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Solid Phase Extraction Method for Caffeine Analysis in Water: A Mini Review

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ABSTRACT

This paper discusses an analytical method namely solid phase extraction that is used to separate caffeine residue present in water samples. The developed method reported is in the aspect of sample extraction, mode operation, and selection of detector, figure of merit on method performance and analysis of real samples. Sorbents namely C_{18} and hydrophilic-lipophilic balance (HLB) have become the best selection for the intended purpose. Adjustments of pH, sample flow rate, sample volume, selection of suitable solvent (conditioning, eluting, and reconstituting sample), extraction time or retention time and other operating conditions for instruments are the main considerations during method developments of analytical works. Liquid or gas chromatography is widely used to detect analytes because it is highly selective and sensitive for trace analysis. The recovery assay determined is always high but it can be affected when extracted sample is introduced with the derivative agent prior to analysis. The concentration levels are commonly observed to be high in aquatic samples when the study area is linked to discharge activities, either directly or indirectly from a treatment plant. In cases of multi-residue analysis, caffeine is one of the high active pharmaceutical compounds reported and has become a dominant fraction of micro pollutants.

1. Introduction

Caffeine is one of the stimulant drugs widely used in pharmaceutical, cosmetic, food or beverage industries. This compound is listed by the United States Environmental Protection Agency as a part of chemical compound that is produced in greater volume across the world. The emergence of caffeine in aquatic environments is widely reported in literatures, not only in wastewater but also in marine, lake, river, and groundwater. In fact, the occurrence of caffeine at trace amount levels becomes a good source of chemical waste marker related to sanitation problems [1-5]. High solubility, low octanol/water partition coefficient and insignificant volatility chemical properties cause this pollutant to be stable and ideal in most conditions of the environment. The estimated half-life of caffeine is between 3 days to > 3 months, depending on the aquatic type of environment [6, 7]. In fact, caffeine is metabolised in the human body mainly to paraxanthine, which is not found in plants or food [8]. Furthermore, after consuming caffeine, 0.5 to 10% is excreted, mostly in the urine that leads to its identification as primarily of anthropogenic origin [9-12].

Solid phase extraction is the most widespread method for the extraction of a large volume sample. Optimisation works rely on a suitable condition for sorbent extraction such as pH sample, type of sample, nature of sorbent composition, suitability of elution solvent, and flow rate program [13]. The ability to extract a broad range of multi compounds simultaneously under one condition becomes a necessity when sampling and sample extraction is the limiting factor of analytical procedure [14, 15]. In general, the working principle of solid phase extraction is based on normal phase, reversed phase or ion exchange. Faster, less labour-intensive sample manipulation and high concentration factors are a few examples of the advantages when this technique is applied to extract the sample [16]. The purpose of using solid phase extraction is not only to preconcentrate sample but eliminate interfering or impurities of the component from the matrix. Major concern on the efficacy of this method is linked to the selectivity of analytes toward sorbent. Therefore, it is very crucial to choose a suitable sorbent; either for single or multi-compound extractions. The best method will become the first choice if the procedure is easy to handle, has minimum steps, less time consuming, good recovery and reproducibility [17].

The aim of this review paper is to discuss the knowledge (advantage and limitation) on the application of solid phase extraction towards caffeine analysis. The research work detailed in this paper focuses on the extraction of caffeine from water samples. Method development elucidated in this paper is according to particular sorbent types, namely hydrophilic-lipophilic balance, C_{18} and other composition of sorbents.

2. Type of Sorbents

2.1 Hydrophilic-Lipophilic Balance Sorbent

Extraction technique for stimulant (caffeine), anti-inflammatory and antiepileptic drugs has been reported in literature. Santos et al. [18] explained that HLB sorbent is one of the effective solid phase extract ants to isolate caffeine from wastewater samples. The method was evaluated based on spiked analytes in filtered wastewater samples. Five hundred (influent) and one thousand millilitre (effluent) were loaded onto the sorbent with the flow rate controlled at 15 mL/min. All compounds were eluted from the sorbent using a low amount of ethyl acetate (3 mL) prior to reconstitution using 0.5 mL methanol. Final determination was achieved using HPLC-DAD equipped with RP-18 column. UV signal for caffeine was set at 273 nm and a peak appeared after 10 minutes. An advantage of this method is caffeine which has the ability to elute from sorbent without adjusting the pH of samples. Meanwhile, the major flaw of this method is the mobile phase used which is the gradient elution type. The time needed for gradient elution to change was every 0, 4.5, 12.5, 18, 27 and 45 minutes to control the amount of methanol, acetonitrile and potassium dihydrogen phosphate solution. Caffeine was detected in all real samples collected from four treatment plants located in Seville city, Spain. Highest concentrations were found at 16.3 µg/L and 4.52 µg/L for influent and effluent, respectively.

HLB sorbent type was utilised by Verenitch et al. [19] to determine acid drugs and caffeine residue in wastewater and receiving waters. Caffeine was extracted separately from acid drugs since the author noticed that the extraction yield was destroyed when derivatisation steps were introduced to the sample prior to analysis using gas chromatography- mass spectrometry. Caffeine was extracted using offline mode and the final eluent was desorbed from the sorbent using a combination of methanol (1

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mL) and methanol: MTBE (6 mL). After the extracted sample was dried, it was then dissolved in light petroleum solution (0.1 till 1 mL) depending on the type of samples. Precursor ion m/z 194 was chosen for caffeine in MS/MS analysis. Since the objective work aimed to extract multiresidue compounds, it seemed less practicable when more than 30 minutes was required for the peak of caffeine to appear in the chromatogram. Coefficient of linear calibration curve was found lowest among the compound studied, $r^2 = 0.989$ but the detection limit was remarkably low at 20 ng/L. In comparison to other compounds, caffeine was noted as having a relatively poor detection limit. Real water samples analysis indicated caffeine was present at the range of not detected to 8132 ng/L in which effluent from the treatment plant gave a higher concentration compared to receiving water.

Analysis of caffeine occurrence in Rochor Canal and Marina Bay's surface water was successfully performed when samples were extracted using low capacity HLB sorbent (150 mg). Wu et al. [20] started the extraction work with conditioning the sorbent using methanol and deionised water. Sample was adjusted to acidic condition at pH2 controlled by an addition of HCl solution. Eluting process was complete once the sorbent was loaded with methanol and a combination of methanol: acetone solvent. Before the extracted sample was ready to inject, it was reconstituted with 0.1% formic acid in methanol solvent. Chromatographic separation was successfully carried out using LC-MS/MS analysis in positive mode ionisation. Caffeine was identified based on precursor ion m/z 194.8. The figure of merit was not well explained, except the detection limit was achieved at 0.5 ng/L for all compounds; in specific, 0.1 ng/mL for caffeine. In real water samples analysis, caffeine was measured within the range of 0.37 to 1.35 ng/mL. The authors also discussed that good correlation between caffeine and faecal coliform was exhibited at high density area population which was linked to the assumption that both pollutants were remarked as good waste markers.

Dokmeci et al. [21] found the usage of HLB sorbent to be the best selection for extraction of caffeine simultaneously with ibuprofen, naproxen, diclofenac (non-steroidal anti-inflammatory drugs) and salicylic acids (analgesic). Sorbent performance was compared among HLB, MCX, and C_{18} types. Best recovery for caffeine was exhibited at 74.50% for HLB, higher than MCX (69.10%) and C_{18} (65.30%), respectively. The suitability of pH 2 was found to reach the optimum condition for other compounds but very poor for caffeine (35%). It was believed that the adjustment of pH is necessary for derivatised based compounds but presents a disadvantage for caffeine analysis. Final determination was performed by using gas chromatography – mass spectrometry. Detection limit was achieved at 5.6 ng/L and good linearity with R^2 at 0.999 (range 4 – 46 µg/L). Analysis of surface and wastewater collected from Çerkezköy region was performed in this study. It was found that the concentration levels of caffeine were within the range from not detected to 121.2 ng/L which was the highest concentration detected during summer.

Tahrim et al. [22] explicated that the usage of HLB sorbent type is ideal to isolate 10 target pharmaceutical compounds including caffeine. Extracted samples were eluted using ethyl acetate. Chromatographic separation using C_{18} column was performed based on analysis using positive ionisation mode of liquid chromatography-mass spectrometry. Optimal condition was achieved by using gradient elution consisting of 0.1% formic acid in deionised water and 100% of acetonitrile, respectively. The flow rate of mobile phase was set up at 0.30 mL/min. Caffeine was detected at the retention time of 7.71 with m/z 195. Caffeine was detected in all samples taken from a sewage treatment plant located in Kuala Lumpur, Malaysia. The total number of samples was 5 from raw sewage and 5 from the effluent stage, respectively. Nonetheless, the concentration levels of pollutant were not well explained.

An analysis of multi-class pharmaceutical was also reported by Al-Qaim et al. [23]. Caffeine was extracted together with six compounds namely prazosin, enalapril maleate, carbamazepine, nifedipine, levonorgestrel and simvastatin. Sorbent HLB was identified to be the most suitable to extract all compounds compared to ENVI-Chrom P and LC-SAX sorbent type. The method only required a low amount of sample (100 ml), loaded onto the sorbent at 9 mL/min. The extracted sample was then eluted using 5 ml ethyl acetate. Final determination was done using LC-ESI-TOF/MS in positive mode ionisation. An advantage of this method was sample was extracted without adjusting the pH, which led to low risk of sample damage. Furthermore, the total run time was only 16.1 min, in which caffeine first appeared first in the chromatogram after 6 minutes. Validation work of the developed method indicated that the bias measurement was high for caffeine such as relative standard deviation for repeatability test (5.7 – 20.1%) and reproducibility test (11.4%) after three consecutive weeks. The method was tested using an analysis of river water sample. The sample was collected from Tangkas River, Malaysia and the concentration of caffeine found was 257 ng/L.

In another study, Al-Qaim et al. [24] explicated that low capacity of HLB sorbent can perform well when the extraction process reaches optimum condition. In general, the sorbent was initially conditioned by passing it through a mixture of organic solvents, namely methyl tert-butyl ether, methanol and deionised water. The sample was then loaded into the sorbent at a desired flow rate followed by the washing process using deionised water. Elution process was completed through an addition of a mixture solution (methyl tert-butyl ether, acetone-MeOH 21:9 and acetone-MeOH 9:21) onto the sorbent at the desired flow rate. Concentration of targeted analytes was achieved when the sample was pre-concentrated under nitrogen stream. Chromatographic separation was done through HPLC-UV analysis. Caffeine was detected at a retention time of 0.6 minute. Detection limit was achieved at 0.066 µg/L, which was enough for a routine analysis, especially wastewater analysis. The bias of repeatability measurement obtained was low which less than 3.29%. The method was also considered robust in terms of the mobile phase flow rate and volume injection adjustment of ±2. Analysis of caffeine in real samples indicated that the concentration levels were measured at 31.7 – 50.1 µg/L. Quantitative analysis was checked using TOF-MS positive ionisation mode with m/z 195.

HLB sorbent was chosen by Thomas and Foster [25] to simultaneously determine caffeine, ibuprofen, naproxen, ketoprofen, mefenamic acid, diclofenac and triclosan. Sample was extracted using 60 mg HLB at a loading rate of 15 mL/min. After completely passing through the cartridge, sorbent was pre-eluted using hexane to remove lipophilic compound, followed by 3 mL ethyl acetate. Final volume of extractant was 100 µL after reconstituting with ethyl acetate. Before determination using GCMS, analyte was derived using a silylating agent, namely N,O-bis[Trimethylsilyl] trifluoroacetamide (BSTFA) at 60 °C for 20 minute. The runtime of GC-MS analysis was 45 minutes to complete the separation of all compounds. A major flaw of this method was related to low recovery obtained for caffeine, which was only 34% for triplicate measurement. This problem was linked to incomplete retention on the solid phase extraction column. Indeed, derivative reaction is not necessary for cases of caffeine analysis. Relative standard deviation for developed method was calculated at 2.7%. Analysis of wastewater samples collected from a treatment plant located in Virginia, USA indicated that caffeine was present at 36 ng/L.

Baena-Nogueras et al. [26] successfully utilised HLB sorbent to simultaneously extract 83 pharmaceutical active compounds in water samples in their work. The main parameters involved to find the optimum condition was sorbent size, suitability of pH samples, addition of complexing agent, and combination of elution solvents. The work flow was designed based on the one variable at a time method. The flow rate of extraction was set up at 2 mL/min. Final detection was determined by using ultra-pure liquid chromatography tandem mass spectrometry. Optimum condition was achieved when the sample was introduced into an acidic or neutral condition. No enhancement of recovery was achieved for caffeine extraction when the complexing agent Na_2EDTA was introduced in the sample. Relative recovery was considered low for caffeine (68%) which was linked to an adjustment of pH sample at a low level, pH 2. Bias measurement, RSD was also high since it was associated to multi-compounds analysis in which some compounds only produced low yield of extractions. Another figure of merit, the detection limit (0.1 ng/L), was remarkably good to trace at a low-level concentration. Caffeine is one of the most detected compounds in this study (7.2 – 522 ng/L), which method was tested using real samples collected from Huelva estuary and Cadiz bay.

Afonso-Oliveras et al. [27] had successfully developed a simple extraction procedure combined with a highly sensitive instrument, namely the liquid chromatography – tandem mass spectrometry. Caffeine was extracted together with 22 pharmaceutical compounds from different therapeutic classes. The extraction was based on the analysis using HLB as the main sorbent. Targeted analytes were eluted from the sorbent using a low volume of methanol solvent (5 mL). Optimisation work was build up based on a factorial experimental design. The efficacies test on method performance was associated to three factors, namely pH, sample volume and ionic strength. The Pareto chart elucidated that adjustment of pH and an addition of ionic strength (sodium chloride) had the greatest effect on method recovery. In specific, caffeine was having less effect on salt percentage compared to other compounds. Caffeine was identified based on a retention time of 19.7 min using positive ionisation mode. Validation of the extraction method proved that the proposed technique was working well, but to isolate caffeine, the measurement of intra-day or inter-day gave high percentages of relative standard deviation which were 7.92 – 11.4% and 9.04 – 13.3% respectively. Detection limit was taken into account at 2.35 ng/L. Applicability of the developed method was tested through analysis of wastewater samples. Samples were taken from wastewater treatment plants located at Gran Canaria, Spain. Caffeine was found at varied levels, ranging from 0.099 μg/L till 91.5 μg/L. Summary of method extraction and performance was tabulated in Table 1.

Table 1 Descriptive of latent information in method extraction by using HLB sorbent type

Sorbent Capacity (mg)	Elution Solvent	Retention Time (minute)	Instrument	Detection Limit (μg/L)	Recovery (%)	Concentration Levels (μg/L)	Ref.
60	Ethyl acetate	> 10	HPLC-DAD	0.07[a] 0.03[b]	78	0.56 – 6.80	[18]
200	Methanol and MTBE	30.67	GC-MS/MS	0.02	110.6	ND – 8.13	[19]
150	Methanol and acetone	NA	LC-MS/MS	0.10	NA	0.37 – 1.35	[20]
60	Hexane, ethyl acetate and methanol	8.32	GC-MS	0.005	74.5	ND – 0.12	[21]
60	Ethyl acetate	7.71	LC-MS	NA	NA	NA	[22]
60	Ethyl acetate	6.50	LC-MS	NA	120	0.25	[23]
60	Methanol, acetone and MTBE	0.60	HPLC-UV	0.06	87.5	31.70 – 50.10	[24]
60	Hexane and ethyl acetate	26.07	GC-MS	0.019	34	0.036	[25]
500	Methanol	2.72	LC-MS/MS	0.08[c]	68	0.007 – 0.52	[26]
500	Methanol	19.70	LC-MS/MS	0.002	75.99	0.099 – 91.5	[27]

[a] Influent; [b] Effluent; [c] Concentration at nanogram per liter

2.2 C_{18} Sorbent

Ternes et al. [28] investigated the capability of C_{18} sorbent to extract caffeine and other neutral types of pharmaceuticals. The extracted compounds were eluted using only a small amount of methanol solvent. Final determination was quantified and qualified using liquid chromatography equipped with electrospray ionisation tandem mass spectrometry (ESI-MS). Caffeine was first eluted at a retention time of 8.91 minute. Despite the overall recoveries achieving higher than 80%, the performance of C_{18} for caffeine analysis was only 66% in the spiked sample. Furthermore, the recovery values became lower in the surface and effluent samples. In fact, the application of standard addition using surrogates seemed less effective for the case of caffeine analysis. The reduction was believed to occur due to matrix impurities that led to sorption deficiencies and signal suppression in the electrospray interface. Method quantification limit was calculated at 0.10 μg/L and 0.025 μg/L for influent and effluent, respectively. Method performance was tested using real sample taken from a treatment plant and selected rivers in Germany. Caffeine was measured high in the influent samples with a mean value of 147 μg/L while the effluent sample only reached a maximum concentration of 1.9 μg/L. For river water sample analysis, the maximum concentration was quantified at 0.88 μg/L, in which only 11 samples were classified to be below the limit.

C_{18} sorbent was identified to be the best sorbent for caffeine extraction in a method development proposed by Togola and Budzinski [13]. Targeted compounds were extracted simultaneously with other acidic and natural compounds. Peak identification was quantified through gas chromatography mass spectrometry. Since the separation was performed on gas chromatography, the derivatization step was required for other compounds; nonetheless, caffeine was detected well without *N*-methyl-*N*-(trimethylsilyl) trifluoroacetamide (MSTFA). On the preliminary assessment, authors found that the performance of HLB sorbent was most suitable for acidic compounds (aspirin, ibuprofen, diclofenac, naproxen, gemfibrozil, and clofibric acid) but gave poor recovery for neutral compounds including caffeine. A major flaw of this method was the extraction procedure which was performed separately after selection of the best sorbent. Despite the work findings being good, the laboratory work was time consuming, especially the incubation process for derivatization to complete which was 35 minutes.

Detection limit for caffeine was accounted for at 0.7 ng/L. Recovery was achieved at 70.6% in the spiked sample and eluted using a solvent mixture (acetone and ethyl acetate). Caffeine contamination was assessed through wastewater and surface water analyses. The concentration levels were varied from 3.5 to 159.8 ng/L and 2.6 to 3257.2 ng/L for surface and effluent, respectively. Estuary area has been remarked as receiving an aquatic ecosystem having a high impact on caffeine contamination. The authors also elucidated about the fluctuation of pharmaceutical residue not only depending on usage demand, but linked to seasonal and the efficacy of treatment system as well.

Alahmad and Alawi [29] developed a solid phase extraction method to determine five pharmaceutical compounds including caffeine in wastewater samples. Sorbent type, C_{18} was chosen to isolate all targeted analytes from the matrix samples. Caffeine was eluted from the sorbent using 8 mL ethyl acetate at a slow loading rate of 3 mL/min. Chromatographic separation was achieved by using C_8 column in HPLC-UV detector. Mobile phase consisted of the combination of water, acetonitrile and 0.1% trifluoracetic acid. Peak resolution for caffeine appeared at a retention time, t_R = 3.22 minutes and the flow rate was 1 mL/min. The method showed good performance in validation work such as having a low detection limit (0.6 μg/L) and an acceptable range for recoveries (99.8 – 100.8%) at ppb concentration levels. Caffeine residue was found to be higher in sewage treatment plant compared to other pharmaceuticals. Frequency of detection was 100% for all sampling locations with a maximum concentration reaching 1076 μg/L. Concentration of caffeine was found higher in all influent treatment plants compared to the effluent stage. The treatment system used in Abu-Nusair, Wadi Alseir and Baqa'a, Jordan was capable to remove caffeine till 65%.

A comparative method performance of C_{18} sorbent between online and offline mode operations has been evaluated by Moret et al. [30]. For offline operating procedure, sample was extracted using a commercial sorbent with the capacity of 3 mL 500 mg. Meanwhile, the sorbent for online mode consisted of a mini column filled with 100 mg Accubond II ODS particles. Caffeine was eluted by using methanol mixture: water (2 mL) for offline extraction while only 0.3 mL methanol used in the online procedure. Final determination for both techniques used the HLPC-UV. Recoveries for extraction method was found higher (>90%) when methanol was introduced in the elution volume. A volume of 0.3 mL methanol was chosen to completely elute caffeine from 100 mg sorbent for online extraction. Detection limit was found better when online method applied a quantitative analysis in which the extraction method gave LODs of 10 ng/L and 100 ng/L (online), respectively. In contrast, intra-day precision was calculated lower in offline mode, <6% compared to <12% in online operation. In the analysis of real samples, the authors revealed that the online mode is not suitable to apply in the extraction of wastewater samples. The abundance of organic matter led to reducing the method efficacies and most samples were identified as below the detection limit. When same sample was introduced into offline method, caffeine was completely identified with maximum concentration level 120 μg/L.

Ismail et al. [31] reported that the development of tandem extraction technique (HLB-C_{18}) was useful to extract caffeine and other six pharmaceutical compounds in wastewater samples. Caffeine was eluted from C_{18} sorbent using 9 mL of a combination of ethyl acetate and acetone. Each sample (500 mL) was loaded onto the sorbent at 15 mL/min. Caffeine was separated using HPLC-DAD and the maximum intensity (280 nm) was found at a retention time of 4 minutes. The method was successfully applied to determine caffeine in wastewater sample. For instance, the analysis of wastewater collected from a treatment plant in Shah Alam, Malaysia found that caffeine residue varied from 0.4 till 24.5 mg/L. There were a few drawbacks of this method such as the separation of seven compounds required a different elution program and the combination of mobile phase needed two instruments, namely HPLC-DAD and HPLC-FLD to separate all compounds. The method may be suitable if the research work aims to separate multi compounds but it is less effective with only caffeine as the main subject. In fact, the positioning of cartridge was also restricted for HLB to be on top of C_{18} sorbent to achieve 87.4% recovery of method analysis.

C_{18} Strata X type was chosen by Edwards et al. [32] to extract caffeine in surface and wastewater from selected treatment plants in Barbados, West Indies. Surface and wastewater samples were priory acidified using HCl (pH 2) before being passed through a cartridge at a loading rate of 5 ml/min. The extracted caffeine was eluted from the sorbent using 100 mL chloroform at a flow rate of 1 mL/min. Later, the extracted caffeine was dried under nitrogen stream followed by reconstitution with 1 mL of methanol. The final extract was analysed using GC-MS equipped with non-polar column DB-5ms. The total runtime was 10 minutes and the caffeine peak was shown at retention time, t_R = 8.4 min. Good performance was shown through the recovery assay (90 – 100%) and low detection limit was achieved at 0.2 ng/L. The method was tested using real samples which explicated that the surface water samples contained 0.1 – 6.9 μg/L while the wastewater samples were in the range from 0.1 to 43 μg/L.

Jagoda et al. [33] successfully utilised C_{18} sorbent to isolate caffeine from river water samples. Method extraction was performed offline and final determination was achieved by using gas chromatography – mass spectrometry. The sorbent was conditioned using different combinations of solvents (methanol: water, ethyl acetate: acetone) at ratio 1:1. Sample loading was controlled at a flow rate from 0.08 to 0.18 cm^3/s and caffeine was desorbed from the sorbent by using ethyl acetate and acetone solvent. The extracted samples underwent a drying process using vacuum concentrator and were reconstituted using methanol, before being injected to the GC-MS port. No optimisation work was provided in this study since their work aimed to perform monitoring work. Caffeine residue was detected in all 12-point sampling along the Rudawa River, located in Poland. The concentration levels varied from 14.4 to 380 ng/dm^3. Higher concentration of caffeine was exhibited to be close to anthropogenically active areas and human settlements.

Offline extraction technique was also developed by Archana et al. [34] for the determination of caffeine simultaneously with ciprofloxacin, acetaminophen, benzophenone and irgasan. The targeted compounds were extracted by using C_{18} sorbent type before final detection with HPLC-PDA. The efficacy of method performance was tested using different adjustments of pH sample. Sample for acid extraction was controlled through an addition of hydrochloric acid while base extraction was established using ammonium hydroxide solution. The conditioning process was similarly performed except for an addition of acidified water after loading methanol and deionised water on the sorbent for acid mode extraction. Another step for extraction was proposed with the same manner. Chromatographic separation was successfully carried out based on isocratic mode which was a combination of methanol and acetic acid used as the mobile phase. Maximum intensity for caffeine was set at 273 nm with a retention time identified at 2.90 minute. Good performance was shown through validation of work analysis as having high linearity (0.99), low detection limit (0.09 µg/L) and bias measurement achieved at 0.23%. Recoveries for method (80%) and instrument accuracy (93%) were calculated within the acceptable range for part per billion concentrations. Caffeine was measured at different concentrations when acid and base extractions were applied which ranged from 36.67 – 102.84 µg/L and 0.58 – 119.02 µg/L, respectively. Matrix samples were collected from a treatment plant and river located in Nagpur, India. Summary of method extraction and performance was tabulated in Table 2.

Table 2 Descriptive of latent information in method extraction by using C_{18} sorbent type

Sorbent Capacity (mg)	Elution Solvent	Retention Time (minute)	Instrument	Detection Limit (µg/L)	Recovery (%)	Concentration Levels (µg/L)	Ref.
500	Methanol	8.91	LC-MS/MS	0.10[a] 0.025[b]	66	0.88 – 147	[28]
200	Acetone and ethyl acetate	15.30	GC-MS	0.7[c]	70.6	3.5 – 159.8 2.6 – 3257.2[bc]	[13]
500	Ethyl acetate	3.22	HLPC-UV	0.6	99.8 – 100.8	1076	[29]
500	Methanol and water	0.1	HPLC-UV	0.1	>90	120	[30]
1000	Ethyl acetate and acetone	4.00	HPLC-DAD	0.013	87.4	0.4 – 24.5[d]	[31]
2000	Chloroform	8.40	GC-MS	0.2[c]	90 – 100	0.1 – 43	[32]
500	Ethyl acetate and acetone	-	GC-MS	-	-	14.4 – 380[c]	[33]
500	Methanol and acetone	2.90	HPLC-PDA	0.09	80	0.56 – 119.02	[34]

[a] Influent; [b] Effluent; [c] Concentration at nanogram per liter; [d] Concentration at milligram per liter

2.3 Other Types of Sorbent

The efficacies of pre-column sorbent for caffeine determination were tested by Chen et al. [35]. Four different types of sorbents, namely C_{18}, PLRP-1, PLRP-s and Bond Elute ENV were chosen during this study. Qualitative and quantitative analyses were performed by using HPLC-DAD. Caffeine was detected at wavelength 210 nm and acetonitrile was used as the mobile phase (gradient method). PLRP-s type was chosen as the best sorbent to elute analysis with recoveries achieved till 97.8% and detection limit was calculated at 0.1 µg/L for every 50 mL spiked sample. The bias for repeatability test was found low in the range of 2.6 – 3.9% for every 5 times of measurement. The interference of non-targeted compound was successfully eliminated when phosphoric acid 0.001% v/v, diluted in deionised water, was introduced during the pre-column back wash. Nonetheless, the efficiency of extraction method was found depleted to 85.5% of recovery analysis. Analysis of real samples indicated that the method had successfully extracted caffeine with varied concentrations from not detected to 15.2 µg/L. Samples were taken from two sewage treatment plants located in Bolivar and Hall Head, Australia.

A pre-treatment of multi-class pharmaceutical compounds through solid phase extraction technique has been developed by Cardoso et al. [36]. The main target included sulfamethoxazole, diclofenac, atenolol, fluoxetine and caffeine. They were isolated from the matrix sample using a polymeric based sorbent, Strata X. The optimisation work involved two compartment instrumental conditions (LC-MS/MS) for method performance. Instrumental sensitivity was tested based on the selection of mobile phase and ionisation mode. A combination of methanol and water was chosen as the most suitable solution for separating all compounds. For extraction analysis, efficacy of sorbent, selection of sorbent type and volume were tested to achieve the highest recoveries. Final condition was fixed at Strata X as the best sorbent, and 4 mL of methanol was used as the elution solvent. Calibration curve was achieved at a satisfactory level > 0.990 for all compounds including caffeine in regard to analytes spiked into the solvent, supply water or surface water. Accuracy of method performance was explicated through a validation work. For example, recoveries of spiked caffeine were achieved at 91 – 118% by using three concentration levels. Bias measurement was obtained low at 2.5% of relative standard deviation. Quantitative analysis had no proven data since no pharmaceutical compound was detected during this study.

Khalik et al. [37] found that a research work constructed using experimental design is an effective approach to optimise solid phase extraction for caffeine analysis. Central composite design, 2^3 was used to find the optimum condition for flow rate, elution volume and suitability of pH sample. Caffeine was successfully eluted from Oasis MCX sorbent using 0.75% ammonium hydroxide in methanol at a loading rate of sample of 1.2 ml/min. The good resolution of peak area was obtained at 2 min for chromatographic separation using HPLC-UV. Detection limit was achieved at 0.02 µg/L and recoveries were ranged from 80.9 to 93.7% at three concentration levels. The disadvantage of this method was it consumed more time to load the sample since the flow rate was controlled at a low speed. Analysis of real samples indicated that the caffeine was detected at concentration levels from 0.64 to 59.01 µg/L. Higher concentration was found to be near the point source of pollution such as drainage input from the university cafeteria entering the storm water channel.

Gonçalves et al. [38] chose Strata-X to isolate caffiene residue in river water samples. Sorbent was conditioned with a combination of methanol and ultrapure water with the ratio 1:1. Analytes were recovered from the sorbent using methanol and followed by the reconsituting process with methanol: water (30:70 v/v). The extracted samples were determined by using high performance liquid chromatography equipped with a diode array detector. Figures of merit such as detection limit (0.05 µg/L), recovery (85.7%) and linearity ($r^2 = 0.99$) were achieved during this study. The method was then applied for sample analysis from Paquequer River, which was collected three times (February, March and October 2007). The authors found that concentration levels were varied from below the quantification limit till 47.5 µg/L. The most affected area was a location close to Teresópolis city, Brazil. High correlation between caffeine and ammonia was linked to a discharge originating from the sewage, either using septic tank or direct discharge.

3. Conclusion

Solid phase extraction is an ideal extraction technique to isolate caffeine residue from water matrices. HLB and C_{18} are sorbent types widely used for intended purposes. Liquid or gas chromatography has become the best selection for the determination of caffeine content in water samples. The detection limit achieved was varied but most of the cases reached low at sub part per billion of concentration levels. Recovery of the developed method was obtained at satisfactory level and became easily traceable when analysed as a single analyte. Derivatisation step for gas chromatography analysis seemed to not be applicable to enhance the sensitivity of caffeine detection. Caffeine analysis in water samples has a wide range of concentration levels and the amount is usually higher from influent and effluent wastewater. Modification on polymeric sorbent or a hybrid of the extraction techniques may become new prospects for the separation of this compound in future works.

References

[1] Z. Chen, P. Pavelic, P. Dillon, R. Naidu, Determination of caffeine as a tracer of sewage effluent in natural waters by on-line solid-phase extraction and liquid chromatography with diode-array detection, Water Res. 36 (2002) 4830-4838.

[2] I.J Buerge, T. Poiger, M.D. Müller, H.R. Buser, Caffeine, an anthropogenic marker for wastewater contamination of surface waters, Environ. Sci. Technol. 37 (2003) 691-700.

[3] S. Kurissery, N. Kanavillil, S. Verenitch, A. Mazumder, Caffeine as an anthropogenic marker of domestic waste: a study from Lake Simcoe watershed, Ecol. Indic. 23 (2012) 501-508.

[4] F.Y. Lim, S.L. Ong, J. Hu, Recent advances in the use of chemical markers for tracing wastewater contamination in aquatic environment: a review, Water 9 (2017) 143-169.

[5] C.C. Montagner, G.A. Umbuzeiro, C. Pasquini, W.F. Jardim, Caffeine as an indicator of estrogenic activity in source water, Environ. Sci. Process Impacts 16 (2014) 1866-1869.

[6] M.J. Benotti, B.J. Brownawell, Microbial degradation of pharmaceuticals in estuarine and coastal seawater, Environ. Pollut. 157 (2009) 994-1002.

[7] S. Sauvé, K. Aboulfadl, S. Dorner, P. Payment, G. Deschamps, et al, Fecal coliforms, caffeine and carbamazepine in storm water collection systems in a large urban area, Chemosphere 86 (2012) 118-123.

[8] O. Hillebrand, K. Nödler, T. Licha, M. Sauter, T. Geyer, Caffeine as an indicator for the quantification of untreated wastewater in karst systems, Water Res. 46 (2012) 395-402.

[9] A.P. Ferreira, Caffeine as an environmental indicator for assessing urban aquatic ecosystems, Cad. Saúde Pública. 21 (2005) 1884-1892.

[10] C. Paulo, F.L. Gomes, I.N. Tomita, Á.J Santos-neto, M. Zaiat, Rapid determination of 12 antibiotics and caffeine in sewage and bioreactor effluent by online column-switching liquid chromatography/tandem mass spectrometry, Anal. Bioanal. Chem. 407 (2015) 8787-8801.

[11] P.N. Patil, Caffeine in various samples and their analysis with HPLC – A review, Int. J. Pharm. Sci. Rev. Res. 16 (2012) 76-83.

[12] I. Senta, E. Gracia-Lor, A. Borsotti, E. Zuccato, S. Castiglioni, Wastewater analysis to monitor use of caffeine and nicotine and evaluation of their metabolites as biomarkers for population size assessment, Water Res. 74 (2015) 23-33.

[13] A. Togola, H. Budzinski, Analytical development for analysis of pharmaceuticals in water samples by SPE and GC–MS, Anal. Bioanal. Chem. 388 (2007) 627-635.

[14] A. Andrade-Eiroa, M. Canle, V. Leroy-Cancellieri, V. Cerdà, Solid-phase extraction of organic compounds: a critical review (part I), Trends Anal. Chem. 80 (2016) 641-654.

[15] S. Weigel, R. Kallenborn, H. Hühnerfuss, Simultaneous solid-phase extraction of acidic, neutral and basic pharmaceuticals from aqueous samples at ambient (neutral) pH and their determination by gas chromatography–mass spectrometry, J. Chromatogr. A 1023 (2004) 183-195.

[16] C. Lombardi, Solid phase extraction, Chem. New Zealand 1 (2015) 88-90.

[17] N. Abd-Talib, S.H. Mohd-Setapar, A.K. Khamis, The benefits and limitations of methods development in solid phase extraction: mini review, J. Teknologi Sci. Eng. 69 (2014) 69-72.

[18] J.L. Santos, I. Aparicio, E. Alonso, M. Callejón, Simultaneous determination of pharmaceutically active compounds in wastewater samples by solid phase extraction and high-performance liquid chromatography with diode array and fluorescence detectors, Anal. Chim. Acta. 550 (2005) 116-122.

[19] S.S. Verenitch, C.J. Lowe, A. Mazumder, Determination of acidic drugs and caffeine in municipal wastewaters and receiving waters by gas chromatography–ion trap tandem mass spectrometry, J. Chromatogr. A 1116 (2006) 193-203.

[20] J. Wu, J. Yue, R. Hu, Z. Yang, L. Zhang, Use of caffeine and human pharmaceutical compounds to identify sewage contamination, World Acad. Sci. Eng. Tech. 44 (2008) 438-442.

[21] A.H. Dökmeci, K. Sezer, İ. Dökmeci, H. İbar, Determination of selected acidic pharmaceuticals and caffeine in Ergene basin, in Turkey, Global NEST J. 15 (2013) 431-439.

[22] N.A. Tahrim, M.P. Abdullah, Y.F.A. Aziz, Determination of human pharmaceuticals in pre-and post-sewage treatment, AIP Conf. Proc. 1571 (2013) 760-764.

[23] F.F. Al-Qaim, M.P. Abdullah, M.R. Othman, J. Latip, W. Afiq, A validation method development for simultaneous LC-ESI-TOF/MS analysis of some pharmaceuticals in Tangkas river-Malaysia, J. Braz. Chem. Soc. 25 (2014) 271-281.

[24] F.F. Al-Qaim, S.H. Jusof, M.P. Abdullah, Z.H. Mussa, N.A. Tahrim, W.M.A.W.M. Khalik, M.R. Othman, Determination of caffeine in surface water using solid phase extraction and high-performance liquid chromatography, Malay. J. Anal. Sci. 21 (2017) 95-104.

[25] P.M. Thomas, G.D. Foster, Determination of nonsteroidal anti-inflammatory drugs, caffeine, and triclosan in wastewater by gas chromatography–mass spectrometry, J. Environ. Sci. Health. Part A 39 (2004) 1969-1978.

[26] R.M. Baena-Nogueras, M.G. Pintado-Herrera, E. González-Mazo, P.A. Lara-Martín, Determination of pharmaceuticals in coastal systems using solid phase extraction (SPE) followed by ultra-performance liquid chromatography–tandem mass spectrometry (UPLC-MS/MS), Curr. Anal. Chem. 12 (2016) 183-201.

[27] C. Afonso-Olivares, T. Čadková, Z. Sosa-Ferrera, J.J. Santana-Rodríguez, L. Nováková, Simplified solid-phase extraction procedure combined with liquid chromatography tandem–mass spectrometry for multiresidue assessment of pharmaceutical compounds in environmental liquid samples, J. Chromatogr. A 1487 (2017) 54-63.

[28] T. Ternes, M. Bonerz, T. Schmidt, Determination of neutral pharmaceuticals in wastewater and rivers by liquid chromatography–electrospray tandem mass spectrometry. J. Chromatogr. A 938 (2001) 175-185.

[29] W.R. Alahmad, M.A. Alawi, HPLC/UV/Fluorescence detection of several pharmaceuticals in sewage treatment plant wastewaters of Jordan, Fresen. Environ. Bull. 19 (2010) 805-810.

[30] S. Moret, M. Hidalgo, J.M. Sanchez, Simple and fast methods based on solid-phase extraction coupled to liquid chromatography with UV detection for the monitoring of caffeine in natural, and wastewater as marker of anthropogenic impact, ISRN Chromatogr. 2012 (2012) 1-7.

[31] L. Ismail, R. Osman, N. Saim, Tandem solid phase extraction for the determination of pharmaceuticals in wastewater, Malay. J. Anal. Sci. 17 (2013) 262-271.

[32] Q.A. Edwards, S.M. Kulikov, L.D. Garner-O'Neale, Caffeine in surface and wastewaters in Barbados, Springer Plus, West Indies, 2015.

[33] A. Jagoda, W. Żukowski, B. Dąbrowska, Investigations of the presence of caffeine in the Rudawa River, Kraków, Poland, Environ. Monitor. Assess. 187 (2015) 566-578.

[34] G. Archana, R. Dhodapkar, A. Kumar, Offline solid-phase extraction for preconcentration of pharmaceuticals and personal care products in environmental water and their simultaneous determination using the reversed phase high-performance liquid chromatography method, Environ. Monitor. Assess. 188 (2016) 512-522.

[35] Z. Chen, P. Pavelic, P. Dillon, R. Naidu, Determination of caffeine as a tracer of sewage effluent in natural waters by on-line solid-phase extraction and liquid chromatography with diode-array detection, Water Res. 36 (2002) 4830-4838.

[36] L.V. Cardoso, D. Tomasini, M.R. Sampaio, S.S. Caldas, N. Kleemann, E.G. Primel, et al, Optimization and validation of a method using SPE and LC-APCI-MS/MS for determination of pharmaceuticals in surface and public supply water, J. Braz. Chem. Soc. 22 (2011) 1944-1952.

[37] W.M.A.W.M. Khalik, M.P. Abdullah, F.K. Baharudin, S. A. Zulkepli, Optimization of extraction procedure for determination of caffeine residue in water, J. Mater. Environ. Sci. 7 (2016) 720-728.

[38] E.S. Gonçalves, S.V. Rodrigues, E.V.D. Silva-Filho, The use of caffeine as a chemical marker of domestic wastewater contamination in surface waters: seasonal and spatial variations in Teresópolis, Brazil, Rev. Ambient. Água. 12 (2017) 192-202.