

Review

Recent Advances in the Use of Chemical Markers for Tracing Wastewater Contamination in Aquatic Environment: A Review

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Abstract: There has been increasing research focus on the detection and occurrence of wastewater contamination in aquatic environment. Wastewater treatment plants receive effluents containing various chemical pollutants. These chemicals may not be fully removed during treatment and could potentially enter the receiving water bodies. Detection of these chemical pollutants and source identification could be a challenging research task due to the diversified chemical and functional groups, concentration levels and fate and transportation mechanisms of these pollutants in the environment. Chemical markers such as pharmaceuticals and personal care products, artificial sweeteners, fluorescent whitening agents, sterols and stanols, and nitrate and nitrogen isotopics have been widely used by most research as markers. These markers served as indicators of wastewater contamination to the receiving bodies due to their frequent usage, resistance to biodegradability and, more importantly, anthropogenic origin. These markers are commonly used in combination to identify the contaminant source of different origins. This article discusses the main chemical markers that are used to identify wastewater contamination in receiving bodies, the current trends, and approach to select suitable chemical markers.

Keywords: chemical markers; wastewater contamination; pharmaceuticals and personal care products; artificial sweeteners; fluorescent whitening agents; sterols and stanols

1. Introduction

Climate change, increasing population growth and reduced reliable supply of water resources have created many challenges to sustainable water supply management. Inappropriate management of wastewater from both domestic and industry had led to many unfortunate adverse health issues, such as diarrhea and cholera infections. This has hindered socio-economic development, especially in developing countries. In water-stressed countries, stormwater is recognized as a valuable water resource [1]. However, urban stormwater runoff is identified as a significant source of contamination to surface water [2–4]. This observation has significant implication as runoff may eventually enter rivers and/or reservoirs which served as drinking water source [5,6]. In addition, surface water contamination attributed by wastewater has always been an area of research and engineering interest.

Contaminants from domestic sewage could enter surface water by either direct/indirect discharge or discharged of treated effluents from wastewater treatment plants (WWTPs). For example, combined sewer overflows (CSOs) have been identified as major causes of fecal contaminant after rainfall events [7,8] and sewage exfiltration from aged/leaking sewer infrastructure during dry period had been reported to contaminate surface water [9–11]. In addition, urban runoff, untreated or partially treated sewage, illicit connections and broken/poor pipe materials have also been identified as sources of wastewater contaminations to surface water [12,13].

It is challenging to distinguish contaminants originated from raw sewage from other sources in surface water. To identify contaminant inputs from raw wastewater, various techniques using molecular markers (chemical, microbial, or combination of both) have been widely practiced [14–17].

Fecal indicator bacteria such as *Escherichia coli* (*E. coli*) and *enterococci* have been widely used as microbial markers to investigate sources and extent of wastewater contamination. However, the presence of fecal indicator bacteria does not always relate to the source of fecal contamination. New development in microbial source tracking (MST) has established tools to identify and discriminate sources of wastewater contamination, i.e., between human and non-human, and among different animals [18–22]. These include molecular methods to establish the library of DNA profiles for fecal bacteria, protozoan and viruses. The most widely applied methods for molecular fingerprinting are denaturing gradient gel electrophoresis, temperature gradient gel electrophoresis and terminal restriction fragment length polymorphism analysis [23–25]. Selection of the appropriate MST markers would provide rapid detection of wastewater contamination directed to the specific source.

In recent years, various chemical markers have been investigated and utilized for identifying the wastewater contamination [26,27]. In the recent studies by Tran et al. [28,29], the research team had demonstrated that pharmaceutical care products (PPCPs) and artificial sweeteners (ASs) could serve as promising markers for detecting sewer leakage.

There have been extensive reports in the two decades related to detection of wastewater contaminates in surface water. This review article served to provide a summary of the current state of knowledge in applying chemical markers for wastewater contamination identification in surface water. This provides valuable insights to the regulatory and engineering communities and could aid in the development of safe water management strategies.

2. Use of Chemicals Markers

A wide range of chemicals has been utilized to detect wastewater contamination in surface water and groundwater. In recent years, numerous studies have successfully utilized PPCPs, ASs, fluorescent whitening agents (FWAs) and fecal sterols/stanols (SSs) to detect contamination of wastewater to surface water and groundwater [14,30–32]. However, it remains highly challenging to accurately predict the extent of wastewater contamination using the methods developed using these chemical markers. Currently, there is no single chemical that could serve as marker for wastewater contamination for all sites accurately. Understanding of land use pattern, types and levels of contaminants in wastewater, fate and transport of chemicals are needed in order to select suitable marker(s). Chemical markers can be divided into three main categories: (a) those produced by humans, e.g., fecal sterol; (b) those that can pass through human bodies, e.g., PPCPs; and (c) those that are associated with sewage contaminated waste system, e.g., detergents [14,33,34]. The use of chemical markers has the advantages of more rapid and reliable detection, source specific and stable compared to microbial markers. The disadvantages of utilizing chemical markers include: (a) the presence of chemical marker does not absolute represent contamination by wastewater; and (b) could lack specificity and can be impacted by environmental factors such as degradation and sorption. One of the key considerations for selecting the suitable chemical markers is the chemical markers should be associated with wastewater sources and occurring in receiving water bodies at specific study area. The specific chemicals that are ubiquitously present and detected in high concentration in raw wastewater could be potentially selected as markers in the studied area. The proposed chemical markers should be specific to wastewater contamination sources. For instance, markers should be absent or detected in significantly lower concentrations in background receiving bodies with no wastewater contamination sources. The use of markers is site-specific and may not be applicable from one location to another. Table 1 provides the list of chemical markers in wastewater contamination assessment in recent research.

Table 1. Summary of chemical markers identified in the literature survey.

Group	Compounds	CAS No.	Reference
Pharmaceuticals and personal care products (PPCPs)	Acetaminophen	103-90-2	[34–37]
	Diclofenac	15307-86-5	[35,38]
	Caffeine	58-08-2	[7,15,17,34–37,39–45]
	Bisphenol A	80-05-7	[9,35]
	Propyl paraben	94-13-3	[35]
	Triclocarbon	101-20-2	[17,35]
	Metoprolol	37350-58-6	[35,46]
	Propranolol	525-66-6	[38]
	Ibuprofen	15687-27-1	[34,38,47]
	Atenolol	29122-68-7	[38]
Artificial sweeteners (ASs)	Carbamazepine	298-46-4	[36,38,43,48–50]
	Oxypurinol	2465-59-0	[51]
	Sucralose	56038-13-2	[52–58]
Artificial sweeteners (ASs)	Acesulfame	55589-62-3	[45,53,59]
	Cyclamate	139-05-9	[59]
	4,4'-bis(2-sulfostyryl)biphenyl	27344-41-8	[60–62]
Fluorescent whitening agents (FWAs)	4,4'-bis[(4-anilino-6-morpholino-1,3,5-triazin-2-yl)amino]stilbene-2,2'-disulfonate	16090-02-1	[60,61,63]
	Coprostanol	360-68-9	[37,64–67]
Sterols/Stanol (SSs)	Epicoprostanol	516-95-0	[64,65,67–69]
	Campestanol	474-60-2	[64,67,68]
	Sitostanol	83-45-4	[64,67,69]
	24-ethylcoprostanol	4736-91-8	[64,67–70]
	24-ethylepicoprostanol	5060-24-2	[64,67]
	Cholesterol	57-88-5	[65–69]
	Cholestanol	80-97-7	[65,67,68]
Isotopic compositions	$\delta^{15}\text{N}$	29817-79-6	[71]
	$\delta^{18}\text{O}$	14797-71-8	[71]
Alternative potential markers	1-aminopropanone	107-10-8	[72–75]
	Boron	7440-42-8	[76,77]
	Total trihalomethanes	-	[71]

2.1. Pharmaceuticals and Personal Care Products (PPCPs)

PPCPs have been found ubiquitously in a wide variety of environmental matrices [78,79]. Most PPCPs of concern are excretion product from urine and feces, and ingredients used in cosmetic products, medicines and agricultural practice. PPCPs such as carbamazepine and dithyltoluamide have low adsorption capacity and are poorly removed in wastewater treatment systems. Thus, these PPCPs would eventually enter surface water system through effluent discharge from the wastewater treatment plants (WTPs) [29,80]. Continual improvement in chemical detection methodologies has substantially facilitated the detection and quantification of PPCPs at ultra-trace levels. The main advantages of using PPCPs as marker are more rapid analysis response time and greater specificity [81].

Yang et al. [82] reported both treated and untreated wastewater were important sources of PPCPs. They detected caffeine (865 ng/L), acetaminophen (339 ng/L) and ciprofloxacin (304 ng/L) in Shijing River. Caffeine was found to have a high correlation (correlation coefficients between 0.62 and 0.98) with total nitrogen, ammonium and cumulative fluorescence excitation emission matrix volume. In US and Europe, more than 80 PPCPs were detected at concentrations of up to mg/L level in different water bodies [78,83,84]. Based on the research carried out by Vystvna et al. [85], it was suggested that diclofenac, caffeine and carbamazepine are useful chemical markers for tracing wastewater contamination in France and Ukraine. Similarly, the use of persistent marker (carbamazepine) and labile markers (acetaminophen and salicylic acid) has been successfully applied to detect wastewater contamination in surface water and groundwaters by Tran et al. [29]. Foolad et al. [86] also tested sewage molecular markers using soil columns under different conditions e.g., transportation of markers in both abiotic and biotic columns and effect of different concentrations of acetate as an

easily biodegradable primary substrate on the removal of markers. Their results demonstrated acesulfame, carbamazepine, crotamiton, cyclamate and saccharine were suitable to be used as sewage molecular markers as these compounds are stable against sorption and biodegradation processes. In contrast, transport of acetaminophen, caffeine and diethyltoluamide were limited by both sorption and biodegradation processes and were not considered as useful markers. Gasser et al. [87] investigated the treated effluents from a wastewater recharge site that discharged to a surrounding active aquifer. They concluded that carbamazepine could be used as a marker to predict the wastewater stream contamination even when carbamazepine was degraded to a large extent. The authors recommended carbamazepine as universal tracer since it has low background concentration and a change in its concentration between different wastewater sites will not significantly affect its efficiency as leak detector. In Canada, caffeine was identified as potential indicator to track the domestic wastewater [41], while in another study in Japan, Nakada et al. [80] found that crotamiton and carbamazepine were useful as conservative markers in freshwater and coastal environments.

The use of PPCPs as markers could vary among different sites. Spatial variations and effects of seasonal change need to be investigated for different locations and weather conditions. Generally, caffeine and carbamazepine are the most widely used markers to evaluate the wastewater contamination from the published literature. The suitability of PPCPs as wastewater contamination markers is largely dependent on persistency and whether they are detected at high frequency at pollution sources and receiving bodies. Many studies have investigated and indicated the use of PPCPs as useful wastewater tracer. However, not all the PPCPs are derived from fecal source. For instance, caffeine could be derived from household sinks or plants. Detection of high level of caffeine could be a good indicator for wastewater contamination but could not indicate fecal pollution [88]. Therefore, combination of other indicators could provide better understanding of wastewater contamination especially source-specific. It is recommended to have background knowledge about land use pattern, type of PPCPs in the wastewater source and information about wastewater input to track the origin of pollution.

2.2. Artificial Sweeteners (ASs)

ASs such as acesulfame (ACE), saccharin (SAC), sucralose (SUC), aspartame (ASP) and cyclamate (CYC) are used as sugar substitutes in food and beverages due to their low caloric characteristics. These compounds represent an emerging class of micropollutants and have been of environmental concerns. Some ASs could pass through human bodies without being affected by metabolism processes and enter the environment through human excretions [89–91]. Studies of occurrence, fate, transformation and elimination of ASs have increased rapidly in the recent years [86,92]. ASs have been reported in rivers receiving effluents from WWTPs (ACE up to 14,200 ng/L and SUC up to 1800 ng/L) and in surface water (SAC up to 310 ng/L and CYC up to 1960 ng/L) [93–95]. Perkola and Sainio [96] found that ACS and SAC were detected in all tested samples (twelve rivers and three lakes in Finland), whereas CYC and SUC in 98% and 56% of the samples, respectively. They further concluded that the levels of ACE and SUC in rivers correlated linearly with population equivalents of the wastewater treatment plants located within the catchment areas (Rivers Aura, Kokemakim Kymi, Porvoo, Vantaa and Vuoksi). They also found that concentrations of SAC and CYC were source-specific. Due to their recalcitrance to transformation, persistence, high water solubility, low adsorption capacity on soils, reliable analytical method and short analysis time, ASs have been considered as ideal wastewater markers [26,97]. Batchu [98] developed an online solid phase extraction and liquid chromatography with high resolution mass spectrometry for the detection of sucralose in aqueous samples and applied this method to detect sucralose in 17 oceanic and estuarine sites in Broward County. Sucralose was detected in 78% of the samples (8 to 148 ng/L), with the exception of the WWTP ocean outfall where the measured concentration was 8418 ng/L. Buerge et al. [89] first reported the occurrence of four ASs (ACE, CYC, SAC, and SUC) in aquatic environment in Switzerland. These four ASs were found at concentrations of 2–65 µg/L in untreated wastewater. They further demonstrated that ACE can be a promising marker of domestic wastewater contamination in surface water and

groundwater. Zirlewagen et al. [59] proposed that CYC could be served as powerful indicator due to its higher input concentration and higher stability. Review from Tollefsen et al. [99] reported that the removal efficiencies of SUC in sewage treatment plant (STP) were as low as 5%–20%. In other study, Soh et al. [100] noted removal efficiencies of SUC as high as 32%–48% using advanced cleaning technologies and adapted inoculums. However, it has been documented that the breakdown of SUC is slow and incomplete under realistic (STP) operational conditions [99]. For this reason, SUC has been proposed as chemical markers for wastewater contamination. Scheurer et al. [97] reported that compounds with a pronounced stability during wastewater treatment are ACE, SUC and CBZ. They found that CBZ and ACE could be used to predict the source accurately if the influence of point sources and regional differences is limited. It was shown that ratio of persistent organic could be used to estimate certain wastewater impact and the occurrence of other trace pollutants. Apart from their use as wastewater markers, ASs had also been proven as powerful tracers for detecting landfill leachate plumes in groundwater. Roy et al. [101] showed that SAC and CYC could be used as tracers for current and legacy landfill contamination.

Most of the literature findings showed that acesulfame and sucralose are the most widely used ASs to trace wastewater contamination in aquatic environment because of their high detection frequencies and low adsorption capacities onto soil. The concentrations and detection frequencies of ASs may vary for different water matrices and locations. SUC had been proposed as a promising marker for wastewater contamination in US [52,54]. Oppenheimer et al. [54] proposed an analytical framework utilizing ratios of carbamazepine to sucralose and gadolinium anomaly to sucralose to distinguish sources of anthropogenic loading to impaired water bodies. The authors noted that SUC was an effective marker as it appears to be ubiquitous in the human diet and stable in the environment. However, it may not be applicable universally for other regions. For instance, Tran et al. [29] found that SUC is not a suitable marker of wastewater contamination in Singapore due to its low detection frequencies in Singapore's surface water and groundwater. On the other hand, SUC was not detected in 54 samples from Tastatt (Germany). The concentrations were below detection limit of 50 ng/L. However, this did not confirm the samples were free from sewer contamination [102]. In another study conducted by James et al. [103], the authors found that SUC was not a good marker for wastewater from septic tanks. They noted low correlation between sucralose concentration and bacteria in the septic effluent. Results from these studies showed that the use of SUC as marker was site-specific. Hence, it is necessary to study the occurrence and fate of ASs and hydrological conditions prior to selecting the appropriate ASs markers for the study sites. Other ASs (besides acesulfame and sucralose) are usually present at high concentrations in wastewater and not detected in surface water samples. In this connection, research should be directed to study the fate and transport of ASs. Sorption and biodegradation behaviors of ASs in soil and aquatic environment should be investigated. In addition, further investigation on the use of both persistent indicators (ACE and SUC) and other biodegradable indicators is warranted.

2.3. Fluorescent Whitening Agents (FWAs)

Fluorescent whitening agents (FWA) is a class of detergent compounds that absorb ultraviolet light and emit light in the blue range [104]. FWAs are active ingredient in laundry detergent and are used worldwide in remarkably large quantities. The extensive usage of FWAs has raised environmental concern due to the high water solubility and recalcitrant nature of this compound and the tendency to accumulate on sewage sludge. These characteristics are the reason for poor removal of FWAs in wastewater treatment system. Stoll and Giger [61] carried out a river monitoring program in Switzerland. The FWAs concentrations were detected to be between 6 ng/L and 120 ng/L for diaminostilbene (DAS 1) and between 10 ng/L and 70 ng/L for distyrylbiphenyl (DSBP). Mass balance indicated that 13% of FWAs consumed were released to surface waters. This observation suggested FWAs can potentially serve as promising marker for wastewater contamination. One of the greatest advantages of using FWAs as chemical marker is the method to detect these compounds is relatively simple, fast and inexpensive [105]. Some fluorometers allow additional features of

detecting FWAs in real time (continuous-flow reading). For instance, DAS 1 and DSBP have been successfully applied as chemical markers to detect wastewater contamination [60,61,63]. A study was performed on mountain river impacted by FWAs from both domestic and industrial sources [106]. The authors found that variations of fluorescence decay at $\lambda_{\text{ex}} = 360$ nm could explain the potential FWA sources from laundry greywater (domestic source) and paper and textile mills (industrial sources). It was suggested that $\lambda_{\text{ex}} = 280$ nm could also be considered as an indicator of FWA pollution in river. In a study conducted in Nottingham, d-limonene was detected in 50% of the raw sewage samples and was suggested as useful marker to detect wastewater contamination [71].

Although FWAs have been successfully used for detecting wastewater contamination in surface water, contradictory results were reported. Dickerson et al. [107] reported that detection of FWAs could be interfered by humics and dissolved carbons present in wastewater and surface waters by fluorometry. In addition, previous studies found FWAs could be photo-degraded in environment [60,63]. Another drawback of using FWAs as marker is the lack of correlation between FWAs and fecal bacteria [105]. Therefore, FWAs as tracer to detect wastewater contamination in receiving bodies should be used with caution. More research is needed on the behavior and fate of FWAs to confirm its application as a chemical marker of wastewater contamination.

2.4. Sterols/Stanol (SSs)

Sterols are a family of lipid compounds with a steroid ring structure and they are important constituent of cells [108]. They are present naturally in plants (campesterol, stigmasterol and β -sitosteril) and animals (cholesterol and coprostanol) [67,108]. Sterols can be converted to stanols through biohydrogenation by bacteria that are present in the digestive track of some warm-blooded animals [109]. The presence of SSs in the environmental matrices can be identified as fecal contamination since stanols produced by the reducing bacteria are only present in feces. For instance, coprostanol (COP) was found to constitute 40%–60% of the total sterols present in human waste [109,110]. COP was suggested as a marker for human-derived pollution due to its persistence during transportation in the environment [111]. However, Writer et al. [112] highlighted the use of COP as sole marker was inaccurate. The authors introduced a ratio of COP to cholestanol (CSA) + cholesterol (CSE) to trace sewage contamination, with COP represents sewage source and CSE represents both sewage and non-sewage sources. COP concentrations in bed sediments were noted to be greater than 0.010 $\mu\text{g/g}$. Comparison of geochemical data and the hydrologic model showed that sediment bound COP could be transported to settling basin at Lake Pepin and Pool 19. Writer et al. [113] showed that the combined use of geochemical data and a mass balance hydrological model enabled a better understanding of contaminant transport in Mississippi river. The ratio of $\text{COP} + \frac{\text{ECOP}}{\Sigma \text{Sterols}}$ reported by Sherwin et al. [114] could be utilized to detect untreated sewage contamination when values are above 0.2. Several SSs ratio developed enables level of wastewater contamination and pollution source identified, e.g., human and non-human (Tables 2 and 3). However, not all values were within the range of SSs ratio from the previous literatures. Hence, more studies are needed to verify the pollution sources. Multi-metric approaches together with SSs ratio are highly recommended for specific-pollution source.

Isobe et al. [68] studied the fecal pollution using SSs in tropical countries where serious sewage pollution had occurred. A total of 59 sampling stations were investigated and analyzed for chemical markers (SSs) and microbiological markers (fecal coliforms and fecal streptococci). The relationship between both bacteriological and chemical indicators fluctuated among different environmental settings due to the vast number of variables used in the study. Isobe et al. [68] noted that *E. coli* showed significant correlation ($r^2 = 0.86$) with coprostanol in samples collected in Malaysia and Vietnam. This was the first work which applied coprostanol (and other SSs) successfully as fecal pollution tracer in Southeast Asia. The results suggested that improvement of the sewage treatment systems in the studied area were needed. Understanding the degradation rates and persistence of SSs in sediments and aquatic environment, and contribution of stanols to sediments can be helpful for tracing wastewater contamination. In addition, transformation and degradation between sterols and stanols

could impact the detection of SSs. Nishimura and Koyama [70] reported that stanols from Lake Suwa could be degraded and survived in sediments as compared with stenols. They noted that stanols in the surface sediment was originated from living organisms. In another study, it was noted that COP and CSE were converted to epicoprostanol (ECOP) and CSA, respectively, under anoxic conditions [115]. The conversion is a function of environmental parameters such as temperature, acidity, redox potential, etc. Therefore, understanding the conditions of transportation and impact of the environmental parameters is crucial for the selection of suitable SSs as markers.

Table 2. SSs Indices for identification of wastewater contamination.

SS Ratio	Level of Wastewater Contamination			Reference
	Certain	Unsure	No Contamination	
$\frac{\text{Coprostanol}}{\text{Coprostanol} + \text{Cholestanol}}$	>0.7	0.3–0.7	<0.3	[65,67,69,112,115–123]
$\frac{\text{Coprostanol} + \text{Epicoprostanol}}{\text{Coprostanol} + \text{Epicoprostanol} + \text{Cholestanol}}$	>0.7	0.3–0.7	<0.3	[67,120,121]
$\frac{\text{Epicoprostanol}}{\text{Coprostanol}}$	<0.2	0.2–0.8	>0.8	[65,124]
$\frac{\text{Coprostanol}}{\text{Cholesterol}}$	>1.0	-	<1.0	[108,115,118,121,123,125–129]
$\frac{\text{Coprostanol}}{(\text{Cholestanol} + \text{cholesterol})}$	>0.06	-	-	[69,112,123,130]
$\frac{\text{Coprostanol}}{\text{Epicoprostanol}}$	>1.5	-	<1.5	[115,118,121,128]

Table 3. Ratio of SSs for source assignment.

SS Ratio	Value	Origin	Reference
$\frac{\text{Coprostanol} + \text{Epicoprostanol}}{\text{Cholesterol}}$	>3.7	Pig	[131,132]
	<0.7	Chicken, cow	
$\frac{\text{Campesterol} + \text{Sitosterol}}{\text{Cholesterol}}$	30–75	Human and herbivore	[122]
	>1.5	Pig, chicken, cow	[131,132]
$\frac{\text{Epicoprostanol}}{\text{Coprostanol} + \text{Cholestanol}}$	<1	Human	[132,133]
	>0.1	Cattle, horse, deer	
$\frac{\text{Sitosterol}}{\text{Coprostanol}}$	<0.01	Human	[69,134]
	>1.0	Bovine manures	
$\frac{\text{Coprostanol}}{\text{Coprostanol} + 24\text{-ethylcoprostanol}}$	<1.0	Human or porcine feces	[69,135]
	>0.73	Human	
$\frac{24\text{-ethylcholesterol}}{24\text{-ethylcoprostanol}}$	<0.38	Herbivores	[136,137]
	>4	Plant decay	
$\frac{\text{Coprostanol}}{24\text{-Ethylcoprostanol}}$	<1	Fecal source	[136]
	>1	Human	
	>0.8	Human	
	<1	Herbivore	[136]

2.5. Nitrate and Nitrogen Isotopic Signatures

High nutrient concentrations in water bodies may be an indication of wastewater contamination. Nitrate was found to be present in wastewater effluents as well as in ground and surface waters [139–141]. Utilizing nitrate as a marker for wastewater contamination has the advantage of having simple detection method and short analysis time. In particular, recent technologies enable on-site measurement. A study was carried out to track anthropogenic inputs using various markers such as caffeine, indicator bacteria and nutrients to distinguish human and non-human contamination

sources in southwest Georgia (US) [15]. Elevated caffeine and nitrate were correlated to population centers and their associated wastewater treatment plants. Significant correlations between caffeine and nitrate (R between 0.60 and 0.77) and fecal coliform were evident but they occurred irregularly. The authors found that, in rural area, higher levels of caffeine and nitrate were linked to population centers and their associated wastewater treatment plants. They found that bacteria were detected at higher concentration at downstream and did not follow dilution trend. This is an indication of natural sources. Furthermore, Peeler et al. [15] noted that higher bacterial levels were detected in a wetland free from human influence but heavily populated by wildlife. The authors successfully applied multiple markers (caffeine, nitrate and coliform bacteria) in distinguishing human and non-human pollution sources in surface water. Seiler et al. [142] also reported the presence of caffeine and PPCPs in ground water with elevated nitrate concentrations can be useful indicators of recharge from domestic wastewater. The authors highlighted the limitation of using caffeine as markers because it apparently is not conservative and its presence is unpredictable. The use of isotope as wastewater tracers has not been extensively studied. Fenech et al. [33] reported that isotopes could be used to trace contamination of nitrate as nitrate consists of N and O, which have naturally occurring stable isotopes. Although isotope tracers could be useful for the detection of nitrate contamination, they are not able to distinguish the source, e.g., sewage and manure because of the overlapping of sewage and manure $\delta^{15}\text{N}$ value. The authors proposed the combination of isotope tracers and chemical markers (PPCPs and food additives) to differentiate the source of contamination. In addition, Barrett et al. [71] found that nitrogen isotopic signatures from the studied sites could serve as an indication of a sewage source. They showed combination of stable nitrogen isotopes and microbiological indicators can be used competently to identify sewage recharge in shallow groundwater. Although the presence of nitrogen may not be necessarily related to sewage derived contamination, the author compared the mean $\delta^{15}\text{N}$ value of 5.3‰ for raw sewage and this showed clear evidence of isotopic enrichment. This study confirmed the finding of Kreitler [143]. Barrett et al. [71] noted that the reasons for the nitrate to become isotopically heavier during infiltration were the partial volatilization of ammonia and depletion in ^{15}N during decomposition of urea in sewage but it was not the sewage itself that was isotopically enriched. The authors found that groundwater nitrogen isotope data were inconsistent with fecal coliforms results. The authors proposed a combination of microbiological fecal indicators (total coliforms, *E. coli*, fecal streptococci, coliphage and enterovirus) and nitrogen isotopes as a tool for “fingerprinting” of sewage recharge to groundwater.

The disadvantages of using nitrate as markers are: (i) it can be diluted during transportation; and (ii) it undergoes biogeochemical processes which can potentially convert nitrate to the other forms of nitrogen. Even though nitrate is always present in septic discharges, the source of nitrate may not necessarily originate from septic system. Nitrate may come from fertilizers and degradation of soil organic matter. Thus, an integrated approach to combine the use of nitrate and other chemical markers should be used, as it is unlikely that nitrate could serve as an ideal marker for wastewater contamination alone. It is concluded from the previous literature that the presence of nitrate does not confirm the receiving body is free of wastewater contamination. However, this provide additional evidence of potential wastewater contamination e.g., correlation with the bacteria and chemical compounds.

2.6. Alternative Potential Chemicals

The previous sections have described the current chemical markers which are widely used. The reviews carried out suggest the selection of wastewater markers is always site-specific. A number of other potential markers of wastewater contamination have also been identified. Barrett et al. [71] reported that adsorbable organic sulfur may be regarded as potential sewage markers as these compounds are indicators of FWAs in detergent. Previous studies suggested that the combined use of inorganic chemical indicators (boron and chloride), isotopic tracers, selected organic compounds and PPCPs is a useful tool to assess sources of contamination in different hydrologic settings [144,145]. Based on a study conducted by Xu et al. [146], citric acid could be used as markers of grey water in sanitary sewage. They also found that chloride, fluoride and sulfate are useful markers of semiconductor wastewater.

3. Considerations of the Use of Chemical Markers to Detect Wastewater Contamination

The selection of potential chemical markers is dependent on various factors such as land use, population, geology, type and level of pollutants in the sewage, hydro-climatic and environmental conditions. In order to select realistic wastewater markers, it is useful to understand the characteristics of the markers. It is generally agreed that the use of single marker is not sufficient to provide this additional information. Recent trend suggests the use of multiple markers. For instance, ratio of coprostanol/cholesterol can be used to assess the degree of sewage pollution [68,109]. Higher ratio of stigmastanol to other SSs is an indication of presence of fecal matter from herbivorous animals such as cow and sheep [147]. In addition, measurement of related physico-chemical parameters is recommended. The data may be useful to support findings on the source of contamination. In a recent study by De Sousa et al. [38], they showed that measurement of electrical conductivity was not only useful for screening of pollution level, but could also be used to support findings on the contamination sources with the aid of statistical analyses (Principal component analysis (PCA) and correlation). Figure 1 summarizes the approach in selecting the appropriate chemical markers.

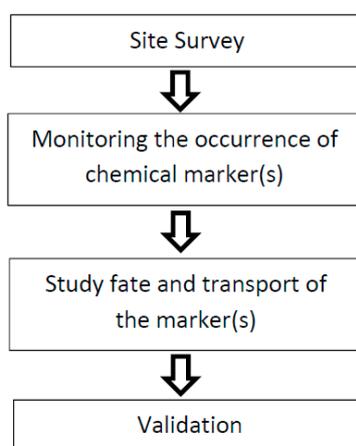


Figure 1. Approach for detecting sewer contamination using chemical markers.

3.1. Site Survey

Chemicals found in wastewater are site- and source- specific. The occurrence, types, transportation and fate of pollutants are largely dependent on human activity, environmental conditions and land use pattern. Thus, selection and consideration of chemical marker(s) in a new site begins with site survey and data collection. Characterization of the specified site/catchment and the potential fecal input are important steps in selecting potential markers. Characterization of site with the evaluation and analysis of the land use, hydrology, population, weather conditions, soil, wastewater treatment processes and other related information could help to identify appropriate potential marker(s) for selection. In addition, types and concentration level of pollutants could be assessed and predicted based on the data collection such as PPCPs consumption data, biodegradation and sorption rates, stability during transportation and fate in soil, and average removal capacity in wastewater treatment plants. Site characterization data should be analyzed and interpreted for a comprehensive assessment such of potential source. For example, food and beverages wastes from food courts and restaurant can be a source of ASs. This information suggests that ASs could be used to track the pollution as artificial sweeteners (ASSs) were reported to be persistent and poorly removed in conventional WWTPs [29].

3.2. Occurrence and Detection of Chemical Markers

Detecting chemical markers in both wastewater source and receiving bodies can be a challenging task due to dilution during transportation and interference of matrix constitutes in the water samples. The method quantification limits for the markers are recommended to be sub-ppt levels, so that it

can detect the target analytes in receiving bodies. Recently, there have been significant improvement and development in chemical markers quantitation methods to provide high throughput capability and to enhance detection sensitivity. Advances in analytical techniques allow chemical markers to be detected in wastewater.

Detailed monitoring programs are required to investigate the occurrence of potential markers. Concentrations of chemical markers detected in wastewater and surface waters from previous studies are tabulated in Table 4. The sample should be collected at source (wastewater), during transport (canal), and receiving bodies (reservoir, groundwater, surface water) and, moreover, the sampling schedule should cover different weather conditions such as wet and dry periods, different seasonal periods, as well as temporal and spatial distribution. Background samples (without impact by wastewater source) should be collected for comparison. Statistical analysis and indices could be performed and used to identify potential markers. For instance, PCA was used to evaluate the spatial and temporal variation of the chemical parameters and emerging contaminants to select promising markers [38]. Peeler et al. [15] studied the relationship between caffeine and other water quality parameters. It was found that the measurement of caffeine, nutrients and indicator bacteria was useful to distinguish human versus non-human sources of wastewater contamination. In addition, detection ratio and detection frequency are widely used indices to identify chemical markers for wastewater contamination. Fenech et al. [33] proposed the use of acetaminophen, caffeine and carbamazepine as chemical markers at Tullow site as their detection frequencies (>83%) are the highest. In another study, five compounds (benzophenone, ethyl citrate, galaxolide (HHCB), tributyl phosphate and triclosan) with detection frequencies of 50%–70% were proposed as suitable chemical markers for human fecal contamination [14]. Buser et al. [148] highlighted that the concentration ratio of ephemeral compound and a recalcitrant compound should decrease with the increased time in a water body. Glassmeyer et al. [14] applied this ratio in their study and found that it was a useful tool in predicting the composition of compounds in lake as compared to lake's hydraulic residence time and also temporal and spatial distance from a known source in a river.

3.3. Fate and Transport of Chemical Markers

An important factor for consideration in selecting the appropriate markers for wastewater contamination would be to understand their fate and transport in the environment. Transport of chemical markers may be affected by various environmental factors such as dilution and natural attenuation. It was found that adsorption and biodegradation processes were the main transport mechanisms of sewage molecular markers in a subsurface area [149,150]. Yamaji et al. [151] showed that photodegradation affected the fate of FWAs in the lacustrine system significantly, with the DSBP and DAS 1 removal rates of 93%–99% and 44%–63%, respectively. They demonstrated that FWAs and DSBP/DAS 1 ratio were good indicators for studying the role of direct photodegradation in behavior of water-soluble chemicals in aquatic environments. Carbamazepine, benzotriazole and primidone were determined to be suitable markers based on their low sorption affinity to soil, while the use of sulfamethoxazole as a marker was limited by the formation of non-extractable residues at lower pH [152]. Yu et al. [152] also highlighted that organic carbon could impact sorption process. Badruzzaman et al. [153] found that sucralose was the most recalcitrant marker in the environment based on their low removal rate (15%) by adsorption, biodegradation or photolysis. Markers with high attenuation were iohexol (90% by photolysis) and carbamazepine (50% by photolysis). They also noted that atenolol was highly biodegradable (60%–80% by biodegradation and adsorption). Foolad et al. [86] studied the fate of nine target sewage markers and found that acetaminophen (ACT), caffeine (CF) and diethyltoluamide (DEET) were removed completely through biotic soil column due to adsorption and biodegradation processes. It is well-known that the transport of chemical markers from wastewater source to receiving bodies are highly affected by the characteristics of wastewater, degree of dilution, type of sediment, temperature, pH and degradation during transport. Limited study was performed to determine the synergistic and antagonistic effects of markers and their metabolites during transport. Indeed, comprehensive study into the fate and transport of chemicals should be conducted for selecting appropriate markers for wastewater contamination.

Table 4. Concentrations of chemical markers detected in wastewater and surface water.

Chemical Marker	Wastewater			Location	Reference	Surface Water			Location	Reference
	Concentration (ng/L)					Concentration (ng/L)				
	Reporting Limit	Mean	Range			Reported Limit	Mean	Range		
Acetaminophen	5.0		1530–337,035	Singapore	[154]	0.1		nd–12.5	Jiulong River, China	[35]
	119.1	2872.5	120.5–6421.6	Ioannina City, Greece	[155]	5.0		25–1163	Singapore	[154]
	58	10,194	130–26,090	Croatia	[156]	5.0	44.3	na–203.2	Ireland	[36]
Diclofenac	3.0		nd–950	Singapore	[154]	0.1		0.819–11.0	Jiulong River, China	[35]
	77.8	100.8	81.1–143	Ioannina City, Greece	[155]	6.0	55	3–180	Ensanche, Spain	[157]
	30	250	50–540	Croatia	[156]	5.0	5	nd–60	Spain	[156]
Caffeine	10	859	50–4200	Bosnia and Herzegovina, Croatia and Serbia	[158]					
	10.0		4219–359,400	Singapore	[154]	0.1		8.07–3060	Jiulong River, China	[35]
	9.0	32,894	na–47,030	Greater Montreal, Sweden	[39]	30.0		428.2–9699.8	Somes River, Romania	[159]
	10.0	127		US	[52]	5.0		265–14,418	Singapore	[154]
	37.2	26,107.5	17,047.1–36,238.0	Ioannina City, Greece	[155]	10.0		13–300	US	[52]
Chemical Marker	Wastewater			Location	Reference	Surface Water			Location	Reference
	Concentration (ng/L)					Concentration (ng/L)				
	Reporting Limit	Mean	Range			Reported Limit	Mean	Range		
	1.0	1180	52,000–192,000	Almeria, Spain	[160]	9.0	112	na–781	Greater Montreal, Sweden	[39]
	10.0	228	23–776	South Korea	[161]	0.25	65.9	na–216.7	Ireland	[36]
	0.5		5173–17,500	Taipei, Taiwan	[162]	4.3		na–522	Greece	[45]
						10.0	105	2.9–194	South Korea	[161]
Carbamazepine	0.5		6.1–939	Singapore	[154]	30.0		nd–75.1	Somes River, Romania	[159]
	2.0	246	na–618	Greater Montreal, Sweden	[39]	0.3		0.5–53.5	Singapore	[154]
	5.0	416		US	[52]	2.0	5	na–22	Greater Montreal, Sweden	[39]
	0.1		460–1700	Israel	[48]	5.0		31–190	US	[52]
	15.8	98.8	29.8–221.6	Ioannina City, Greece	[155]	0.5	5.8	na–30.1	Ireland	[36]
	na		71–1300	US	[163]					
Bisphenol A	10.0		nd–839	Singapore	[154]	1.0		nd–925	Jiulong River, China	[35]
	7.0	1400	720–3400	Almeria, Spain	[160]	5.0		nd–324	Singapore	[154]
	13	510	nd–2060	Bosnia and Herzegovina, Croatia and Serbia	[158]					

Table 4. Cont.

Chemical Marker	Wastewater			Location	Reference	Surface Water			Location	Reference
	Concentration (ng/L)					Concentration (ng/L)				
	Reporting Limit	Mean	Range			Reported Limit	Mean	Range		
Propyl paraben	300		nd-500	Portugal	[164]	0.1		0.440–69.9	Jiulong River, China	[35]
Metoprolol	12		nd–15.2	Coimbra, Portugal	[39]	0.1		0.788–36.0	Jiulong River, China	[35]
	na	77	22–223	Lyon, Fran	[165]	3.8		39–107	River Vantaa, Finland	[166]
Ibuprofen	350	2633.4	418.2–8890.1	Ioannina City, Greece	[155]	30.0		nd–115.2	Somes River, Romania	[159]
	na		1979–33,764	Tyne, UK	[167]	6.0	1277	1100–5297	Ensanche, Spain	[157]
Oxypurinol	25		2800–26,600	Germany	[51]	25		90–22,600	Germany	[51]
Triclosan	1.0		500–1300	Switzerland	[168]	0.4		nd–74	Switzerland	[168]
			42–213	Switzerland	[169]	0.1		0.11–4.77	Singapore	[170]
		202.7	nd–527.9	Ioannina City, Greece	[155]					
	1.399	547	247–785	Ulsan, Korea	[171]					
	3.0		23–434	Australia	[172]					
Atenelol	11		361–751	Coimbra, Portugal	[173]	30.0	72	nd–250	Spain	[156]
	na	1043	388–2450	Lyon, France	[165]	1.0		nd–560	South Wales, UK	[174]
	66.35	117.82		Llobregat, Spain	[175]	11.8		17–55	River Vantaa, Finland	[166]
Salicylic acid	272.0	42,348.1	4138.4–89,133.5	Ioannina City, Greece	[155]	0.3		nd–302	South Wales, UK	[174]
Chemical Marker	Wastewater			Location	Reference	Surface Water			Location	Reference
	Concentration (ng/L)					Concentration (ng/L)				
	Reporting Limit	Mean	Range			Reported Limit	Mean	Range		
	76.69	674.33		Llobregat, Spain	[175]	13.05	208.17		Llobregat, Spain	[175]
						3.0		7.94–112	Singapore	[170]
Acesulfame	5.0		187–75,093	Singapore	[154]	3.5		5–350	Singapore	[154]
						25		28–9600	Finland	[96]
	3.0		1070–51,200	Shanghai, China	[146]	1.0		na–178	Greece	[45]
	20		24,800–26,700	Spain	[176]	10		400–53,700	Spain	[176]
	0.6	11,600		Tianjin, China	[177]	0.6		2730–4650	Tianjin, China	[177]
Aspartame	15.0		nd–2262	Singapore	[154]	1.0		nd–76.8	Tianjin, China	[177]
	1.0	64.7		Tianjin, China	[177]					
cyclamate	5.0		300–250,348	Singapore	[154]	1.04.0		28–1406	Singapore	[154]
	200		25,900–36,400	Spain	[176]	13.0		nd–210	Finland	[96]
	0.9	27,600		Tianjin, China	[177]	0.9		205–313	Tianjin, China	[177]
saccharin	5.0		500–135,759	Singapore	[154]	3.0		40–810	Singapore	[154]
	500		18,400–22,300	Spain	[176]	25		nd–490	Finland	[96]
	1.1		10,300	Tianjin, China	[177]	1.1		193–746	Tianjin, China	[177]
Sucralose	50.0		100–4719	Singapore	[154]	100.0		120–10,000	US	[52]
	100.0	27,000		US	[52]	200.0		nd–1000	Finland	[96]
	5.7	8418		US	[98]					

Table 4. Cont.

Chemical Marker	Wastewater			Location	Reference	Surface Water			Location	Reference
	Concentration (ng/L)					Concentration (ng/L)				
	Reporting Limit	Mean	Range			Reported Limit	Mean	Range		
	500		3000–5300	Spain	[176]	250		400–5300	Spain	[176]
	6.3	20,600		Tianjin, China	[177]	6.3		287–311	Tianjin, China	[177]
Coprostanol	6000	34,300	32,500–36,800	Northern Italy	[178]	6000	8700	8300–9200	Po River, Italy	[178]
	na	26,700		Malaysia	[66]	10.0		15.5–277.6	Singapore	[125]
	5.8	202,000		Plymouth, UK	[179]	2.0		2–67	Canada	[180]
24-ethylcoprostanol	6000	67,100	63,900–70,200	Northern Italy	[178]					
Cholesterol	na	58,000		Malaysia	[66]	1.3		37–189.6	Singapore	[125]
	5.2	32,000		Plymouth, UK	[179]	3.38		13.9–534	Danubi, Hungary	[181]
Stigmasterol	na	1800		Malaysia	[66]	4.50		nd–188	Danubi, Hungary	[181]
	4.50		170–48,500	Hungary	[181]					
Sitosterol	na	1500		Malaysia	[66]	1.32		21.5–1796	Danubi, Hungary	[181]
	2000		na–2900	US	[14]					
Stigmastanol	na	5600		Malaysia	[66]					
	2000		nd–1200	US	[14]					
Chemical Marker	Wastewater			Location	Reference	Surface Water			Location	Reference
	Concentration (ng/L)					Concentration (ng/L)				
	Reporting Limit	Mean	Range			Reported Limit	Mean	Range		
4,4'-bis[(4-anilino-6-morpholino-1,3,5-triazin-2-yl)amino]stilbene-2,2'-disulfonate	5.0		2900–8200	Tokyo, Japan	[60]	3.0		6–120	Switzerland	[61]
	18.0	42		Taiwan	[182]	5.0	1000		Tokyo, Japan	[60]
						45		nd–485	Japan	[151]
4,4'-bis(2-sulfostyryl)biphenyl	0.4		11,100–21,900	Tokyo, Japan	[60]	3.0		10–70	Switzerland	[61]
	4.0	185		Taiwan	[182]	0.4		100–6400	Tokyo, Japan	[60]
						4.0		Nd-425	Lao-jie river, Taiwan	[182]

Notes: nd = not detected; na = not available.

3.4. Validation

It is essential that markers should be absent or detected in significantly lower concentration in the background samples (no known wastewater sources), higher concentrations should be detected in samples with wastewater sources contribution. Glassmeyer et al. [14] collected a wide range of samples which consisted of samples from upstream, downstream, WWTPs, and further downstream in US. The samples collected represent a variety of climatic conditions, population, streams size and treatment capacities of WWTPs. They demonstrated that many compounds present in WWTP effluent were not found in the upstream sample. In contrast, the concentrations of markers were similar (no statistically different) in WWTP effluent and downstream samples, which indicated that contamination of waste water to river water quality was caused by incomplete pollutant removal in WWTP. The concentrations of markers were found to be diminished with greater distances from WWTP. This may be due to instream processes such as dilution, degradation, sorption, etc. In addition, the authors showed the targeted markers (acetaminophen, caffeine, methyl salicylate) were not found at Michigan (a reference site). This further suggested these targeted markers could potentially serve as chemical markers. The absence of target compounds at the reference site clearly indicates that the target compounds are not detected in unpolluted streams, and therefore could be proposed as chemical markers. Tran et al. [29] found that none of the targeted ASs (ACE, CYC and SAC) were detected in the background groundwater samples. However, these compounds were found in all groundwater samples with known leaking sewer segment. In the same study, ACE and SAC were not found in all the background surface water samples. In contrast, CYC was detected in a relatively low concentration compared to those in potentially impacted surface water samples. The authors suggested that the presence of CYC, SAC and ACE in wastewater and impacted surface water was affected by wastewater contamination. Suitable markers that can be used to detect wastewater contamination should be absent (or detected at relatively lower concentration) in reference site (background samples) and detectable at higher concentration in both wastewater source and contaminated surface water. Hence, samples should be collected at different sites to better evaluate and validate suitability of the markers.

3.5. Ability to Distinguish Sources

Identification of pollution sources will help in the management of wastewater contamination. Selection of appropriate markers enables pollution source tracing, which could distinguish between human and non-human, and discernment among different animals origins. Most of the studies to differentiate pollution sources were based on the use of SSs markers. Source identification and apportionment could be achieved through marker ratio analysis and statistical tools such as (PCA) and multiple linear regression (MLR).

The use of SSs as marker provides additional advantage which can be used to discriminate between human and non-human contamination. In addition, a ratio of $\frac{\beta\text{-cholestanone}}{\alpha\text{-cholestanone} + \beta\text{-cholestanone}}$ was proposed [116]. This ratio indicates human fecal pollution if the ratio is greater than 0.7. Richard and Phillip [183] developed the ratio of $\frac{\text{COP}}{5\beta\text{-stigmasteroi}}$ for source identification, where ratio above 1.5 indicates human fecal pollution. Mudge and Seguel [184] proposed a ratio of $\frac{\text{ECOP}}{\text{COP}}$, where the ratio lower than 0.2 indicates untreated sewage contamination. This index has been used by Froehmer et al. [127] to study Barigui river watershed. The ratios were below 0.20 at most stations and it was concluded that sewage discharged into the river did not undergo prior treatment or incomplete removal of the measured pollutants during treatment. This finding has been confirmed using ratios of isomeric forms of sterols and ketones. A consistent result was obtained for the source identification by the SSs based PCA method and microbial markers in river waters contaminated by fecal matter of unknown origin [64]. The approach developed in this study could be applied to differentiate sources of fecal contaminations in water body where fecal contaminations from human, bovine and porcine co-present. This study also validated the use of PCA method to detect the wastewater contamination sources. McCalley et al. [185] proposed ratio of COP/CSE to elucidate the contributions from biogenic

and sewage sources. For instance, ratio greater than 1 indicates sewage source while ratio less than 1 represents biogenic sources. Leeming et al. [109] applied the various ratios of sterols to differentiate the feces sources between herbivore and omnivore. In another study, Leeming et al. [135] successfully distinguish feces from cows and sheep, humans, hens, dogs and cats with the aid of PCA analysis. Kuroda [186] utilized PPCP analysis, tritium analysis, principal component analysis-multiple linear regression (PCA-MLR), perfluoroalkyl carboxylic acid ratio analysis (PFCAR) and their combined use to identify the sources of perfluoroalkyl acids (PFAAs) in Japan. They noted that the primary source of PFAAs in polluted groundwater were sewage (44.6%) and point sources (45.7%) whilst minor source was street runoff (9.7%). Gregor et al. [187] modeled the selected chemical profiles of different fecal sources using classification and regression tree (CART) analysis. The authors concluded that effluents from human wastes could be identified by the use of FWAs. Tables 2 and 3 summarize the indices for wastewater contamination and marker ratio to distinguish sources of contamination.

It is widely accepted that utilizing multiple chemical markers are useful to distinguish sources of pollution and to distinguish “fresh” vs. “aged” wastewater. For instance, Zirlewagen et al. [59] utilized CYC/ACE ratios to identify fresh untreated wastewater. The authors noted that using ACE as indicator alone could not distinguish between “fresh” and “old” wastewater contamination. Hence, they suggested the combined use of ACE and CYC as marker set could provide additional information of the age of wastewater contamination. Low CYC/ACE ratios could be related to both treated wastewater and untreated wastewater with a minimum residence time of several weeks within the karst system. Higher CYC/ACE ratio was due to recent contamination by untreated wastewater. Tran et al. [28] suggested that the presence of both biodegradable markers (CYC and SAC) and persistent marker (ACE) could be useful to detect fresh wastewater contamination e.g., sewer leakage or overflow discharge. This finding had been validated in few sampling locations in Singapore. The ratio of valsartan and valsartan acid was recommended to identify the age of contamination within the study area, e.g., >1 related to fresh untreated sewage and ≤ 1 for wastewater of higher relative treatment level or residence time [188–190]. However, it is worth mentioning that the occurrence of valsartan and valsartan acid is site-specific and depends on the wastewater characteristics. Sidhu et al. [191] suggested that the presence of caffeine, paracetamol and salicylic acid could explain recent contamination from raw sewage due to high prevalence of human adenovirus and human poly-omavirus found in their study. Further studies on the use of multiple markers to assess “fresh” vs. “aged” wastewater contamination are needed in order to better understand and manage the wastewater contamination issues. It is recommended that combination of few chemical markers (both recalcitrant and biodegradable) and/or microbial markers would be useful to assess the wastewater contamination.

4. Conclusions and Future Trend

Various classes of chemicals have been proposed as chemical markers to detect wastewater contamination. The advantages of using chemical markers are relatively fast and sensitive detection methods, spatially and temporally stable, and source-specific compared with microbial markers. PPCPs and ASs have been shown to be specific to wastewater contamination. Numerous PPCPs and ASs compounds are selected as markers because they are persistent, not effectively removed by WWTPs and stable during transport. The persistent nature of FWAs and their widespread distribution in aquatic environment made them suitable to use as markers for sewage contamination. The limitations of using FWAs as markers include the measurement by fluorometer may be interfered by organic matters in the water samples, and some studies noted lack of relationship between FWAs and fecal bacteria. The use of all chemical markers is region and temporally specific.

It requires extensive efforts to identify effective and specific markers for wastewater contamination. In-depth understanding of catchment site and higher number of representative sampling sites and sampling frequencies covering seasonal variations and different operation of wastewater treatment plant would provide a comprehensive assessment on the selection of suitable markers. Most of the previous studies concluded that there is no universal marker. The combination of markers

(chemicals and microbiological) is highly recommended to identify wastewater contamination and source identification especially in a complex catchment. Focus on selection of appropriate chemical markers may provide useful information such as source identification, identification of recent or prior sewage contamination and effectiveness of rehabilitation works. Latest advances in analytical methods allow detection of emerging chemical markers, e.g., endocrine disrupting compounds and their metabolites/intermediate at lower detection limit, lower costs and shorter analysis time.

In the future of chemical marker selection, it would be beneficial to evaluate the other emerging contaminants as potential markers for wastewater contamination. Relationship between fecal input and the markers should be checked periodically to assess the specificity and sensitivity of the use of the markers. It is recommended to use appropriate statistical tools to develop indices/ratio for the identification of wastewater contamination sources. Application of statistics techniques such as PCA, CA and DA would be beneficial for the interpretation of experimental data. Furthermore, analyzing data with these statistical techniques assists in the identification of potential chemical markers and could provide valuable information related to specific source of wastewater contamination.

Another research gap to address in future study is the influence of natural source which are not originated from wastewater, e.g., caffeine from *Cola acuminata*. There is limited study about background levels of chemical markers in aquatic systems and the wastewater sources. Further research should be designed to address this research gap to provide more accurate assessment of wastewater contamination and its origin.

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