Chemicals of Emerging Concerns CECs and Their Transformation Products TPs in Aquatic Enlivenment, Current Status and Challenges: A Comprehensive Review

Sahrish Arshad
Master of Philosophy in Chemistry, University of Agriculture Faisalabad, Pakistan
Email: sehrishsen22@gmail.com

Sultan Ahmad Nasir
Master of Philosophy in Chemistry, University of Sargodha
Email: sultannasir046@gmail.com

Muhammad Asif
Master of Philosophy in Chemistry, Riphah International University Islamabad
Email: asif19176@gmail.com

Received on: 01-05-2024 Accepted on: 01-06-2024

Abstract

Environmental research has shifted from legacy contaminants to Chemicals of emerging concerns CECs in the last two decades. CECs and their transformation product TPs are ubiquitously documented in the aquatic environment due to the increased anthropological activities of humans. These CECs and their transformation product TPs have continuously impacted ecosystems and humans. Though current analytical tools and effect-based methods are out of infancy regarding water analysis, following holistic approaches are necessary to improve the gaps in the current water analysis scenario. (1) Prioritization of more environmentally relevant CECs and their TPs by appropriate and standardized analytical and bioanalytical approaches, (2) continuous and regular monitoring of currents European watchlist, priority list, and substances of very high concerns (SOVHC) by all member states, (3) monitoring of spatial, and temporal occurrence of CECs and their TPs over a more extended period by using passive sampling techniques (4) Integration of target, suspect and non-target screening with Effect-directed analysis to assess the toxic causative chemicals in complex mixtures. (5) Polarity extended screening of CECs and their TPs in environmental (water) samples. Furthermore, for assessing the aquatic environmentally relevant CECs and their TPs, appropriate and standardized analytical tools and assessment protocols are required to address TPs' selection, identification, and quantification and their toxicological relevance. So that adequate mitigation measures are taken against CECs and TPs to protect and conserve our environment.

Chemicals of Emerging Concerns CECs and Their Transformation Products TPs in Aquatic Enlivenment, Current Status and Challenges: A Comprehensive Review

Keywords: Chemicals of Emerging Concerns, Transformation Products

Introduction:

Rapid economic growth, urbanization, and lifestyle patterns increase our society's daily use of chemicals for household activities, industrial manufacturing, agricultural applications, personal care, and human and animal healthcare (Llamas et al., 2020). According to one estimate, more than 100,000 chemicals are registered in the EU, and 30,000–70,000 chemicals are used daily. These chemicals from anthropogenic activities have been continuously discharged into aquatic compartments such as freshwater bodies and cause water pollution (Loos et al., 2009; Zhong et al., 2021). Water pollution has become a daunting challenge and everyday problem for our society because water is the source of life and is used for various purposes, such as drinking (Vasilachi et al., 2021). Nowadays, there are increasing concerns about the chemicals of emerging concerns CECs due to their toxicity and potential risks to human health and ecology. The occurrence of CECs in the aqueous environment has been investigated for several years. Still, during the last two decades, the focus of environmental researchers has been shifted from legacy pollutants to the so-called chemicals of emerging concerns CECs (that are directly discharged into the environment through municipal wastewater effluents, urban stormwater, agricultural runoff, and various diffuse sources) (Pal et al., 2010; Schwarzenbach et al., 2006). Chemicals/Contaminants of emerging concern represent a group of compounds currently not regulated (not submitted to a routine monitoring and emission control regime) whose fate, behavior, and (eco)toxicological effects are poorly understood. Still, they may be under scrutiny for future regulation. It is now known that these CECs are not necessarily newly developed chemicals: most CECs are substances that have entered into the environment for decades, but their existence has only recently been detected due to the development of more sensitive analytical methods (Dulio et al., 2018). CECs consist of surfactants, flame retardants, pharmaceuticals, personal care products, gasoline additives and their degradation products, biocides, polar pesticides, degradation products, and various proven or suspected endocrine-disrupting compounds (EDCs). The NORMAN experts regularly revise the list of emerging substances (Emerging Substances et al., 2021).

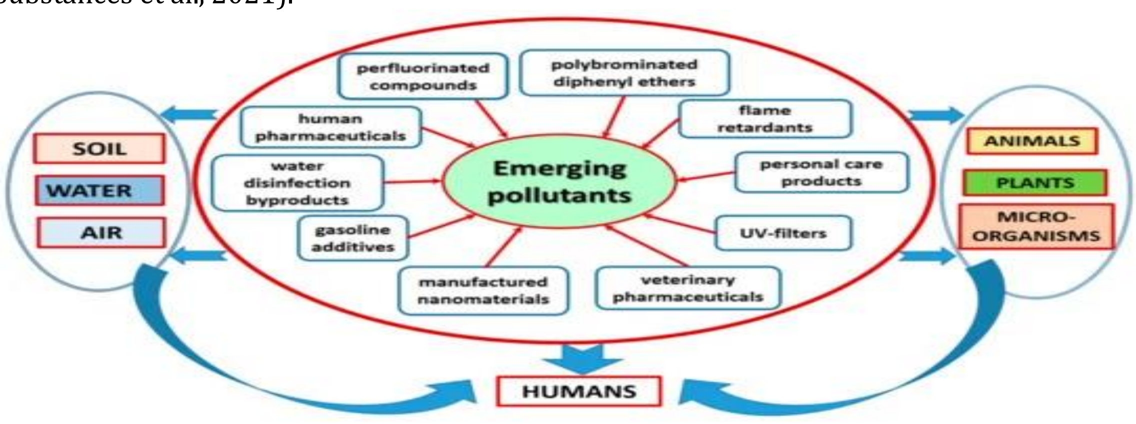

Figure: 1 Category of chemicals of emerging concerns CECs that impact soil, air, water, animals, plants, microorganisms, and humans (Vasilachi et al., 2021).

Ecological Impacts of CECs:

Due to their continuous human consumption and inefficient removal by traditional wastewater treatment processes and other diffuse sources, CECs have been ubiquitously detected in freshwater bodies, drinking water, and the food chain in ng/L to µg/L range. The occurrence of these CECs in the environment may cause unpleasant and toxic effects on aquatic organisms and humans, even their presence at nanogram per litter (ng/L) concentrations. Certain CECs are persistent due to their physicochemical properties and their resistance to degradation (Sousa et al., 2021; Cruzeiro et al., 2016; Sousa et al., 2019). A few CECs are also termed PMT (persistent, mobile, and toxic or vPvMT (very persistent, very mobile, and toxic) due to their persistent, high mobility (solubility) and poisonous nature. These PMT or vPvMT substances can pass through natural barriers like river banks and artificial obstacles in water treatment facilities and cause irreparable damage to the ecosystems (Rüdel et al., 2020). Some CECs are continuous/uncontrolled discharges into the environment and accumulate; these CECs can also be supposed to be "pseudo-persistent" pollutants, which would cause the same exposure potential as regulated persistent pollutants. The occurrence of these CECs in the environment may cause unpleasant and toxic effects on aquatic organisms and humans, even their presence at nanogram per litter (ng/L) concentrations. In recent risk assessment and prioritization schemes with identified concerns including hormonal interference in fishes, genotoxicity, toxicity for reproduction, carcinogenicity in lab animals, endocrine disruption, antibiotic resistance, and immune toxicity (Cruzeiro et al., 2013; Sousa et al., 2019; Zhong et al., 2021). It is tough to estimate the long-term impacts of most CECs on the environment and human health, which is still a daunting challenge. At the same time, the knowledge and awareness of their behavior and hazard/ecological risks are incomplete and limited. Furthermore, the presence of these chemicals as a complex mixture in the aquatic environment can cause additive or synergistic effects, which leads to underestimating the potential impact on marine organisms. Exposure-effects–driven assessment tools describe mixture effects, and then follow-up chemical analysis is used to identify the chemicals that may be responsible for the observed effects (vice versa). Literature suggests the application of specific tools for evaluating the toxic effects of emerging pollutants: environmental risk assessment (ERA), quantitative analysis of the structure-activity relationship (QSAR), the relationship between physicochemical properties and environmental behavior and fate (PPEF), assisted by software tools(Vasilachi et al., 2021).

Because of the pseudo-persistence nature due to their continuous discharge, resistance to degradation of these chemicals in surface and groundwater, climate changes, and the increase of anthropogenic activities may worsen the situation. Since these water bodies are vital for the survival and maintenance of all ecosystems and a source of drinking water, surface water needs to be protected and preserved through detailed study, monitoring programs, risk assessment, and mitigation measures.

Current Regulatory Status of CECs:

The US Environmental Protection Agency (EPA):

Many centuries have responded to this issue regarding the potentially toxic effects on ecology by revising their current water regulations. Comprehensive monitoring of the CECs in the aquatic environment is the core of most management strategies. In the USA, water quality is regulated under the Clean Water Act (CWA) and the Safe Drinking Water Act (SDWA) by the US Environmental Protection Agency (EPA). CECs are incorporated into this regulatory skeleton and the drinking water contaminant candidate list (CCL) mainly through unregulated contaminant monitoring rules (UCMR) and the drinking water contaminant candidate list (CCL) (Bieber et al., 2017; Zhong et al., 2021). According to the Fifth Unregulated Contaminant Monitoring Rule, UCMR 5, 29 per- and polyfluoroalkyl substances [PFAS] and one metal will be monitored from 2023 to 2025 by EPA Methods 533 and 537.1 (Fifth et al., 2021).

The European Union (EU), the water framework directive 16 (2000/60/EC):
In this regard, the European Union (EU) established the Water Framework Directive 16 (2000/60/EC) in 2000 for water policy within the EU, aiming at achieving a sound ecological and chemical status of surface water in the EU. In 2008, the water framework directive (2008/105/EC 2008) was updated, and the first list of 33 priority substances/groups of substances (PSs) that should be monitored within a member of states was made. The Directive 2013/39/EU (2013) again revised its list; a set of 12 new substances were also included in the list, recommending the monitoring of 45 PSs and pointing out the demand for developing new mitigation measures (Pistocchi et al., 2019; Arle et al., 2016). Furthermore, Directive 39/2013/EU also issued a watch list of pollutants for monitoring that may pose a risk to or via the aquatic environment and for which monitoring data is insufficient for better assessments of risks from chemicals present in surface water and supporting future prioritization exercises in the EU (Sousa et al., 2019). This list should be revised every 2 years, and member states must monitor these substances at least once per year for up to four years. This is the first effort within the European Union to incorporate pharmaceuticals and hormones in routine water monitoring (Bieber et al., 2017; Zhong et al., 2021). The watch list was again amended in 2015 (Directive 2015/495/EU), 2018 (Directive 2018/840/EU), and 2020. The latest version of the watch list is included three substances already on the list since 2018 (the insecticide metaflumizone and the antibiotics amoxicillin and ciprofloxacin) and several substances added in 2020: the sulfonamide antibiotic sulfamethoxazole and the diaminopyrimidine antibiotic trimethoprim, the antidepressant venlafaxine and its metabolite O-desmethyl venlafaxine, a group of three azole pharmaceuticals (clotrimazole, fluconazole, and miconazole) and seven azole pesticides (imazalil, miconazole, ketoconazole, miconazole, prochloraz, tebuconazole, tetraconazole), and the fungicides famoxadone and dimoxystrobin (Richards et al., 2021; Chemicals et al., 2021).

NORMAN project:
To cover the gaps in conventional prioritization schemes that often exclude CECs due to data deficiencies, in 2005, the European Commission founded the NORMAN project to promote a permanent network of reference laboratories and research centers, including academia, industry, standardization bodies, and NGOs for the monitoring of contaminants of emerging concern (Brack et al., 2012). As an independent organization, NORMAN plays a vital role as an interface between science and policy, with the benefit of speaking to the European Commission and other public institutions with the “bigger voice” of more than 70 members

from 20 countries (Dulio et al., 2018). Until 18 May 2020, about 1036 candidates have been listed as emerging pollutants most frequently occurring in the environment by the NORMAN Network (Xue et al., 2021).

The European Chemicals Agency (ECHA) and Registration, Evaluation, Authorization, and Restriction of Chemicals (REACH) regulation (EC 1907/2006)

On 1 June 2007, the REACH regulation (EC 1907/2006) (stands for Registration, Evaluation, Authorization, and Restriction of Chemicals) came into force by the European Chemicals Agency (ECHA) (Rüdel et al., 2020). The REACH regulation aims to improve the protection of human health and the environment from the risks that chemicals can pose through the better and earlier identification of the intrinsic properties of chemical substances (Understanding REACH et al., 2020). According to IPCHEM (the Information Platform for Chemical Monitoring), the number of registered and pre-registered substances in REACH regulation is 30,000–50,000 industrial substances chemicals used in daily-use products. However, the current updated (till 15 July 2021) authorized REACH register substances are 23,341 in the European Union. According to IPCHEM (December 2020 report), 3168 substances and compounds have been found in different matrices such as environment, human, food and feed products, and indoor air (IPCheM Portal, 2022; Bopp et al., 2020). The Candidate List of Substances of Very High Concern (SVHCs) was updated on 8 July 2021 by ECHA, and now it contains 219 chemicals that may harm people or the environment (All News, 2022). Of 219 chemicals, 43 substances are already present under the REACH authorization regime. A study (25 studies from 2000 to 2018) revealed that 333 chemicals were found in groundwater and drinking water. Of these 333 chemicals, 142 (43%) represented substances that were registered under REACH (as of May 2017), of which 32 were also utilized as pharmaceuticals, and five were also used as pesticides (Rüdel et al., 2020). Substances registered under REACH already today have a significant risk to drinking water quality. On 15/07/2021, the ECHA made the restriction on manufacture, placing on the market, and use of per- and polyfluoroalkyl substance PFAS in the EU due to their vPvMT and toxic and bioaccumulative nature, both concerning human health as well as the environment (Registry of restriction, 2022). This shows that the current regulations cover only a limited number of chemicals. So, it is a need of the hour to prioritize more environmentally relevant substances by the use of appropriate and standardized analytical approaches and assessment protocols.

Challenge of Persistent, Mobile, and Toxic (PMT) and Very Persistent and Very Mobile and Toxic (vPvMT) Substances:

Those substances that have intrinsic characteristics like persistency (P) mobility (M), and toxicity are termed persistent, mobile, and toxic (PMT) substances. The persistency is due to their low degradation, even if they remain for years in environments. The mobility is because of the high polar nature and lower sorption potential on soil and sediments, so these substances are highly soluble and mobile in water. Furthermore, these substances are highly toxic and are carcinogenic, germ-cell mutagenic, and harmful for reproduction (Hale et al., 2020). Neumann et al. described for the first time (in 2015) the name of these substances as Persistent Mobile and Toxic (PMT) substances and very persistent and very mobile (vPvM) substances, while Reemtsma et al. (2016) presented the name of these substances as

Persistent Mobile Organic Compounds (PMOCs). Due to these properties, these substances can pass through natural barriers like river banks and artificial obstacles in wastewater treatment plants (WWTP) and drinking water treatment facilities, and even granular activated carbon (GAC) filtration, ultrafiltration, advanced oxidation processes (like ozonation) and reverse osmosis are unable to remove these substances effectively (Hale et al., 2020; Emerging contaminants, 2013) once these substances enter the environment, there is irreparable damage to the environment. Furthermore, an analytical and monitoring gap exists for the detection and quantification of these mobile (polar) substances in routine water analysis because conventional analytical methods such as chromatography (GC) and reversed-phase liquid chromatography (RPLC) are unable to detect and quantify most of these substances due to their high polarity, solubility in water and low n-octanol–water partition coefficients (Kow), or low pH-dependent n-octanol–water distribution coefficients (DOW) (Rüdel et al., 2020).

The terms persistent, mobile, and toxic" (PMT) substances and "very persistent and very mobile" (vPvM) substances are also harmonized with the language used within Europe's REACH framework to assess and classify the risks related to industrial chemicals (Registration, Evaluation, Authorization, and Restriction of Chemicals (EC 1907/2006) regulation Annex XIII), and considered PMT and vPvMT substances as equivalent to persistent, bioaccumulative and toxic" PBT, and "very persistent and very bioaccumulative" vPvB (Hale et al., 2020). In October 2020, the European Commission, as part of its Chemical Strategy for Sustainability, decided that by 2022, PMT/vPvM substances should be considered a new SVHC category under REACH. About 260 substances (out of all registered substances under REACH) have been identified as PMT/vPvM by UBA in a research project. Per- and polyfluoroalkyl substances (PFAS) and 1,4-dioxane are examples of PMT/vPvMT substances (Rüdel et al., 2020).

As we have seen in the previous section EPA and ECHA are now taking serious action against Per- and poly-fluoroalkyl substances (PFAS) due to their PMT/vPvMT properties. Because of their continuous emission, inefficient removal by artificial barriers in water treatment facilities, analytical monitoring gap, persistency, mobility over longer distances, toxicity, and high risk associated with PMT/vPvMT substances, these substances can cause irreparable damage to the environment, drinking water resources as well as for human beings. So, there is an urgent need to monitor PMT/vPvMT substances in WWTPs, surface water, and drinking water resources,

Monitoring of Occurrence, Fate, spatial, and seasonal variation of CECs over extended periods:

Anthropogenic organic trace substances have been ubiquitously detected in surface water. These substances enter into the environment via different points and diffuse sources. The distribution and fate of CECs and their TPs in wastewater treatment plants and freshwater bodies depend on many factors such as physio-chemicals properties such as molecular structure, biodegradability. water- and fat solubility, environmental conditions and distribution coefficient, etc. (Emerging contaminants, 2013; Krishi Sanskritil, 2022). The fate of CECs in wastewaters and the environment is better understood by standardized and appropriate sampling techniques. The use of improper sampling approaches is assumed to be the greatest error of reported occurrence data. Most current studies used grab sampling, and grab sampling gives only a snapshot of CECs concentration for a specific point in time. This approach has limitations and does not provide a representative sample and causes uncertainties. If you begin with a poorly chosen sample or If our sample is not representative, then results are meaningless. "Garbage in, garbage out!" So, it would be highly desirable to use a proper sampling strategy. Nowadays time and volume/flow proportional 24h composite samplers are being preferred, because they provide a better estimate of the mean concentration, and also account for fluctuations in inflow (Ort et al., 2010). In SOLUTIONS, researchers suggested passive sampling methods that give better estimates of the time-weighted mean of freely dissolved concentrations of CECs, and high-volume sampling techniques that results in simultaneous access of chemical and bioanalytical analysis, and development of multi-residue methods of higher sensitivity. These sampling techniques offer better exposure estimates and help us to identify the specific toxicological relevance of contaminants (Altenburger et al., 2019). 24h composite and passive sampling methods ensure that representative data is obtained and facilitates a better understanding of spatial and temporal trends of CECs occurrence (Petrie et al., 2015).

Seasonal and spatial monitoring programs are a tool to evaluate the influence of weather conditions (e.g., temperature and precipitation), matrix and environment of water bodies on the fate of the CECs and their TPs, sources of chemicals, their consumption/usage patterns of the target compounds and their degradation rates in WWTPs and the environment (Sousa et al., 2019). A comprehensive understanding of the occurrence and wide distribution of complex trace organic contaminants and their transformation products in freshwater bodies and wastewater treatment plants helps us to predict and mitigate their potential effects on ecological and human health in aquatic environments (Bai et al., 2018). Various studies have reported the occurrence, spatial and temporal distributions of CECs, but the time duration is very short (Reh et al., 2013), and only few studies carried out over extended period (Ashfaq et al, 2019). Due to this reason, the fate and risk assessment of CECs and their TPs are not fully understood, and Therefore, monitoring of CECs and their TPs in the WWTPs and freshwater over an extended period is of great interest.

Transformation Products TPs of CECs:

After the release into the natural water environment and wastewater treatment processes, chemicals of emerging concerns are not completely decomposed but may transform by both abiotic and biotic processes resulting in intermediates that are usually more polar. Transformation products (TPs) are mainly transformed through hydrolysis, oxidation, hydroxylation, conjugation, cleavage, dealkylation, methylation, demethylation, and by different microorganisms. In certain cases, TPs are less toxic than their parent compounds in the aquatic environment, but there is also a large number of examples in which TPs are more toxic in engineered or natural systems and some might show higher sublethal, behavioral, or developmental effects in aquatic organisms or potential adverse effects to human health as compared to the parent compounds (Brack et al., 2019), for example, TCS can transforms to methyl triclosan (MeTCS) and exhibits higher endocrine disruption effects than TCS (Ashfaq et al., 2019).

Most of the studies focus on parent compounds, and very limited studies have reported parent compound and their transformation products together e.g. only a few studies have reported the occurrence of bisphenol A monomethyl ether (BPA-MME) and bisphenol A dimethyl ether (BPA-DME) BPA-MME (transformation products bisphenol A (BPA) (Ashfaq et al., 2018). Furthermore, toxicological data on the effects of these TPs are very poor. All these factors represent a major knowledge gap on occurrence fate and toxicological effects of TPs. The knowledge of transformation pathways and identification of TPs together with parent compounds help us to understand the fate and risk assessments of CECs. Thus, this topic demands further research and, where the action is warranted, appropriate mitigation strategies. Thus, to assess the aquatic environmentally relevant TPs, appropriate and standardized analytical tools and assessment protocols are required to address the selection, identification, and quantification of TPs and their toxicological relevance (Brack et al., 2019).

CECs and their TPs on suspended solids:

During mass load and mass balance calculation in WWTPs and freshwater, only dissolved aqueous concentrations of CECs and their TPs are considered, and concentrations of CECs on suspended solid are ignored which leads to underestimations or under-reporting of fate and occurrence of these chemicals (Ashfaq et al., 2018). Analysis of adsorbed CECs and their TPs on suspended solid is necessary because some chemicals have high affinity due to their high Kow coefficient value. Various CECs including amitriptyline, EMDP, dosulepin, fluoxetine, norfluoxetine, triclosan, ofloxacin, and ciprofloxacin norfluoxetine, triclosan, ofloxacin, and ciprofloxacin have been detected on suspended solid (Petrie et al., 2015). This provides a path for their discharge into the environment which goes undetected and the environmental fate of chemicals on suspended solids is unknown. However, a few studies have considered the CECs on the suspended solids during the mass balance assessment, which may lead to the overestimation or underestimation of the CECs losses and bias for CECs fate (Wang et al., 2018; Ashfaq et al., 2017). So, it is highly recommended to consider the of CECs on suspended solids to better estimate the fate.

Suspect screening and Non-target Screening (NTS) by High-resolution Mass spectrometry HRMS:

While in target screening, the targeted compounds are known and standards are available to allow compound-specific method optimizations, in suspect screening, standards are not necessarily available and in non-target analysis, compounds are unknown, and even the structures of the compounds detected are not necessarily known (Altenburger et al., 2019). The number of selected compounds for watch lists, priority lists, and substance of very concerns will always be limited and the selection process will always be time-consuming. Furthermore, the standards of CECs and their TPs are not available. Thus, it cannot fully represent CECs of recent concern (Schmidt, 2018). To cope with these challenges, HRMS detection based on time-of-flight or Orbitrap analyzers can be used in water analysis to allow suspect and nontarget screening without the use of reference standards, and help us to identify known unknown and unknown unknown in complex matrixes (Brack et al., 2019). Since these HRMS-based instruments can screen and detect a very high number of compounds and their TPs, retention time (RT), fragmentation, exact masses, and isotopic pattern of these compounds can be recorded in databases like MassBank, StoffIdent, ChemSpider, Chemicalize, or DAIOS. These databases can also be integrated with silico prediction tools (e.g., MetFrag, Eawag-PPS, CATABOL, PathPred, Meteor) for the provisional identification of the molecule without the use of reference standards in an analytical approach called 'suspect screening'. Structural confirmation by the application of MS/MS analysis may strengthen the analytical approach and boosts the confidence levels of identification. In non-target screening, the tentative identification of CECs and TPs is made without any previous knowledge. In this strategy, very high-resolution MS is used for obtaining high mass accuracy for verification of the proposed molecular formula and reliable interpretation of the MS/MS spectra (Drewes & Letzel, 2016).

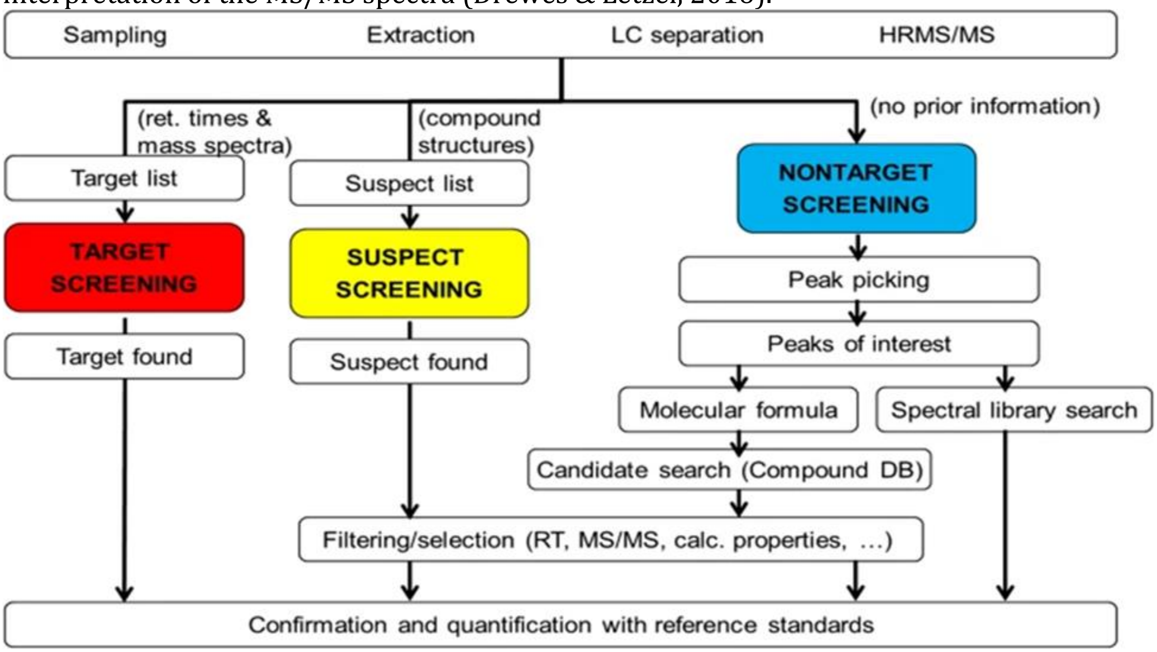

Figure 2. Analytical strategies for the identification and quantification of parent compounds and transformation products (Brack et al., 2019).

Nowadays Two approaches are most commonly used to carry out non-target screening suggested by Schymanski et al. and Krauss et al. Harmonization of data processing, software tools and workflows, availability of open-source MS databases, and data exchange among different software platforms are needed for effective use of non-target screening (Schmidt, 2018; Drewes & Letzel, 2016). The current status-related monitoring of chemicals emerging concern and their transformation products is also complimented with the wide-scope target, suspect, hidden target approaches, and non-target screening (NTS) in combination with effect-directed analysis to guard against and assess the presence and risks of complex mixtures (Brack et al., 2019). As we know that there are thousands of CECs and their TP is present in the aquatic environment but undetected until now due to lack of standards and various others reasons. Several studies have been carried out by the use of NTS, and a lot of work has to be done by utilizing Non-target Screening. So, NTS by HRMS is used to explore the unknown CECs and their TPs. Suspect screening and non-target screening have been successfully applied for real-time monitoring of the Rhine river (Altenburger et al., 2019).

Effect Directed Analysis:

The direct links between exposure to chemicals and effects are not fully understood neither effect-based methods nor chemical analysis alone. This problem was also discussed in the EU-funded project SOLUTIONS, aiming at the development of a more holistic approach to monitor the surface waters in the context of the European Water Framework Directive. A solution-oriented approach has been suggested by the environmental researcher that considers chemical exposures and associated risks in a more integrated manner, for example by combining chemical analyses with effect-based methods. The effect-based analysis is a powerful complementary tool to chemical analysis and should be further implemented in future revisions of the EU WFD (Brack et al., 2018). These bioanalytical tools focus on different biological organization levels and may consist of standardized in vivo and in vitro bioassays, in situ monitoring strategies as well as ecological analyses at the population and community level. The whole toxicity has been evaluated by whole-organism tests, apical endpoints, adaptive stress responses which are caused by complex mixtures of contaminants involving many substances. On the other hand, specific effects on unique receptors in the organism such as endocrine disruption, photosynthesis inhibition, or inhibition of specific enzymes are often evaluated by few individual drivers of mixture toxicity. The identification of these drivers can be a key to the decision on targeted and cost-effective abatement options and needs the integration of effect-based monitoring with chemical analytical tools (Altenburger et al., 2019). Theoretical and experimental assessments tools allow us to evaluate the overall risk to individual organisms or populations of a species, despite the presence of mixtures of hundreds of compounds in environmental matrices. Thus, it is also possible to identify the most significant chemicals contributing to observed effects and will help us to establish cause-effect relationships and provide a focus for potential management measures (Altenburger et al., 2019). Effect-directed analysis (EDA) is a very useful and powerful tool to identify chemicals causing the toxic effect, by chromatographic fractionation which reduces the complexity of the mixtures. Different approaches have been used to demonstrate EDA. An interesting approach is the use of a micro fractionation system that connects LC or even LC×LC separations with a simultaneous collection of fractions in microtiter plates that permits to relate the effect and chemical identity (Wang et al., 2019). Another very effective strategy to prioritize chemicals of emerging concern and their transformation products aquatic water sample by EDA is the application of high-performance thin-layer chromatography (HPTLC-HRMS) in combination with bioassay. HPTLC is used to fractionate samples, then separated zones are subjected to bioassays, and in the final steps, HRMS is utilized to identify chemicals that cause an effect. In this way, HPTLC-HRMS is used with bioassays to facilitate non-target screening for the prioritization of environmentally relevant chemicals in complex mixtures (Stütz et al., 2017; St., 2022). The general workflow is shown in the figure. 3. EDA approach is the most powerful tool so far and the only approach that directly provides cause-effect relationships. Site-specific drivers of toxicity are also identified by Effect-directed analysis (EDA). Limited studies have reported the use of this approach on water and sediments, by using different toxicological endpoints such as endocrine disruption, mutagenicity, dioxin-like effects, and effects on daphnids and algae as well as in wastewater treatment assessments (Brack et al., 2018). So, it is highly recommended to use EDA approach for the prioritization of most environmentally relevant

CECs and their TPs.

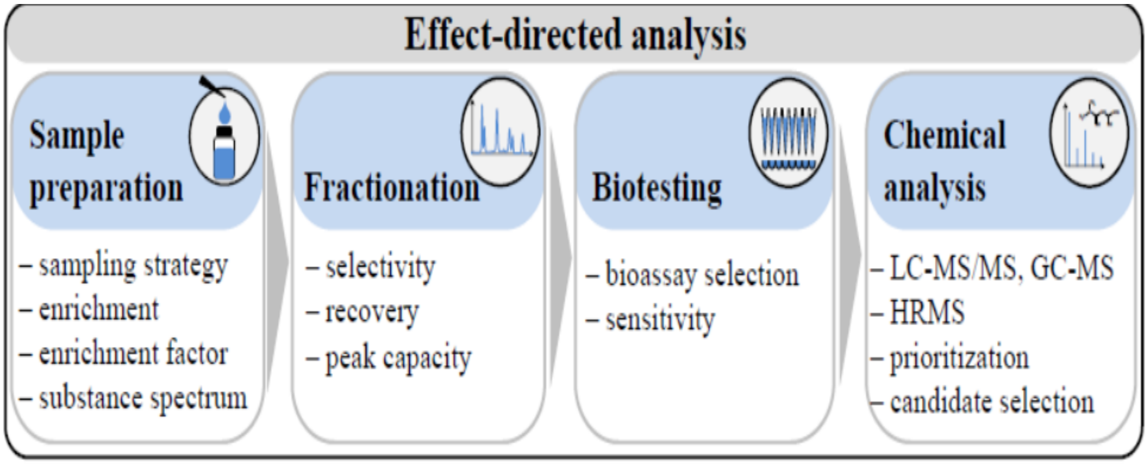

Figure 3. General workflow of effect-directed analysis (Stütz et al., 2017).

Polarity extended monitoring of CECs and their TP (Widening the analytical Window): In addition to fairly polar compounds, water bodies contain a large number of polar and very polar organic compounds due to the very polar nature of water. These water bodies also carry unknown trace organic compounds and their transformation products (TPs). Transformation products (TPs) are often very polar as compared to the parent compound. At the moment, quality of water and pollutant monitoring is carried out largely by liquid chromatography (LC) – (tandem) – mass spectrometry (MS) using reversed-phase (RP) columns for chromatographic separations. Although RPLC-MS is a selective, sensitive and well-established method for the routine monitoring of these regulated and characterized targeted trace organic compounds, it is limited to non-polar to moderately polar molecules (Minkus et al., 2021).

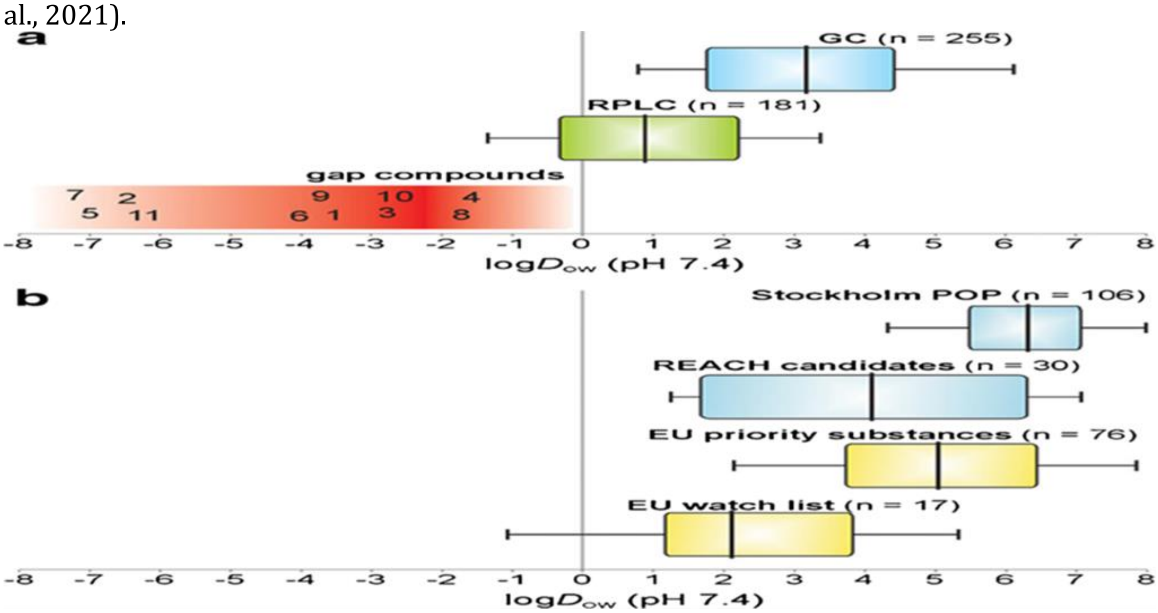

Figure 4. Classification of organic CECs according to their speciation-adjusted partitioning constants between octanol and water (Dow) and analytical gap for very polar organic compounds (Copyright 2016 American Chemical Society) (Schmidt, 2018).

And there is an analytical gap for simultaneous determination of non-polar to very polar organic molecules in water samples in a single run. For the determination and monitoring of a wide polarity range of organic compounds, alternative separation techniques are required. An ideal chromatographic system should provide the separation of non-polar, polar, and very polar compounds in a single run simultaneously. Polarity-enhanced chromatographic methods such as RPLC–HILIC/TOF–MS (using the same mobile phase) and SFC/TOF–MS can fill the gap for the analysis of non-polar, polar, and very polar molecules and are expected to be increasingly used in environmental monitoring in the future, and widening the analytical window (Bieber et al., 2017).

Only a few studies have reported the utilization of this approach, and there is an analytical gap to study a wide polarity range of CECs and their TPs. Furthermore, polarity-enhanced chromatographic methods can also be used to study persistent, mobile, and toxic (PMT) and Very Persistent and Very Mobile and toxic (vPvMT) Substances (Minkus et al., 2020; Bieber & Letzel, 2020).

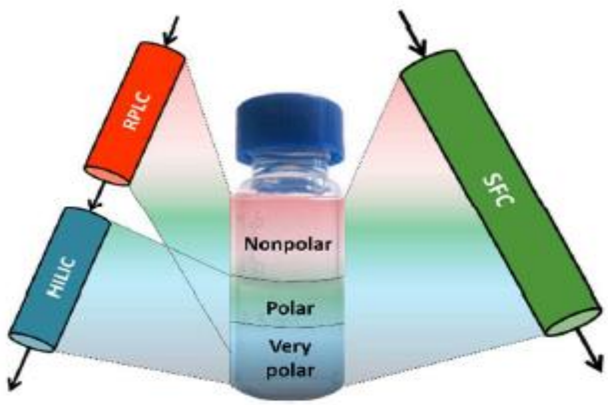

Figure 5. Conceptual diagram of polarity extending monitoring, that covers of Analytical gap for very polar organic compounds (Bieber et al., 2017).

Outlook:

Due to anthropogenic activities of humans, chemicals of emerging concern CECs have been documented in every compartment of the environment, particularly in the aquatic compartment. Contamination of water resources due to CECs is a very concerning issue because water is the source of life and is used for various purposes. If we want to deliver well preserved and protected water reservoirs, and habitat able planet Earth to our grandchildren, then we have to manage the dynamics of chemical innovation, production, consumption, use, disposal, and resulting emission into the aquatic environment, by continues comprehensive monitoring and management strategies, that leads to mitigate their effects on ecosystems.

References:

1. All news. (2022). ECHA. https://echa.europa.eu/-/candidate-list-updated-with-eight-hazardous-chemicals
2. Altenburger, R., Brack, W., Burgess, R. M., Busch, W., Escher, B. I., Focks, A., Mark Hewitt, L., Jacobsen, B. N., Alda, d., Miren López, Ait-Aissa, S., Backhaus, T., Ginebreda, A., Hilscherová, K., Hollender, J., Hollert, H., Neale, P. A., Schulze, T., Schymanski, E. L., Teodorovic, I., .Gothenburg University. (2019). Future water quality monitoring: Improving the balance between exposure and toxicity assessments of real-world pollutant mixtures. Environmental Sciences Europe, 31(1), 1-17. https://doi.org/10.1186/s12302-019-0193-1
3. Altenburger, R., Brack, W., Burgess, R. M., Busch, W., Escher, B. I., Focks, A., Mark Hewitt, L., Jacobsen, B. N., Alda, d., Miren López, Ait-Aissa, S., Backhaus, T., Ginebreda, A., Hilscherová, K., Hollender, J., Hollert, H., Neale, P. A., Schulze, T., Schymanski, E. L., Teodorovic, I., .Gothenburg University. (2019). Future water quality monitoring: Improving the balance between exposure and toxicity assessments of real-world pollutant mixtures. Environmental Sciences Europe, 31(1), 1-17. https://doi.org/10.1186/s12302-019-0193-1
4. Arle, J., Mohaupt, V., & Kirst, I. (2016). Monitoring of surface waters in Germany under the water framework Directive—A review of approaches, methods, and results. Water (Basel), 8(6), 217. https://doi.org/10.3390/w8060217
5. Ashfaq, M., Li, Y., Wang, Y., Chen, W., Wang, H., Chen, X., Wu, W., Huang, Z., Yu, C., & Sun, Q. (2017). Occurrence, fate, and mass balance of different classes of pharmaceuticals and personal care products in an anaerobic-anoxic-oxic wastewater treatment plant in Xiamen, China. Water Research (Oxford), 123, 655-667. https://doi.org/10.1016/j.watres.2017.07.014
6. Ashfaq, M., Li, Y., Wang, Y., Qin, D., Rehman, M. S. U., Rashid, A., Yu, C., & Sun, Q. (2018). Monitoring and mass balance analysis of endocrine-disrupting compounds and their transformation products in an anaerobic-anoxic-oxic wastewater treatment system in Xiamen, china. Chemosphere (Oxford), 204, 170-177. https://doi.org/10.1016/j.chemosphere.2018.04.028
7. Ashfaq, M., Sun, Q., Ma, C., Rashid, A., Li, Y., Mulla, S. I., & Yu, C. (2019). Occurrence, seasonal variation, and risk evaluation of selected endocrine-disrupting compounds and their transformation products in Jiulong river and estuary, china. Marine Pollution Bulletin, 145, 370-376. https://doi.org/10.1016/j.marpolbul.2019.05.016
8. Ashfaq, M., Sun, Q., Zhang, H., Li, Y., Wang, Y., Li, M., Lv, M., Liao, X., & Yu, C. (2018). Occurrence and fate of bisphenol A transformation products, bisphenol A monomethyl ether and bisphenol A dimethyl ether, in wastewater treatment plants and surface water. Journal of Hazardous Materials, 357, 401-407. https://doi.org/10.1016/j.jhazmat.2018.06.022
9. Bai, X., Lutz, A., Carroll, R., Keteles, K., Dahlin, K., Murphy, M., & Nguyen, D. (2018). Occurrence, distribution, and seasonality of emerging contaminants in urban watersheds. Chemosphere (Oxford), 200, 133-142. https://doi.org/10.1016/j.chemosphere.2018.02.106
10. Bieber S and Letzel T (2020) White Paper – Polarity-Extended Chromatography, AFIN-TS Forum; February (1): 1-4.
11. Bieber, S., Greco, G., Grosse, S., & Letzel, T. (2017). RPLC-HILIC and SFC with Mass Spectrometry: Polarity-Extended Organic Molecule Screening in Environmental (Water) Samples. Analytical Chemistry, 89(15), 7907–7914. https://doi.org/10.1021/acs.analchem.7b00859
12. Bopp, S., Franco, A., Cusinato, A., Kephalopoulos, S. & Ceridono, M., Information Platform for Chemical Monitoring IPCHEM (2020) – Update on the state of play of IPCHEM, European Commission, Ispra, 2020, JRC123154.
13. Brack, W., Dulio, V., & Slobodnik, J. (2012). The NORMAN network and its activities on emerging environmental substances with a focus on the effect-directed analysis of complex environmental contamination. Environmental Sciences Europe, 24(1), 1-5. https://doi.org/10.1186/2190-4715-24-29

14. Brack, W., Escher, B. I., Müller, E., Schmitt-Jansen, M., Schulze, T., Slobodnik, J., & Hollert, H. (2018). Towards a holistic and solution-oriented monitoring of chemical status of European water bodies: How to support the EU strategy for a non-toxic environment? Environmental Sciences Europe, 30(1), 1-11. https://doi.org/10.1186/s12302-018-0161-1
15. Brack, W., Hollender, J., de Alda, M. L., Müller, C., Schulze, T., Schymanski, E., Slobodnik, J., & Krauss, M. (2019). High-resolution mass spectrometry to complement monitoring and track emerging chemicals and pollution trends in European water resources. Environmental Sciences Europe, 31(1), 1-6. https://doi.org/10.1186/s12302-019-0230-0
16. Chemicals - Water pollution - Environment - European Commission. (2021). European Commission | Choose your language | Choisir une langue | Wählen Sie eine Sprache. https://ec.europa.eu/environment/water/water-dangersub/index.htm
17. Cruzeiro, C., Rocha, E., Pardal, M. Â., & Rocha, M. J. (2016). Seasonal-spatial survey of pesticides in the most significant estuary of the iberian peninsula – the tagus river estuary. Journal of Cleaner Production, 126, 419-427. https://doi.org/10.1016/j.jclepro.2016.03.005
18. Drewes, J. E., & Letzel, T. /. (2016). Chemicals of emerging concern and their transformation products in the aqueous environment. (). American Chemical Society. https://doi.org/10.1021/bk-2016-1241.ch001
19. Dulio, V., van Bavel, B., Brorström-Lundén, E. et al. Emerging pollutants in the EU: 10 years of NORMAN in support of environmental policies and regulations. Environ Sci Eur 30, 5 (2018). https://doi.org/10.1186/s12302-018-0135-3
20. Emerging contaminants: A tutorial mini-review. (2013). Global NEST Journal, 14(1), 72-79. https://doi.org/10.30955/gnj.000823
21. Emerging substances. (2021.). WELCOME TO THE NORMAN NETWORK | NORMAN. https://www.normandata.eu/?q=node/19
22. Fifth unregulated contaminant monitoring rule. (2021, March 11). US EPA. https://www.epa.gov/dwucmr/fifth-unregulated-contaminant-monitoring-rule
23. Hale, S. E., Arp, H. P. H., Schliebner, I., & Neumann, M. (2020). What's in a name: Persistent, mobile, and toxic (PMT) and very persistent and very mobile (vPvM) substances. Environmental Science & Technology, 54(23), 14790-14792. https://doi.org/10.1021/acs.est.0c05257
24. Hale, S., Arp, H. P., Schliebner, I., & Neumann, M. (2020). Persistent, mobile, and toxic (PMT) and very persistent and very mobile (vPvM) substances pose an equivalent level of concern to persistent, bioaccumulative, and toxic (PBT) and very persistent and very bioaccumulative (vPvB) substances under REACH. https://doi.org/10.1186/s12302-020-00440-4
25. IPCheM Portal. (2022). IPCheM Portal. https://ipchem.jrc.ec.europa.eu/RDSIdiscovery/ipchem/index.html
26. Krishi Sanskriti. (2022). https://www.krishisanskriti.org/vol_image/10Sep201512091935.pdf
27. Llamas, M., Vadillo-Pérez, I., Candela, L., Jiménez-Gavilán, P., Corada-Fernández, C., & Castro-Gámez, A. F. (2020). Screening and distribution of contaminants of emerging concern and regulated organic pollutants in the heavily modified guadalhorce river basin, southern spain. Water (Basel), 12(3012), 3012. https://doi.org/10.3390/w12113012
28. Loos, R., Gawlik, B. M., Locoro, G., Rimaviciute, E., Contini, S., & Bidoglio, G. (2009). EU-wide survey of polar organic persistent pollutants in European river waters. Environmental Pollution (1987), 157(2), 561-568. https://doi.org/10.1016/j.envpol.2008.09.020
29. Minkus, S., Bieber, S., & Letzel, T. (2021). (very) polar organic compounds in the danube river basin: A non-target screening workflow and prioritization strategy for extracting highly confident features electronic supplementary information (ESI) available. see DOI: Analytical Methods, 13(17), 244-254. https://doi.org/10.1039/d1ay00434d
30. Minkus, S., Grosse, S., Bieber, S., Veloutsou, S., & Letzel, T. (2020). Optimized hidden target screening for very polar molecules in surface waters including a compound database inquiry.

Analytical and Bioanalytical Chemistry, 412(20), 4953-4966. https://doi.org/10.1007/s00216-020-02743-0

31. Ort, C., Lawrence, M. G., Reungoat, J., & Mueller, J. F. (2010). Sampling for PPCPs in wastewater systems: Comparison of different sampling modes and optimization strategies. Environmental Science & Technology, 44(16), 6289-6296. https://doi.org/10.1021/es100778d
32. Pal, A., Gin, K. Y., Lin, A. Y., & Reinhard, M. (2010). Impacts of emerging organic contaminants on freshwater resources: Review of recent occurrences, sources, fate, and effects. The Science of the Total Environment, 408(24), 6062-6069. https://doi.org/10.1016/j.scitotenv.2010.09.026
33. Petrie, B., Barden, R., & Kasprzyk-Hordern, B. (2015). A review on emerging contaminants in wastewaters and the environment: Current knowledge, understudied areas and recommendations for future monitoring. Water Research (Oxford), 72, 3-27. https://doi.org/10.1016/j.watres.2014.08.053
34. Pistocchi, A., Dorati, C., Aloe, A., Ginebreda, A., & Marcé, R. (2019). River pollution by priority chemical substances under the water framework directive: A provisional pan-European assessment. The Science of the Total Environment, 662, 434-445. https://doi.org/10.1016/j.scitotenv.2018.12.354
35. Registry of restriction intentions until outcome. (2022). ECHA. https://echa.europa.eu/registry-of-restriction-intentions//dislist/details/0b0236e18663449b
36. Reh, R., Licha, T., Geyer, T., Nödler, K., & Sauter, M. (2013). Occurrence and spatial distribution of organic micro-pollutants in a complex hydrogeological karst system during low flow and high flow periods, results of a two-year study. The Science of the Total Environment, 443, 438-445. https://doi.org/10.1016/j.scitotenv.2012.11.005
37. Richards, L. A., Kumari, R., White, D., Parashar, N., Kumar, A., Ghosh, A., Kumar, S., Chakravorty, B., Lu, C., Civil, W., Lapworth, D. J., Krause, S., Polya, D. A., & Gooddy, D. C. (2021). Emerging organic contaminants in groundwater under a rapidly developing city (Patna) in northern India are dominated by high concentrations of lifestyle chemicals. Environmental Pollution (1987), 268(Pt A), 115765. https://doi.org/10.1016/j.envpol.2020.115765
38. Rüdel, H., Körner, W., Letzel, T., Neumann, M., Nödler, K., & Reemtsma, T. (2020). Persistent, mobile and toxic substances in the environment: A spotlight on current research and regulatory activities. Environmental Sciences Europe, 32(1)https://doi.org/10.1186/s12302-019-0286-x
39. Schmidt, T. C. (2018). Recent trends in water analysis triggering future monitoring of organic micropollutants. Analytical and Bioanalytical Chemistry, 410(17), 3933-3941. https://doi.org/10.1007/s00216-018-1015-9
40. Schwarzenbach, R. P., Escher, B. I., Fenner, K., Hofstetter, T. B., Johnson, C. A., von Gunten, U., & Wehrli, B. (2006). The challenge of micropollutants in aquatic systems. Science (New York, N.Y.), 313(5790), 1072–1077. https://doi.org/10.1126/science.1127291
41. Sousa, J. C. G., Ribeiro, A. R., Barbosa, M. O., Pereira, M. F. R., & Silva, A. M. T. (2018). A review on environmental monitoring of water organic pollutants identified by EU guidelines. Journal of Hazardous Materials, 344, 146-162. https://doi.org/10.1016/j.jhazmat.2017.09.058.
42. Sousa, J. C. G., Ribeiro, A. R., Barbosa, M. O., Ribeiro, C., Tiritan, M. E., Pereira, M. F. R., & Silva, A. M. T. (2019). Monitoring of the 17 EU watch list contaminants of emerging concern in the ave and the Sousa rivers. The Science of the Total Environment, 649, 1083-1095. https://doi.org/10.1016/j.scitotenv.2018.08.309
43. St. (2022). OPUS Hohenheim - Development of strategies for the prioritization of organic trace substances in water by effect-directed analysis - Stütz, Lena. OPUS-Datenbank. https://opus.uni-hohenheim.de/volltexte/2020/1800/
44. Stütz, L., Weiss, S. C., Schulz, W., Schwack, W., & Winzenbacher, R. (2017). Selective two-dimensional effect-directed analysis with thin-layer chromatography. Journal of Chromatography A, 1524, 273-282. https://doi.org/10.1016/j.chroma.2017.10.00948 .

45. Understanding REACH. (2020). ECHA. https://echa.europa.eu/regulations/reach/understanding-reach
46. Vasilachi, I., Asiminicesei, D., Fertu, D., & Gavrilescu, M. (2021). Occurrence and fate of emerging pollutants in water environment and options for their removal. Water (Basel), 13(2), 181. https://doi.org/10.3390/w13020181
47. Wang, Y., Li, Y., Hu, A., Rashid, A., Ashfaq, M., Wang, Y., Wang, H., Luo, H., Yu, C., & Sun, Q. (2018). Monitoring, mass balance, and the fate of pharmaceuticals and personal care products in seven wastewater treatment plants in Xiamen city, China. Journal of Hazardous Materials, 354, 81-90. https://doi.org/10.1016/j.jhazmat.2018.04.064
48. Xue, P., Zhao, Y., Zhao, D., Chi, M., Yin, Y., Xuan, Y., & Wang, X. (2021). Mutagenicity, health risk, and disease burden of exposure to organic micropollutants in water from a drinking water treatment plant in the Yangtze river delta, China. Ecotoxicology and Environmental Safety, 221, 112421-112421. https://doi.org/10.1016/j.ecoenv.2021.112421.
49. Zhong, M., Wang, T., Zhao, W., Huang, J., Wang, B., Blaney, L., Bu, Q., & Yu, G. (2021). Emerging Organic Contaminants in Chinese Surface Water: Identification of Priority Pollutants. Engineering.