.21 µg/L [26], at WWTPs of South Africa, from 15-20 µg/L [27] and in municipal waste effluents of Pachuca, Mexico from 20-47 µg/L [28]. Same drug was found in an Umgeni river system of South Africa up to 59.3 µg/L concentration [29]. The observed concentrations of the target pharmaceuticals in this study are in agreement with reported data in the literature [30-32].

Table 7. **Concentration of naproxen in waste and tap water samples.**

Naproxen in wastewater		Naproxen in tap water	
Sample Number	***Concentration (µg/L)***	***Sample Number***	***Concentration (µg/L)***
W1	115.46	T1	31.21
W2	255.73	T2	13.96
W3	26.80	T3	14.02
W4	479.79	T4	328.95
W5	266.16	T5	126.49
W6	244.10	T6	55.211
W7	377.25	T7	327.49
W8	41.43	T8	27.2
W9	75.09	T9	8.96
W10	54.71	T10	14.02
W11	601.64	T11	65.31
W12	148.10	T12	26.05
W13	681.09	T13	123.38
W14	537.55	T14	141.89
W15	76.56	T15	25.78
W16	827.61	T16	28.74
W17	114.39	T17	97.96
W18	119.78	T18	99.98
W19	91.42	T19	37.33
W20	254.69	T20	34.28

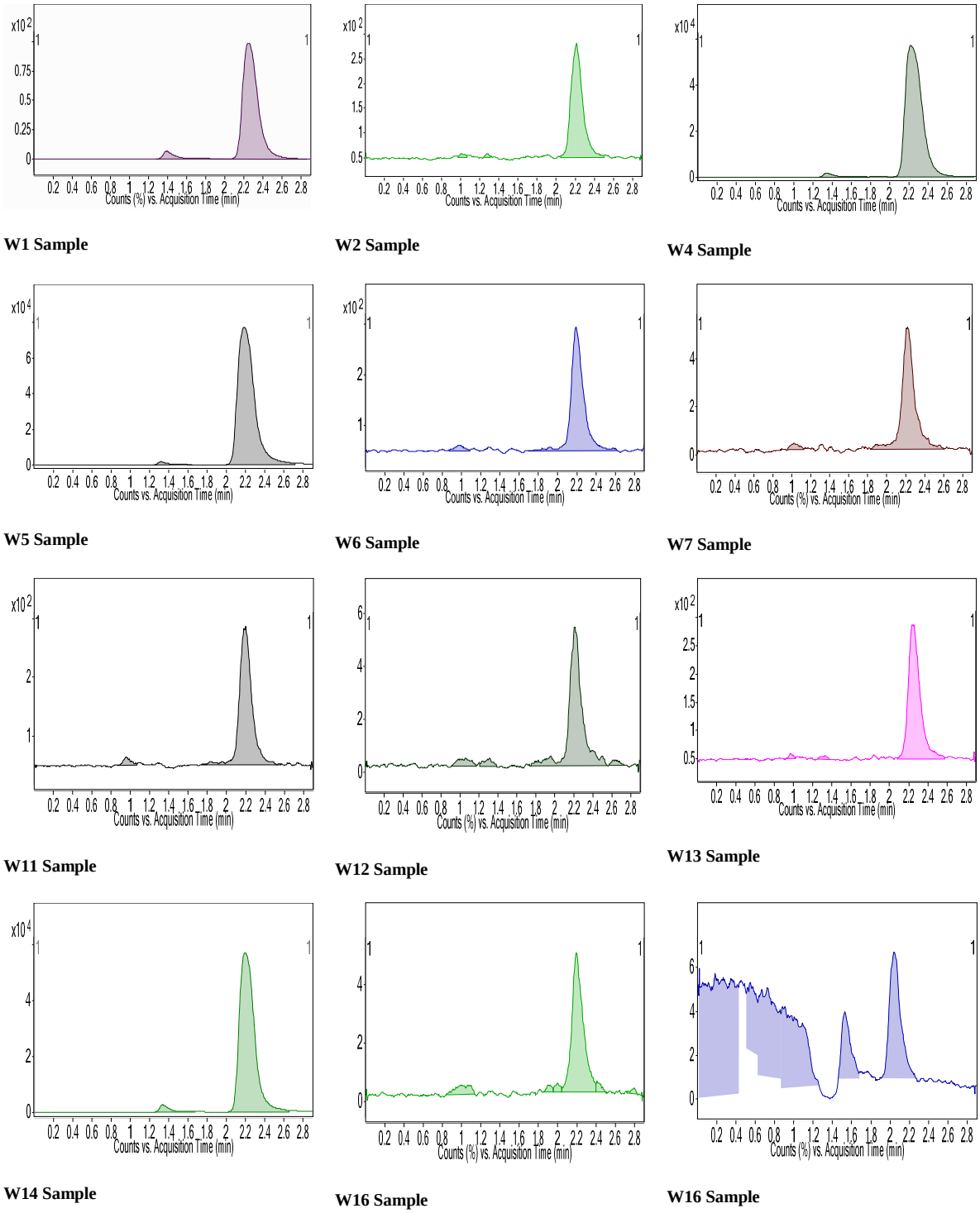


Figure 9. **MRM chromatograms of naproxen in waste water**

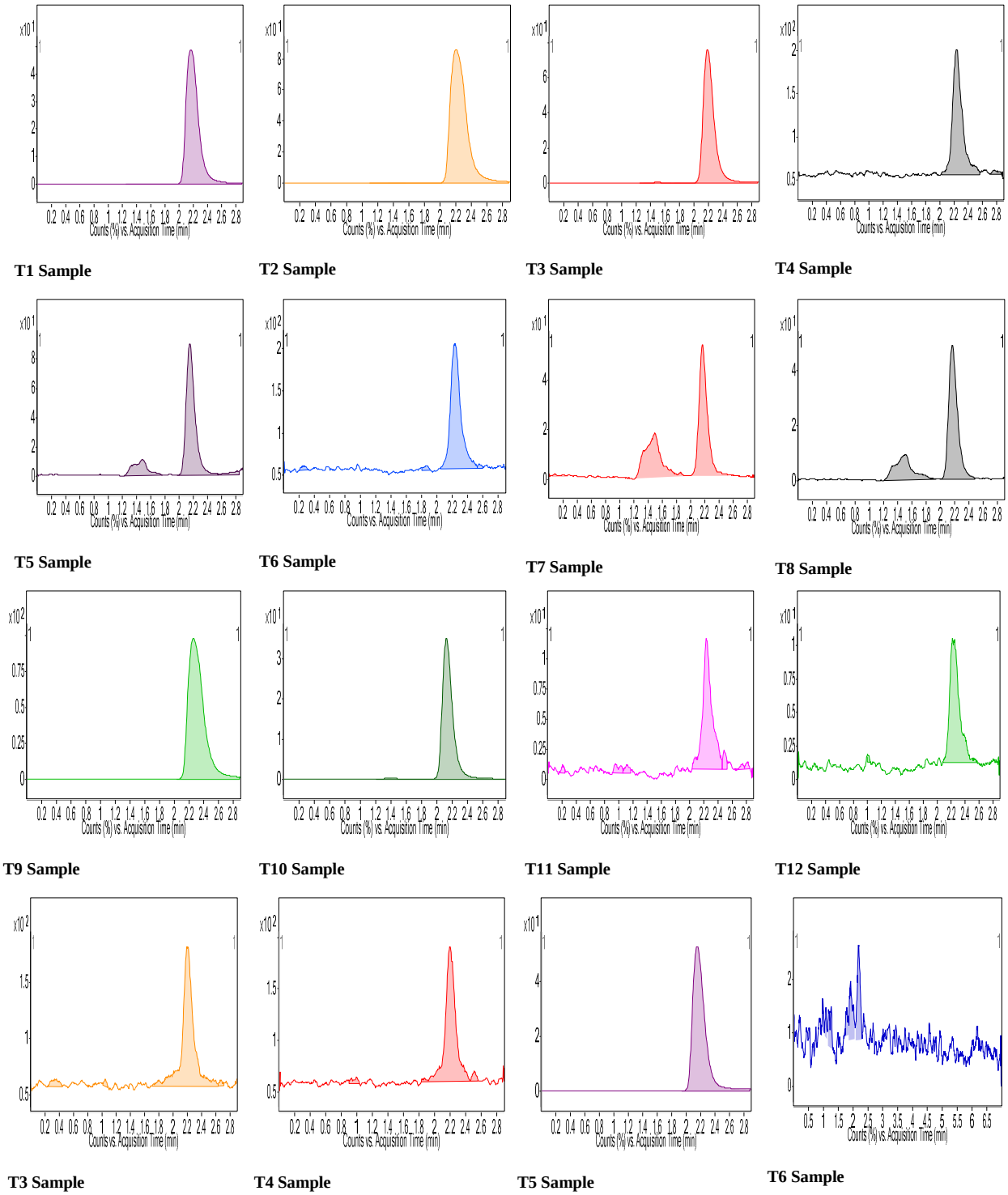
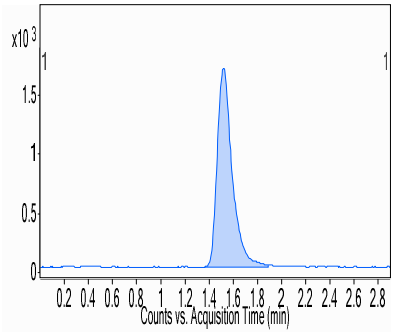
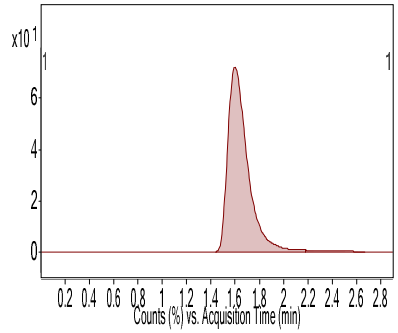


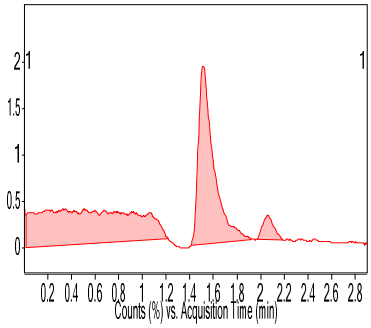
Figure 10. **MRM chromatograms for naproxen in tap water samples**



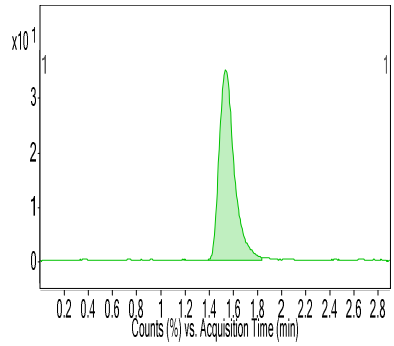
W1 Sample



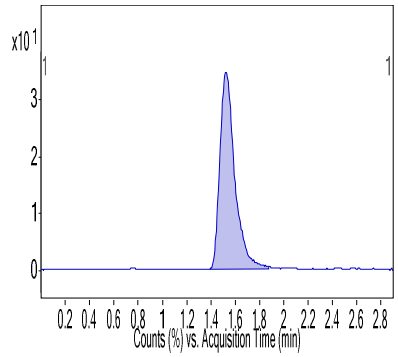
W2 Sample



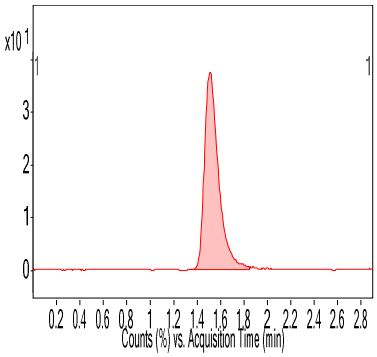
W3 Sample



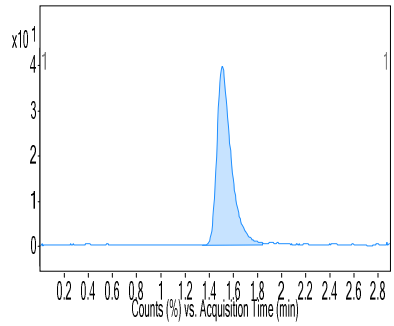
W6 Sample



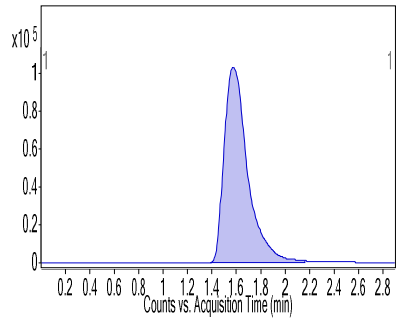
W7 Sample



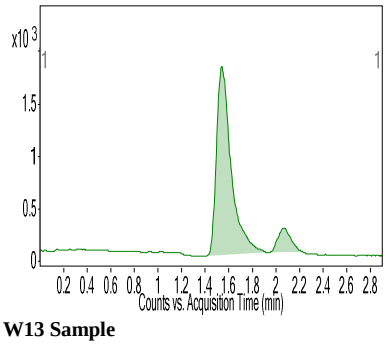
W8 Sample



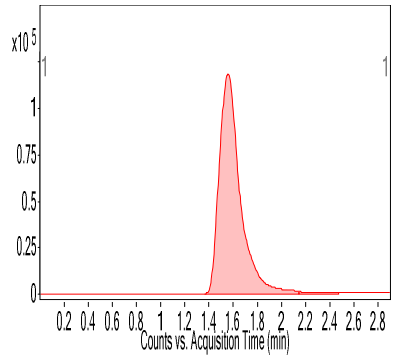
W9 Sample



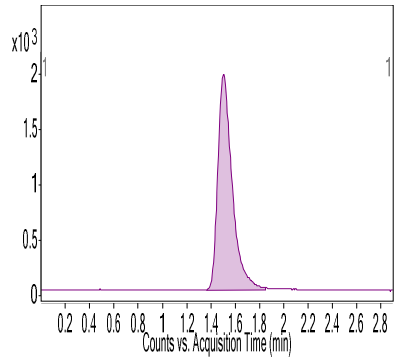
W10 Sample



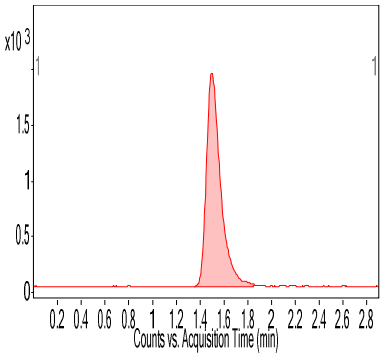
W13 Sample



W14 Sample



W16 Sample



W19 Sample

Figure 11. **MRM chromatograms of acetylsalicylic acid in wastewater samples**

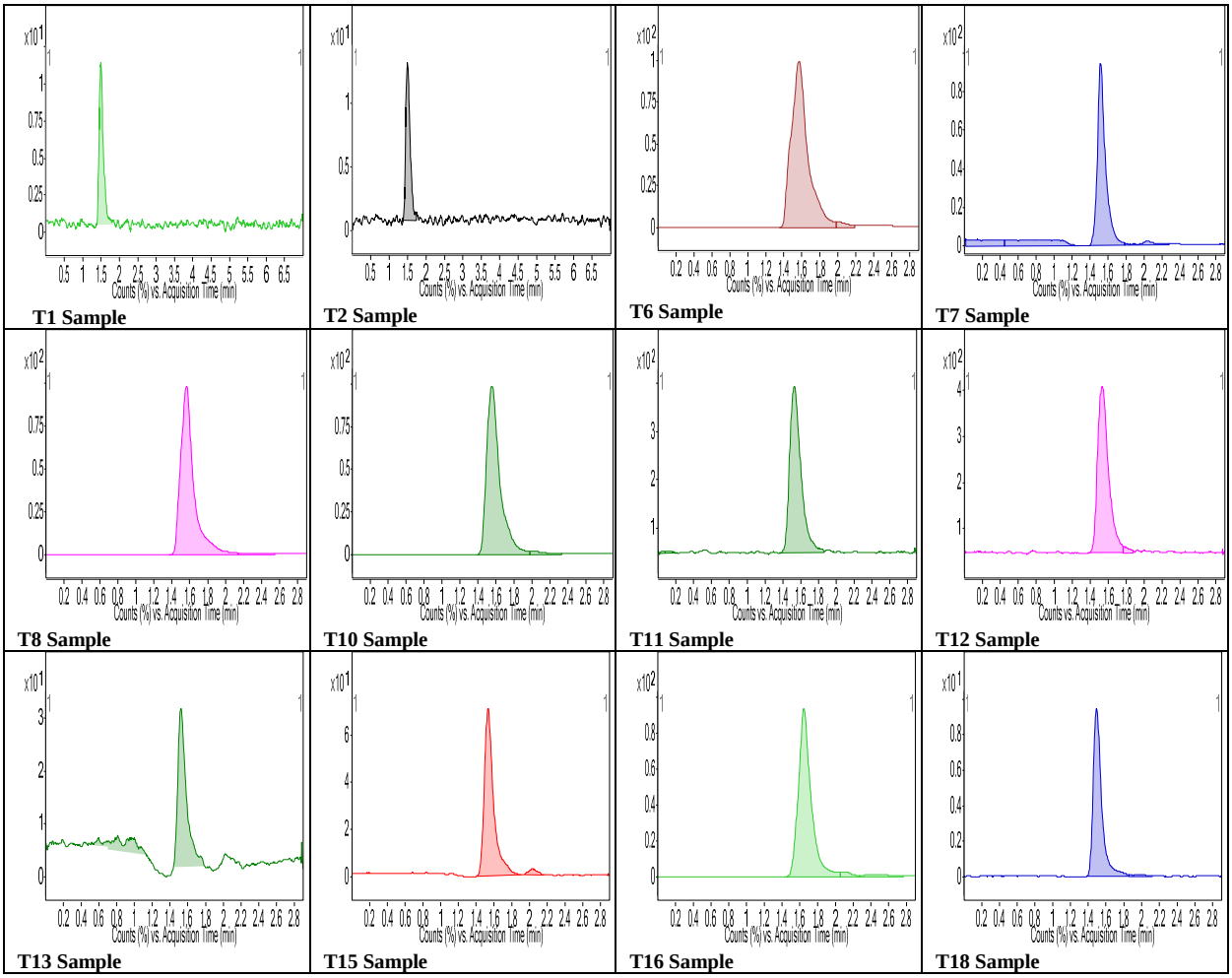


Figure 12. **MRM chromatograms for acetylsalicylic acid in tap water samples**

Table 8. **Concentration of acetylsalicylic acid in waste and tap water samples.**

Acetylsalicylic acid in wastewater		Acetylsalicylic acid in tap water	
Sample Number	***Concentration (µg/L)***	***Sample Number***	***Concentration (µg/L)***
W1	99.79	T1	62.27
W2	75.64	T2	56.90
W3	51.24	T3	BDL
W4	BDL	T4	BDL
W5	7.38	T5	BDL
W6	52.48	T6	8.55
W7	83.09	T7	30.85
W8	108.16	T8	7.42
W9	190.06	T9	ND
W10	186.89	T10	10.1
W11	8.12	T11	5.47
W12	7.35	T12	6.76
W13	12.02	T13	6.80
W14	23.29	T14	BDL
W15	22.63	T15	9.15
W16	48.01	T16	8.12
W17	24.83	T17	BDL
W18	25.12	T18	6.49
W19	52.85	T19	ND
W20	7.81	T20	BDL

Risk Assessment

Risk assessment can be calculated by many ways but the most common and reliable method is to measure, Risk Quotient (RQ) value by using Minimum Therapeutic Dose (MTD) of drugs [33].

RQ = $Cmx2/MTDx10^3$ where Cm=measured concentration in µg/L [34].

RQ value of both drugs (Table 9-10) is <<1 (order of 10^{-3} – 10^{-5}) in all samples indicating No observed adverse effect level (NOAEL) but it will contribute to combined water matrix effect, however continuous intake of these drugs combined with other drugs may be harmful and longtime use even in minor quantities may pose a serious risk to humans health [35].

Table 9. **Risk Quotient values of naproxen.**

Sample code	Naproxen in tap water		
	Measured Conc. (µg/L)	RQ value	Remarks
T1	31.21	$2.4x10^{-4}$	*NOAEL
T2	13.96	$1.1x10^{-4}$	NOAEL
T3	14.02	$1.1x10^{-4}$	NOAEL
T4	328.95	$2.6x10^{-3}$	NOAEL
T5	126.49	$1.0x10^{-3}$	NOAEL
T6	55.211	$4.4x10^{-4}$	NOAEL
T7	327.49	$2.6x10^{-3}$	NOAEL
T8	27.2	$2.1x10^{-4}$	NOAEL
T9	8.96	$7.1x10^{-5}$	NOAEL
T10	14.02	$1.1x10^{-4}$	NOAEL
T11	65.31	$5.2x10^{-4}$	NOAEL
T12	26.05	$2.0x10^{-4}$	NOAEL
T13	123.38	$9.8x10^{-4}$	NOAEL
T14	141.89	$1.1x10^{-3}$	NOAEL
T15	25.78	$2.0x10^{-4}$	NOAEL
T16	28.74	$2.2x10^{-4}$	NOAEL
T17	97.96	$7.8x10^{-4}$	NOAEL
T18	99.98	$7.9x10^{-4}$	NOAEL
T19	37.33	$2.9x10^{-4}$	NOAEL
T20	34.28	$2.7x10^{-4}$	NOAEL

*Where NOAEL = No observed adverse effect level

Table 10. **Risk Quotient values of acetylsalicylic acid.**

Sample code	Acetylsalicylic acid in tap water		
	Measured Conc. (µg/L)	RQ value	Remarks
T1	62.27	$4.1x10^{-3}$	NOAEL
T2	56.90	$3.7x10^{-3}$	NOAEL
T3	BDL*	BDL	NOAEL
T4	BDL	BDL	NOAEL
T5	BDL	BDL	NOAEL
T6	8.55	$2.2x10^{-3}$	NOAEL
T7	30.85	$2.0x10^{-3}$	NOAEL
T8	7.42	$2.6x10^{-3}$	NOAEL
T9	ND*	ND	NOAEL
T10	10.91	$1.2x10^{-3}$	NOAEL
T11	5.47	$1.4x10^{-3}$	NOAEL
T12	6.76	$4.5x10^{-3}$	NOAEL
T13	6.80	$4.5x10^{-3}$	NOAEL
T14	BDL	BDL	NOAEL
T15	9.15	$2.4x10^{-3}$	NOAEL
T16	8.12	$2.7x10^{-3}$	NOAEL
T17	BDL	BDL	NOAEL
T18	6.49	$1.7x10^{-3}$	NOAEL
T19	ND	ND	NOAEL
T20	BDL	BDL	NOAEL

*Where NOAEL = No observed adverse effect level

Conclusions

SPE-LC-MS/MS technique has been successfully applied for the detection and quantification of naproxen and acetylsalicylic acid to check their impacts on the environment. Both pharmaceuticals were found in waste and tap water sources of municipal area of Sukkur city. Naproxen was found comparatively in higher concentration range 26.80 to 827.61 µg/L and 8.96 to 328.95 µg/L, while low concentration of Acetylsalicylic acid was observed ranges

between 7.38 to 190.06 µg/L and 5.47 to 62.27 µg/L in waste and tap water samples respectively. The results obtained are comparable with the data reported in literature. Human health risk was assessed by Risk Quotient approach. The calculated values regarding risk factor were substantially low to cause any harm to the consumer's health but may pose a danger synergistically.

References

1. S. Bibi, R. L. Khan, R. Nazir, P. Khan, H. U. Rehman, S. K. Shakir, S. Naz, M. A. Waheed and R. Jan, *World Appl. Sci. J.*, 34 (2016) 15. https://doi:10.5829/idosi.wasj.2016.34.1.10252
2. Q. Sun, M. Li, C. Ma, X. Chen, X. Xie, and C. P. Yu, *Environ. Pollut.*, 208 (2016) 371. https://doi.org/10.1016/j.envpol.2015.10.003
3. S. Alrumman, S. Keshk and A. El Kott. *Amer. J. Environ. Eng.*, 6 (2016) 88. https://doi: 10.5923/j.ajee.20160603.02
4. M. J. Pawari and S. Gawande. *Int. J. Eng. Res. Gen. Sci.*, 3 (2015) 773. https://doi: 10.12691/jephh-6-3-2.
5. S. M. Kamble, *Int. J. Sci. Res. Pubs*, 4 (2014) 1. https://doi:10.1.1.429.3175.
6. F. D. Owa, *Mediterr. J. Soc. Sci.*, 4 (2013) 65. https://doi: 10.5901/mjss.2013.v4n8p65
7. I. Reinholds, I. Pugajeva, I. Perkons, E. Lundanes, J. Rusko, G. Kizane, V. Nikolajeva, O. Mutere, Z. Petrina, L. Baumane and V. Bartkevics. *Int. J. Environ. Sci. Tech.*, 14 (2017) 1969. https://doi.org/10.1007/s13762-017-1290-6
8. S. Castiglioni, R. Bagnati, R. Fanelli, F. Pomati, D. Calamari and E. Zuccato, *Environ. Sci. Tech.*, 40 (2006) 357. https://doi.org/10.1021/es050991m
9. A. Kaleniecka and P. K. Zarzycki, *Arch. Physio. G. Res.*, 19 (2015) 39. http://apgr.wssp.edu.pl/wp-content/uploads/2015/10/artykul-4.pdf.
10. C. I. Kosma, D. A. Lambropoulou and T. A. Albanis, *Sci. Total Environ.*, 466 (2014) 421. https://doi.org/10.1016/j.scitotenv.2013.07.044
11. T. Kosjek, E. Heath and A. Krbavcic, *Environ. Int.*, 31 (2005) 679. https://doi.org/10.1016/j.envint.2004.12.001
12. O. Olarinmoye, A. Bakare, O. Ugwumbaand and A. Hein, *J. Environ. Chem. Ecotoxicol.*, 8 (2016) 14. http:// doi:10.5897/JECE2015.0364
13. H. Li, Z. Dong, Q. Weng, C. C. Chang and B. Liu, *W. Environ. Res.*, 87 (2015) 1849. https://doi.org/10.2175/106143015X14338845156425
14. M. Scheurell, S. Franke, R. M. Shah and H. Huhnerfuss, *Chemos.*, 77 (2009) 870. https://doi.org/10.1016/j.chemosphere.2009.07.066
15. A. Marchlewicz, D. Domaradzka, U. Guzik and D. Wojcieszyńska, *Water, Air Soil Pollut.*, 227 (2016) 197. https://doi.org/10.1007/s11270-016-2893-0
16. S. Straube, M. R. Tramèr, R. A. Moore, S. Derry and H. J. McQuay. *BMC Gastroenterol.*, 9 (2009) 41. https://doi.org/10.1186/1471-230X-9-41
17. D. Stülten, S. Zühlke, M. Lamshöft and M. Spiteller, *Sci. Total Environ.*, 405 (2008) 310. https://doi.org/10.1016/j.scitotenv.2008.05.036
18. G. L. Brun, M. Bernier, R. Losier, K. Doe, P. Jackman and H. B. Lee, *Environ. Toxicol. Chem.*, 25 (2006) 2163.

https://doi.org/10.1897/05-426R.1
19. M. D. Celiz, J. Tso and D. S. Aga, *Environ. Toxicol Chem.*, 28 (2009) 2473. https://doi.org/10.1897/09-173.1
20. L. H. Santos, A. N. Araújo, A. Fachini, A. Pena, C. Delerue-Matos and M.C.B.S.M. Montenegro, *J. Hazard. Mater*, 175 (2010) 45. https://doi.org/10.1016/j.jhazmat.2009.10.100
21. US EPA. Method 1694, *Water Sci. Tech. Eng. Anal. Divis.*, (2007). HPLC/MS/MS, EPA-821-R-08-002
22. A. Togola and H. Budzinski, *Anal. Bioanal. Chem.*, 388 (2007) 627. https://doi.org/10.1007/s00216-007-1251-x
23. G. Shanmugam, S. Sampath, K. K. Selvaraj, D. J. Larsson and B. R. Ramaswamy, *Environ. Sci. Pollut. Res.*, 21 (2014) 921. https://doi.org/10.1007/s11356-013-1957-6
24. I. A. Kandhar and A. K. Ansari, *Mehran University Res. J. Eng. Technol.*, 21 (2002) 141. https://inis.iaea.org/search/search.aspx?orig_q=journal:%22ISSN%200254-7821%22
25. B. P. Gumbi, B. Moodley, G. Birungi and P. G. Ndungu. *Chemos.*, 168 (2017) 1042. https://doi.org/10.1016/j.chemosphere.2016.10.105
26. L. M. Madikizela and L. Chimuka, *Water SA*, 43 (2013) 264. https://doi: 10.4314/wsa.v43i2.10
27. T. Deblonde, C. Cossu-Leguille and P. Hartemann, *Int. J. Hyg. Environ. Health*, 214 (2011) 442. https://doi.org/10.1016/j.ijheh.2011.08.002
28. K. Aguilar-Arteaga, J. A. Rodriguez, J. M. Miranda, J. Medina and E. Barrado, *Talanta*, 80 (2010) 1152. https://doi.org/10.1016/j.talanta.2009.08.042
29. C. Lacey, S. Basha, A. Morrissey and J. M. Tobin, *Environ. Monit. Asses.*, 184 (2012) 1049. https://doi.org/10.1007/s10661-011-2020-z
30. A. Y. Lin, T. H. Yu and C. F Lin, *Chemos.*, 74 (2008) 131. https://doi.org/10.1016/j.chemosphere.2008.08.027
31. A. E. B. Kermia, D. Fouial-Djebbar and M. Trari. *Compt. Rend. Chi.*, 19 (2016) 963. https://doi.org/10.1016/j.crci.2016.05.005
32. M. Villanueva-Rodríguez, R. Bello-Mendoza, A. Hernández-Ramírez and E. J. Ruiz-Ruiz, *Environ. Tech.*, 40 (2019) 2436. https://doi.org/10.1080/09593330.2018.1442880
33. World Health Organization. (2012). Pharmaceuticals in drinking-water. ISBN 978 92 4 150208 5
34. B. W. Schwab, E. P. Hayes, J. M. Fiori, F. J. Mastrocco, N. M. Roden, D. Cragin, R. D. Meyerhoff, J. D. Vincent and P. D. Anderson, *Regulat. Toxicol. Pharm.*, 42 (2005) 296. https://doi.org/10.1016/j.yrtph.2005.05.005
35. N. Mater, F. Geret, L. Castillo, V. Faucet-Marquis, C. Albasi and A. Pfohl-Leszkowicz, *Environ. Int.*, 63 (2014) 191. https://doi.org/10.1016/j.envint.2013.11.011