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REVIEW ARTICLE

Surface-enhanced Raman spectroscopy for emerging contaminant analysis in drinking water

Seo Won Cho[1,2], **Haoran Wei** (✉)[1,2]

1 Environmental Chemistry and Technology Program, University of Wisconsin–Madison, Madison, WI 53706, USA
2 Department of Civil and Environmental Engineering, University of Wisconsin–Madison, Madison, WI 53706, USA

HIGHLIGHTS

- Definition of emerging contaminants in drinking water is introduced.
- SERS and standard methods for emerging contaminant analysis are compared.
- Enhancement factor and accessibility of SERS hot spots are equally important.
- SERS sensors should be tailored according to emerging contaminant properties.
- Challenges to meet drinking water regulatory guidelines are discussed.

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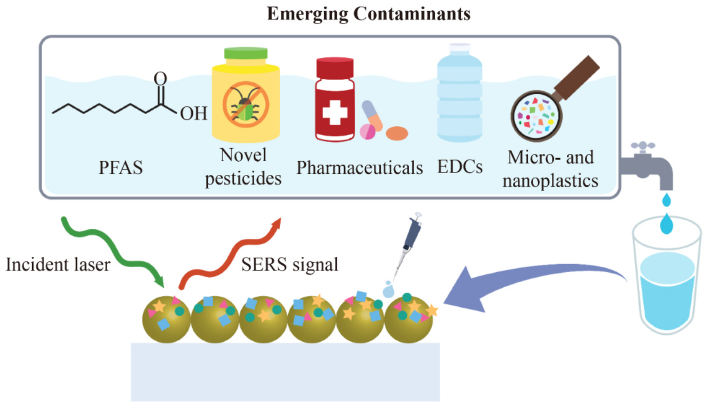
GRAPHIC ABSTRACT



ABSTRACT

Emerging contaminants (ECs) in drinking water pose threats to public health due to their environmental prevalence and potential toxicity. The occurrence of ECs in our drinking water supplies depends on their physicochemical properties, discharging rate, and susceptibility to removal by water treatment processes. Uncertain health effects of long-term exposure to ECs justify their regular monitoring in drinking water supplies. In this review article, we will summarize the current status and future opportunities of surface-enhanced Raman spectroscopy (SERS) for EC analysis in drinking water. Working principles of SERS are first introduced and a comparison of SERS and liquid chromatography-tandem mass spectrometry in terms of cost, time, sensitivity, and availability is made. Subsequently, we discuss the strategies for designing effective SERS sensors for EC analysis based on five categories—per- and polyfluoroalkyl substances, novel pesticides, pharmaceuticals, endocrine-disrupting chemicals, and microplastics. In addition to maximizing the intrinsic enhancement factors of SERS substrates, strategies to improve hot spot accessibilities to the targeting ECs are equally important. This is a review article focusing on SERS analysis of ECs in drinking water. The discussions are not only guided by numerous endeavors to advance SERS technology but also by the drinking water regulatory policy.

1 Introduction

Emerging contaminants (ECs), or contaminants of emerging concern (CECs), have frequently appeared in scientific literature, governmental reports, newspapers, and so on, but a unified and clear definition of ECs by the authorities for environmental protection and management is still missing. The United States Environmental Protection Agency (U.S. EPA) describes ECs as “chemicals that are increasingly detected at low levels in surface water and may have an impact on aquatic life” (U.S. EPA, 2022). The United States Geological Survey describes

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✉ Corresponding author
E-mail: haoran.wei3@wisc.edu

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ECs as “chemicals making it into our lakes and rivers and having a detrimental effect on aquatic species or non-aquatic species via food web accumulation” (USGS, 2019). A recent review article describes ECs as “new contaminants with uncertain effects but the potential for significant harm” (Khan et al., 2022). These descriptions from different perspectives, such as occurrence, impact on natural waters, and toxicity, provide the readers a general impression rather than a strict definition of what emerging contaminants are. Accordingly, whether a chemical can be considered as an EC might be subjective and strongly depends on public perception, so the list of ECs will also change as time evolves. At the beginning of this review article, we will first set up the boundary for our following discussions by proposing a more specific definition of ECs in terms of drinking water safety.

In the perspective of drinking water safety, ECs refer to any potentially hazardous matter, including organic chemicals, inorganic ions, and pathogens, that are detectable in drinking water supplies and pose potential risks to human health. Therefore, the frequent occurrence of a pollutant in drinking water is the first criterion that qualifies it as an emerging contaminant. In this situation, a large population may be subject to chronic exposure to such pollutants via drinking water. The second criterion that qualifies a pollutant as an emerging contaminant is its potential adverse effects on human health. ECs occur in drinking water at very low concentrations (usually below one part per billion) that will not elicit any acute toxicities to humans. However, their long-term effects on human health remain largely uncertain. From the perspective of risk assessment, risk equals to the product of exposure and toxicity. For a specific EC, the product of its certain exposure (ubiquitous occurrence) and uncertain toxicity (unknown long-term effect) gives an uncertain but potentially high risk to humans (Fig. 1).

The prevalence of emerging contaminants in drinking water sources, including both surface water and groundwater, has raised increasing concerns about drinking water safety (Houtman, 2010; Schriks et al., 2010). ECs enter freshwater systems primarily via treated municipal/industrial wastewater effluents and urban/agricultural runoffs (Fawell and Ong, 2012; Meng et al., 2021). The occurrence and fate of ECs in drinking water sources are determined by their physicochemical properties. Higher water solubility, stronger polarity, and lower octanol-water partition coefficient (K_{ow}) endow the contaminants with higher mobility in the water stream and thus a higher chance to reach tap water (Jones-Lepp et al., 2012). On the contrary, hydrophobic contaminants are more likely to be sequestered by activated sludge, sediments, and soils, and thus are much less frequently detected in drinking water supplies (Petrović et al., 2003). The pervasive use of emerging contaminants also affects their fate in drinking water sources. For example, azithromycin, a widely used macrolide antibiotic, is considered pseudo-persistent in the Colorado River and its tributaries because of its heavy use in the US and high tendency to be discharged into natural streams (Jones-Lepp et al., 2012; Bu et al., 2016). Despite their varying sources and physicochemical properties, many ECs can make their way into our drinking water supplies and form a “cocktail” of chemicals with potential toxicities to humans. Therefore, frequent, and large-scale monitoring of ECs in drinking water supplies is highly desirable to protect public health. Unfortunately, high-spatiotemporal-resolution mapping of ECs in drinking water is currently limited by the expensive and time-consuming analytical methods.

Surface-enhanced Raman spectroscopy (SERS) is an emerging and ultrasensitive analytical tool that has been widely used for chemical analysis (Langer et al., 2020; Wang and Wei, 2022; Wei and Cho, 2022). SERS originates from a unique optical phenomenon called localized surface plasmon resonance (LSPR), where the conduction electrons of a metal nanoparticle collectively oscillate as a result of an impinging electromagnetic wave with specific frequencies (Haynes et al., 2005; Schlücker, 2014). As a result of LSPR, the electric field within the nanoscale proximity of the metal nanoparticle surfaces is significantly enhanced, which in turn will enhance the Raman scattering of a molecule that locates within this enhanced electric field. The enhancement of the Raman cross-section of a molecule can be $>10^{10}$ fold when the molecular electronic levels match the incident photon energy or there is charge transfer between the molecule and the metal nanoparticle. In thess situations, single molecule detection can be achieved (Kneipp et al., 1997;

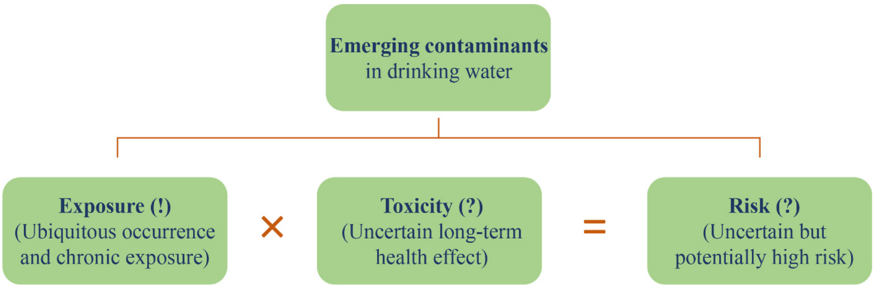

Fig. 1 Schematic illustrating the definition of emerging contaminants in drinking water.

Camden et al., 2008; Le Ru and Etchegoin, 2012). Because of their unique dielectric functions, gold or silver nanoparticles (AuNPs or AgNPs) support an LSPR at visible light wavelengths, which can be excited by the 532-, 633-, and 785-nm lasers commonly equipped in commercial Raman spectrometers. SERS exhibits several unique advantages over traditional analytical methods. 1) *In situ* and real-time measurement – SERS signals can be continuously collected from a water sample without the need for sample pretreatment and injection. 2) Extreme sensitivity – single molecule detection has been regularly reported even in complex matrices. 3) Fingerprint selectivity – a Raman spectrum is like the fingerprint of a molecule, so we can recognize individual chemicals based on their characteristic Raman spectra even in a complex mixture.

This review paper summarizes the recent progress on SERS analysis of typical ECs in drinking water supplies. It serves the researchers in the environmental science and engineering communities who are looking for rapid and inexpensive methods for emerging contaminant quantification. It also provides insights into the design, optimization, and implementation of SERS-based sensors based on the unique physicochemical properties of various emerging contaminants. This paper will be exclusively focused on drinking water matrices because 1) the regulations on emerging contaminants in drinking water are the most common and stringent, making it easy to place the discussions on the technological advances of SERS sensors in the context of EC regulatory policies; 2) drinking water is relatively clean compared to other water matrices (e.g., landfill leachate), which provides opportunities for the development of in-line SERS sensors without water sample pretreatment. In the following sections, we will first compare SERS with traditional analytical methods from the perspectives of cost, time, sensitivity, and accessibility. Subsequently, we will elaborate on the technological advances of SERS sensors for the detection of per- and polyfluoroalkyl substances (PFAS), novel pesticides, pharmaceuticals, endocrine-disrupting chemicals (EDCs), and microplastics, respectively. Finally, we will discuss the future opportunities and the challenges that need to be overcome in order to meet the regulatory guidelines for ECs in drinking water supplies.

2 Comparisons between SERS and traditional analytical methods

Similar to infrared spectroscopy (IR), SERS also provides abundant information on the relative motions of atoms within a molecule, which are fingerprinting characteristics of a molecule and thus can be used for pollutant identification (Mulvaney and Keating, 2000). Unlike IR that is sensitive to chemical bonds with large dipole moment change, SERS has a different selection rule that offers complementary vibrational information on primarily symmetric bonds, such as benzene rings and C=C bonds (Long, 1977). As a result, SERS does not produce high intensities for the vibrational modes of water molecules and thus can be directly used for pollutant analysis in aqueous phases. Compared with fluorescence spectroscopy, SERS exhibits higher photostability and much more information (usually tens of bonding vibrational modes) about the target molecule (Han et al., 2009). Owing to the narrow full width at half maximum (FWHM) of a Raman band, SERS can differentiate similar chemicals even in a complex mixture based on the unique patterns of their Raman bands (Zavaleta et al., 2009; Dougan and Faulds, 2012). Despite the above-mentioned unique advantages, SERS also shares some common advantages with other optical spectroscopy. First, SERS spectra are almost instantly collected, thus enabling rapid and even real-time analysis. Second, technologies for Raman spectrometer miniaturization have been evolving fast, which pushes many handheld Raman spectrometers into the market and drives down the price significantly. The availability of portable Raman spectrometers paves the way for field-deployable SERS analysis of water pollutants.

In order to justify the use of SERS for water pollutant analysis, it is imperative to elaborate on its advantages and disadvantages over standard analytical methods. For ECs with high water solubility (the primary targets of this study), the standard methods established by the U.S. EPA are predominantly based on liquid chromatography-tandem mass spectrometry (LC-MS/MS), e.g., Method 537.1 for PFAS analysis in drinking water (Shoemaker and Tettenhorst, 2020). Despite the high sensitivity and precision of these standard methods, they are also very expensive and time-consuming (Ferrer and Thurman, 2003; Richardson, 2009). First, the water samples need to be collected manually and transported back to a specialized laboratory for analysis. Complex pretreatment steps are usually required, such as prefiltration, preconcentration by solid phase extraction, organic solvent elution, and rotary evaporation. Subsequently, isotopic internal/surrogate standards will be added to the pretreated water samples before they can be injected into the LC-MS/MS for quantitative analysis. In addition, the operation and maintenance of LC-MS/MS requires well-trained personnel and highly specialized laboratories, which restrains its accessibility to ordinary people (Jansen et al., 2005).

As mentioned above, SERS provides an alternative option for emerging contaminant analysis that can potentially overcome the disadvantages of LC-MS/MS (Fang et al., 2016; Gao et al., 2021). SERS is a simple, rapid, and nondestructive technique that allows pollutant analysis both in laboratory and field settings (Halvorson and Vikesland, 2010; Zhou et al., 2020; Wang et al., 2021b). The schematic for conducting a typical SERS analysis is shown in Fig. 2. First, water samples containing ECs will be deposited onto an SERS substrate to ensure the contact of pollutants with plasmonic nanoparticles (Cho et al., 2012; Ouyang et al., 2017). Subsequently, a laser is irradiated on the SERS substrate and then the Raman scatterings will be collected, dispersed, and detected. This "light-in-and-light-out" paradigm significantly reduces the complexity of water sample pretreatment and the time for analysis (Halvorson and Vikesland, 2010; Hakonen et al., 2018). The cost for SERS analysis is also substantially lower than that for LC-MS/MS because it does not need organic solvents and isotopic internal standards. The small size of a Raman spectrometer also makes it possible to conduct SERS analysis in the field (Gahlaut et al., 2020). However, the limit of detection (LOD) of ECs that direct SERS can achieve is usually higher than 1 μg/L, e.g., 5 μg/L for imidacloprid analysis by colloidal AuNPs (Hou et al., 2015; Stewart et al., 2015; Wei and Vikesland, 2015), while LC-MS/MS can achieve an LOD down to the sub-ng/L level with the assistance of solid-phase extraction (Enevoldsen and Juhler, 2010; Bai et al., 2022; Lin et al., 2023). Functionalization of SERS substrates with EC-capturing molecular traps (e.g., aptamers) and/or Raman reporters can bring the LOD further down to the sub-ng/L level (Wang et al., 2016; Cho et al., 2020). In addition, the surface affinity between SERS substrates and analytes (Wei and Vikesland, 2015; Fang et al., 2016) and the complex water matrices (Pérez-Jiménez et al., 2020) sometimes compromise the sensitivity and selectivity of SERS for EC analysis, although many research effort has been devoted to overcoming these disadvantages (Oakley et al., 2012; Yaseen et al., 2018). The comparisons between SERS and LC-MS/MS are summarized in Table 1.

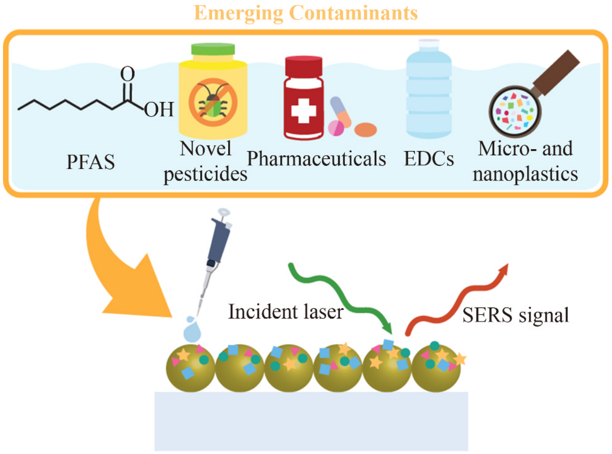

Fig. 2 Schematic of the working principle of a typical SERS sensor for EC analysis.

In addition to sensitivity, reproducibility is another key parameter to characterize the performance of SERS for EC quantification (Grys et al., 2021). Variations of SERS intensities among parallel measurements primarily originate from the heterogeneous distribution of SERS hot spots across one SERS substrate and/or among different batches of SERS substrates. When AuNPs or AgNPs are very close to each other, a significant enhancement of the electric field will occur within the gaps between the nanoparticles, which are called SERS "hot spots" (Moskovits, 2005; Ou et al., 2011). Hot spots are essential for ultrasensitive SERS analysis, but their non-uniform distribution is also the cause of irreproducible SERS signals (Wei et al., 2018b2019). There are two major approaches to improve the reproducibility of SERS measurement: 1) making highly uniform SERS substrates and 2) employing internal standards to calibrate the varying SERS signals (März et al., 2009; Shen et al., 2015). The first approach usually requires lithographic methods to create uniform nanoarrays on a wafer (Huebner et al., 2008; Cinel et al., 2015), which is too expensive to be used for routine environmental monitoring. The second approach requires the functionalization of SERS substrates with other chemicals that exhibit similar Raman cross-sections with the target analytes. These internal standards occupy the precious hot spot volume and can potentially lower the sensitivity for EC analysis. Recently, we developed a "chemical free" method to calibrate SERS signals using the elastic scatterings from laser amplified spontaneous emission as the internal standard and significantly reduced the point-to-point and batch-to-batch SERS signal variations (Wei et al., 2019; Wei et al., 2018). Owing to the research efforts to improve SERS

Table 1 A summary of the advantages and disadvantages of SERS and LC-MS/MS

Analytical method	Advantages	Disadvantages
SERS	• Simple sample pretreatment • Rapid and non-destructive sample analysis • Field deployable • Lower measurement cost (~5–10 $/h) • Lower instrumental cost (~10–30 k$)	• Higher LOD (> 1 μg/L for direct SERS; down to sub-ng/L level for indirect SERS) • Limited to analytes with high affinity to plasmonic nanoparticles • Mediocre reproducibility • Interference by complex water matrices
LC-MS/MS	• Lower LOD (down to sub-ng/L level) • High precision • Standard methods published by the environmental regulatory authorities	• Time-consuming sample pretreatment & analysis • Requiring well-trained personnel • Higher measurement cost (~50–80$/h) • Higher instrumental cost (~500 k$)

reproducibility, the relative standard deviations for SERS measurement can be readily lowered to <5% (Wei et al., 2019; Xu et al., 2020b), making SERS highly promising for the quantitative analysis of ECs in drinking water.

3 SERS analysis of emerging contaminants

In this section, we will summarize the recent progress on SERS analysis of typical emerging contaminants in drinking water, including PFAS, novel pesticides, pharmaceuticals, endocrine-disrupting chemicals, and microplastics (Fig. 2). We will focus on the peer-reviewed publications after 2015 and frame our discussions on the sensitivity, reproducibility, and selectivity of SERS and if they can meet EC regulations or health advisories in drinking water.

PFAS. Per- and polyfluoroalkyl substances are one type of emerging contaminants that have received the most public awareness due to their ubiquity, persistence, and toxicity (Cousins et al., 2020; Zhao et al., 2019; Fenton et al., 2021). The unique hydrophobicity and lipophobicity make PFAS popular ingredients in industrial and consumer products such as food packaging, non-stick cookware, waterproof apparel, lubricants, and firefighting foams. Known as the "forever chemicals", PFAS can remain in natural environments for many years due to their extremely strong carbon-fluorine backbone and a lack of microbial metabolic pathways to efficiently decompose these man-made chemicals (Fang et al., 2016; Cousins et al., 2020; Qiao et al., 2021; Evich et al., 2022). After being used for over 70 years, PFAS have reached every corner of the world and raised enormous public health concerns, e.g., deleterious immune, metabolic, and reproductive effects and increased risks of cancer (Blake and Fenton, 2020). U.S. EPA Method 537.1 describes the standard steps that need to be adopted to detect 18 PFAS in potable water based on solid phase extraction plus LC-MS/MS (Shoemaker and Tettenhorst, 2020). Despite its high sensitivity and reliability, the standard method has limitations in high cost, time-consuming pretreatment steps, and inaptness for onsite measurement (Bai et al., 2022).

SERS was recently employed in order to overcome these limitations (Fang et al., 2016; Bai et al., 2022). Among myriads of PFAS congeners, perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), and 6:2 fluorotelomer sulfonate (6:2 FTS) were selected for SERS analysis (Fang et al., 2016). Individual PFAS was first conjugated with a cationic dye (i.e., ethyl violet, EV) to form an ion pair, which was subsequently deposited onto Ag nanoparticle-graphene oxide (AgNP-GO) nanocomposites. Both the reduced aqueous solubility of the ion pairs and the hydrophobicity of the GO enhanced the loading of EV to AgNPs. Therefore, the concentrations of PFAS were quantified based on the induced enhancement of SERS intensities of EV. This method achieved the best LOD, 50 μg/L, for PFOA. A similar method achieved an LOD of 11 μg/L for PFOA using crystal violet (CV) as the cationic dye and an Ag superstructure array as the SERS substrate (Bai et al., 2022). Both methods can only detect PFOA at a low-μg/L level, which is still 6–7 orders of magnitude higher than its health advisory level (HAL) recently issued by the U.S. EPA (i.e., 0.004 ng/L) (U.S. EPA, 2022b). In addition, these indirect SERS methods measured the Raman signals from the dyes instead of PFAS, so the co-existing non-fluorinated surfactants can produce significant interferences to PFAS quantification. Therefore, a label-free and ultrasensitive method is highly desired to advance the SERS analysis of PFAS in drinking water (Ong et al., 2020).

Novel pesticides. Pesticides play an important role in optimizing landscape configuration and promoting agricultural production. While legacy pesticides, such as DDT and atrazine, have either been banned or limited for use, many novel pesticides have been increasingly used and detected in drinking water. These novel pesticides have not been regulated yet, but their long-term influence on human health should not be overlooked. In this section, we will primarily focus on neonicotinoids to illustrate how SERS advances pesticide analysis in drinking water. Neonicotinoids were introduced into the market in 1991 and now are one of the most widely used classes of insecticides (Bass et al., 2015). Chemically resembling nicotine, neonicotinoids bind with nicotinic acetylcholine receptors in the central nervous system of insects, which makes them active against a wide range of insects and selectively toxic to the pests (Bass et al., 2015; Hladik et al., 2018). The high water solubility of neonicotinoids makes them easily taken up by plant roots and distributed throughout the stem, leaves, flowers, and fruits of the plants (Wood and Goulson, 2017). The systemic nature of neonicotinoids allows the versatile use in the form of seed coatings, soil drench, and foliar sprays (Goulson, 2013). Despite the advantages, their potential high toxicities to non-targeted organisms, such as honeybees and bumblebees, pose a significant risk to our ecosystem (Blacquière et al., 2012).

Conventionally, neonicotinoid detection consists of two steps: sample pretreatment and analysis. Liquid-liquid extraction, solid-phase extraction, and their derivatives have been used for neonicotinoid preconcentration followed by gas chromatography and liquid chromatography-based analysis (Selahle et al., 2021). As elaborated previously, SERS is much faster and cheaper than these standard methods (Selahle et al., 2021; Yang et al., 2021). Among different types of neonicotinoids, N-nitroguanidines (imidacloprid, thiamethoxam, and clothianidin), N-cyanoamidines (acetamiprid and thiacloprid), and nitromethylene (nitenpyram) were used for SERS analysis (Dowgiallo and Guenther, 2019; Creedon et al., 2020; Gao et al., 2021; Puente et al., 2022). These studies predominantly targeted to analyze neonicotinoid residues on fruits (apples and peaches), vegetables (cabbage, spinach, and corn), tea leaves (green tea), and grains (wheat) using a variety of SERS substrates listed in Table 2. We believe that the strategies that were used for SERS analysis of neonicotinoids in the extracts of agricultural products will provide useful guidance for their analysis in drinking water.

Citrate-coated AuNP colloidal SERS substrates were used for the analysis of 21 pesticides, including neonicotinoids, organothiophosphates, fungicides, insect repellents, and so on (Dowgiallo and Guenther, 2019). A large range of LOD from 0.001–10 mg/L was achieved, which can be attributed to the different Raman cross-sections of the pesticides and their different affinities toward AuNP surfaces. However, many of the

Table 2 A summary of SERS-based sensors for emerging contaminant analysis

EC categories	ECs	SERS substrates/labels	Water matrices	LOD (µg/L)	Regulations/Advisories	Ref.
PFAS	PFOA, PFOS, and 6:2 FTS	AgNP-graphene oxide/ethyl violet	Groundwater	50	U.S. EPA HAL: PFOA 0.004 ng/L and PFOS 0.02 ng/L in drinking water	Fang et al. (2016)
	PFOA	Ag nanoclusters on silica microspheres/crystal violet	DI water	11		Bai et al. (2022)
Novel pesticides	Acetamiprid	Au and Ag nanostructures covered on SiO_2	DI water	9	U.S. EPA DWLOC: 80 µg/L (chronic exposure for children 1–6 years old)	Atanasov et al. (2020a)
		AuNPs on Ti_3C_2/SiO_2/PDMS surface	DI water	2×10^{-6}		Gao et al. (2021)
		Colloidal AuNPs	Acetone	10		Dowgiallo and Guenther (2019)
	Clothianidin	Ag layer on nanostructured PVDF film	Methanol-DI water (1:1)	1	Minnesota Department of Health guidance: 200 µg/L	Creedon et al. (2020)
		AuNPs on Ti_3C_2/SiO_2/PDMS surface	DI Water	2×10^{-6}		Gao et al. (2021)
		Colloidal AuNPs	Methanol	10^3		Dowgiallo and Guenther (2019)
		Silver dendrite/electropolymerized molecular identifier/AgNP sandwich hybrids	Ethanol	0.03		Zhao et al. (2020)
	Imidacloprid	Ag layer on nanostructured PVDF film	Methanol-DI water (1:1)	1	Minnesota Department of Health guidance: 2 µg/L	Creedon et al. (2020)
		Citrate-coated AuNP colloid	Methanol-DI Water (1:1)	5		Hou et al. (2015)
		AuNPs on Ti_3C_2/SiO_2/PDMS surface	DI water	1×10^{-6}		Gao et al. (2021)
		Colloidal AuNP	Acetone	100		Dowgiallo and Guenther (2019)
	Nitenpyram	Fern-like Ag dendrites on filter paper	Apple surface	0.3	None	Wang et al. (2019)
		Ag nanospheres and nanocubes	Acetone	3×10^5		Puente et al. (2022)
	Thiacloprid	Ag and Au nanostructures on alumina ceramic	DI water	10^5	U.S. EPA DWLOC: 38 µg/L	Atanasov et al. (2020b)
		Cysteamine-modified silver-coated gold nanoparticles	Liquid milk	23		Hussain et al. (2020)
	Thiamethoxam	AuNPs on Ti_3C_2/SiO_2/PDMS surface	DI water	2×10^{-6}	Minnesota Department of Health guidance: 200 µg/L	Gao et al. (2021)
		Colloidal AuNP	Acetone	100		Dowgiallo and Guenther (2019)
Pharmaceuticals	Sulfamethoxazole	Sepiolite/chitosan/AgNPs	DI water	20	Minnesota Department of Health guidance: 100 µg/L	Hu et al. (2022)
		Ag layer on a nanostructured quartz wafer	DI water/lake, river, tap water	0.05/0.6		Patze et al. (2017)
		Hydroxylamine-coated AgNP colloid	Human urine	2×10^3		Markina et al. (2020)
	Diclofenac	Thiocholine-functionalized AgNP colloid	DI water	6×10^3	None	Stewart et al. (2015)
		Au nanogrid	DI water	3×10^{-4}		Cho et al. (2020)
	Carbamazepine	AuNPs within bacterial cellulose mat	DI water	2	Minnesota Department of Health guidance: 40 µg/L	Wei and Vikesland (2015)

(*Continued*)

EC categories	ECs	SERS substrates/labels	Water matrices	LOD (μg/L)	Regulations/Advisories	Ref.
		Au@Ag core-shell NP colloid	Saliva	0.3		Chen et al. (2021)
Endocrine-disrupting chemicals	17β-estradiol	Au@Ag core-shell NP colloid/Cy3	DI water	3×10^{-4}	Japan MRC: 0.08 μg/L (E2) and 0.02 μg/L (17α-ethinylestradiol)	Pu et al. (2019)
		AuNPs on a magnetic bead/MGITC	Human serum	7×10^{-4}		Wang et al. (2016)
	Total steroid estrogens	Au@Ag core-shell NP colloid/4-MBA	Multiple surface waters	10^{-3}		Liu et al. (2019)
Micro- and nanoplastics	PS micro- and nanoplastics (50–1,000 nm)	Ag nanowires	KI solution	0.1	California SDWA	Yang et al. (2022)
	PS and PMMA micro- and nanoplastics (360–5,000 nm)	Klarite	DI water	2.625×10^{4}		Xu et al. (2020a)
	PS, PE, and PP micro- and nanoplastics (100 nm)	AgNPs	Pure water and sea water	4×10^{4}		Lv et al. (2020)
	PET, PE, PVC, PP, PS, and PC microplastics (80–150 μm)	Sponge supported AuNPs	Ultrapure water, sea water, rainwater, river water, snow water, and tap water	1×10^{3}		Yin et al. (2021)
	PET microplastics	AuNP doped filter paper	water	10^{5}		Xu et al. (2022)
	PS sub-micro- (161 nm) and nanoplastics (33 nm)	AuNPs (46 nm and 14 nm)	SDS and KPS solution (solution obtained from milling)	$10^{4}/2\times10^{4}$		Caldwell et al. (2021)
	PS and PMMA microspheres	AuNPs@V-shaped anodized aluminum oxide (AAO) substrate	DI water	5×10^{7}		Liu et al. (2022)
	PS nanoplastics (~50 nm)	AgNPs	River water	5×10^{3}		Zhou et al. (2021)
	PS sub-microplastics (600 nm)	Au nanourchins	DI water	1–5 particles		Lee and Fang (2022)
	PS nanoplastics (500 nm)	Ag nanowire membrane	Seafood market water and seawater	1		Yang et al. (2022)

measurements were conducted in the presence of organic solvents (acetone for acetamiprid, imidacloprid, and thiamethoxam; methanol for clothianidin), which generated strong interferences that can limit further LOD reduction. Creedon et al. developed an SERS substrate by depositing a silver film onto a nanostructured polyvinylidene fluoride (PVDF) film and applied it for imidacloprid and clothianidin analysis (Creedon et al., 2020). Raman spectra were acquired following drop coating the methanol-DI water (1:1) solutions of imidacloprid and clothianidin onto the SERS substrate. As shown in Fig. 3, low-concentration imidacloprid and clothianidin (1 μg/L) solutions both exhibited well-resolved features in their Raman spectra, indicating that SERS is extremely sensitive for neonicotinoid analysis. However, apparent discrepancies between Raman spectra of low-concentration samples and high-concentration or bulk samples were observed, which was attributed to the different orientations of the molecules adsorbed onto silver surfaces. Further improvement of analysis sensitivity can be achieved by water sample preconcentration. For example, Gao et al. concentrated the analytes in a water sample droplet into a tiny spot by photothermally heating the droplet on a superhydrophobic surface and achieved an LOD of femtomolar level for clothianidin, thiamethoxam, imidacloprid, and acetamiprid. (Gao et al., 2021) The significantly lower detection limits of pesticides compared to the U.S. EPA drinking water levels of comparison (DWLOC) and the health guidance in Minnesota suggest that SERS is a sensitive tool for monitoring pesticides in drinking water (Table 2).

Pharmaceuticals. A survey from a Germany's research project on pharmaceutical residue in drinking water reported that 23% of the liquid pharmaceuticals and 7% of tablets are discarded by the consumers as household garbage or flushed away via toilets (World Health Organization, 2012). As indicated, a tremendous amount of pharmaceuticals ends up in landfill leachate and sewage, which eventually gather in wastewater treatment plants. Both wastewater treatment and drinking water

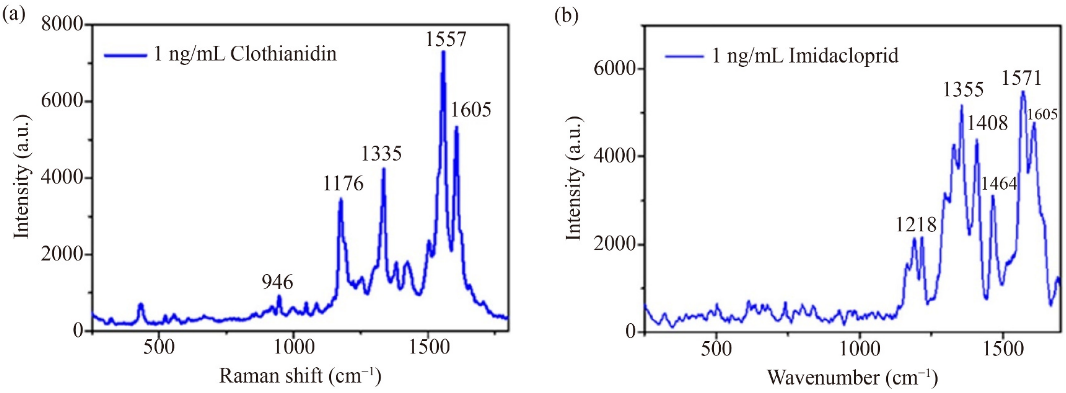

Fig. 3 SERS spectra of clothianidin and imidacloprid that were collected after deposition of their methanol-water solutions (1 μg/L) onto the Ag film@PVDF SERS substrate. Reprinted (adapted) with permission from Creedon et al. (2020). Highly sensitive SERS detection of neonicotinoid pesticides. Complete Raman spectral assignment of clothianidin and imidacloprid. *Journal of Physical Chemistry A*, 124(36): 7238–7247. Copyright 2020 American Chemical Society.

treatment plants are not designed to remove these pharmaceuticals, so they are ubiquitously detected in drinking water sources and finished drinking waters (Jelić et al., 2012; Simazaki et al., 2015; Sun et al., 2015; aus der Beek et al., 2016). In this section, we select three of the most frequently detected pharmaceuticals in various natural and engineered water systems, i.e., sulfamethoxazole, carbamazepine, and diclofenac, as examples to elucidate the strategies that have been adopted to advance their SERS analysis.

Sulfamethoxazole at a 20 μg/L level was detected by filtering a 2 mL solution (pH = 1.8) through an AgNP-decorated membrane (Hu et al., 2022). The membrane skeleton consisting of sepiolite and chitosan efficiently concentrated sulfamethoxazole and improved the sensitivity of SERS analysis. Patze et al. integrated a microfluidic device with a silver-coated nanostructured quartz wafer and achieved an LOD of 0.05 and 0.6 μg/L for DI water and lake/river/tap water matrices, respectively (Patze et al., 2017). Sulfamethoxazole solution was continuously fed to the SERS substrate, thus avoiding the overheating of the SERS substrate, and ensuring a highly reproducible environment for Raman spectrum collection. Sulfamethoxazole has two p*K*a values of 1.6 and 5.7 for its amine groups, indicating that it exhibits relatively low affinity to mostly negatively charged plasmonic nanoparticles under circumneutral pH (Boreen et al., 2004).

This situation aggravates for molecules with even lower pK_a values. Carbamazepine has a very low p*K*a (2.3), making it a neutral molecule that weakly associates with citrate-coated AuNPs. Therefore, the SERS intensities of carbamazepine bands were very low under circumneutral pH. To circumvent this issue, Wei et al. adjusted the pH of the carbamazepine solution to 2.0 before mixing it with AuNP colloid (Wei and Vikesland, 2015). The electrostatic attraction between the positively charged carbamazepine and negatively charged citrate significantly enhanced the affinity between them and achieved an LOD of 2 μg/L (Fig. 4). In addition to adjusting pH, electrostatic forces can be regulated by surface functionalization of the plasmonic nanoparticles. Citrate- and hydroxylamine-coated AgNPs were functionalized with thiocholine, whose quaternary amine groups provided strong positive charges even under alkaline solutions (Stewart et al., 2015). In this way, the anionic pharmaceutical – diclofenac was detected using SERS with an LOD of 6,000 μg/L. This much higher LOD than carbamazepine and sulfamethoxazole can be attributed to the competitive adsorption of co-existing anions with diclofenac. The use of recognition elements can also enhance the affinity of diclofenac to SERS substrates. As shown in Fig. 5(a), Cho et al. recently developed a monolithic gold nanogrid SERS substrate consisting of crossed gold nanowires (Cho et al., 2020). After functionalization of the gold nanogrid with a diclofenac-targeting aptamer, this substrate can capture diclofenac to its surface and detect it

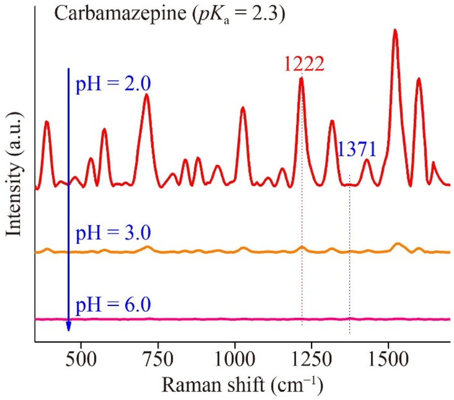

Fig. 4 Raman spectra of carbamazepine collected from an AuNP/bacterial cellulose SERS substrate under pH of 2.0, 3.0, and 6.0 (Wei and Vikesland, 2015). This is an open access article distributed under the terms of the Creative Commons CC BY license, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

down to 3 × 10^{-4} μg/L. Numerous attempts to enhance the sensitivity of SERS sensors for pharmaceutical analysis have lowered the LOD below the Minnesota Department of Health guidance by up to three orders of magnitude (Table 2).

Endocrine-disrupting chemicals. Many synthetic chemicals can disrupt the endocrine system of humans via mimicking, stimulating, or inhibiting natural hormones. EDCs have been frequently detected in drinking water and its chronic exposure could be linked to developmental and reproductive anomalies (Benotti et al., 2009; Wee and Aris, 2017; Liu et al., 2021). Many synthetic chemicals demonstrate endocrine-disrupting effects, such as atrazine, bisphenol A, nonylphenol, and 17β-estradiol (E2). The strategies to detect triazine-containing or aromatic EDCs are similar to what were discussed before, so we will only focus on 17β-estradiol in this section because of its unique molecular structure.

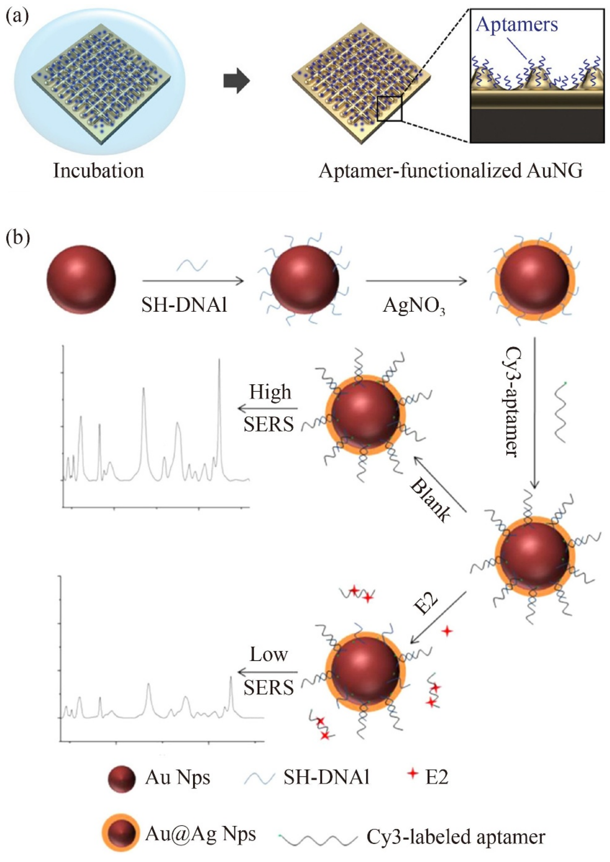

Fig. 5 Schematics of (a) aptamer functionalization on a gold nanogrid SERS substrate and (b) strategy for labeled SERS analysis of 17β-estradiol (Pu et al., 2019; Cho et al., 2020). Reprinted with permission from (Yeon Sik Jung, et al. 2020). Selective, quantitative, and multiplexed surface-enhanced Raman spectroscopy using aptamer-functionalized monolithic plasmonic nanogrids derived from cross-point nano-welding. Advanced Functional Materials, 30: 2000612. Copyright 2020 John Wiley and Sons. Reprinted with permission from Hongbin Pu, Xiaohui Xie, Dawen Sun, et al. (2019). Double-strand DNA functionalized Au@Ag NPs for ultrasensitive detection of 17β-estradiol using surface-enhanced Raman spectroscopy. Talanta, 195: 419–425. Copyright 2019 Elsevier.

Given its low Raman cross-section, 17β-estradiol was primarily detected by SERS with the assistance of a highly Raman effective label. As shown in Fig. 5(b), Au@Ag core-shell nanoparticles were first functionalized with a single-stranded DNA that is complementary to the E2-targeting aptamer (Pu et al., 2019). After adding the E2-targeting aptamer, the core-shell NPs aggregated as a result of DNA hybridization while the Cy3 label that was pre-attached to the aptamer gave rise to a strong SERS signal. However, when 17β-estradiol was added, the strong interaction between 17β-estradiol and the aptamer removed the aptamer from nanoparticle surfaces, thus reducing the SERS intensity of Cy3 substantially. This detection strategy achieved an extremely low LOD of 3 × 10^{-4} μg/L. A similar competition strategy achieved an LOD of 7 × 10^{-4} μg/L for 17β-estradiol analysis using an antibody as the recognition element and malachite green-isothiocyanate (MGITC) as the SERS label (Wang et al., 2016). Recently, an SERS strategy was reported to analyze the total steroid estrogens (TE), including 17β-estradiol, estrone (TE1), and ethinyl estradiol (TEE2) (Liu et al., 2019). The TE-targeting aptamer exhibited a similar binding affinity with the three individual steroid estrogens. Two batches of Au@Ag core-shell nanoparticles were functionalized with the TE-targeting aptamer and the complementary DNA, respectively. Dimers were formed after mixing them together because of DNA hybridization. Subsequently, the Raman label – 4-mercaptobenzoic acid (4-MBA) was coated on the surfaces of both nanoparticles. Whenever any of the three steroid estrogens were present either individually or as a mixture, the strong interactions between the aptamer and the steroid estrogens reduced the distance between the nanoparticles and created SERS hot spots. This strategy achieved an LOD down to 10^{-3} μg/L in multiple environmental waters. As shown in Table 2, SERS can achieve LOD of steroid estrogens that are well below the maximum recommended concentrations (MRCs) in drinking water in Japan with the assistance of SERS labels and recognition elements.

Microplastics. Since their commercial production in the 1950s, plastics have penetrated our lives not just in the form of daily products such as plastic water bottles and food containers but also in the form of small plastic debris, i.e., micro- (< 5 mm) and nanoplastics (< 100 nm) (Thompson et al., 2004; Hale et al., 2020). Such small plastic particles are generated either intentionally or unintentionally from the industrial production of daily products. Microbeads in cosmetics and personal care products are one example, however, the production of microbeads is now banned in the U.S. by Microbead-Free Waters Act of 2015 (van Wezel et al., 2016). Another major source of plastic particles is the secondary microplastics from the physicochemical degradation of plastic wastes and washing of synthetic garments. Owing to their lightweight, as-produced plastic particles can be transported by atmosphere and water into our environment (Qiu et al., 2020).

The environmentally released microplastics pose direct threat to both humans and ecosystems as well as indirect threat that is caused by the pollutants adsorbed to the microplastics (Wang et al., 2021a; Wu et al., 2022). Microplastics have a high adsorption capacity that makes them retain a large number of organic and inorganic pollutants while the biofilms formed on microplastics further attracts pathogenic microorganisms such as algae (He et al., 2022). The plastic particles consumed via food and drinking water act as neurotoxins and exert oxidative stress to humans, aquatic and soil organisms, and cause developmental and reproductive problems (Lei et al., 2018; Qin et al., 2021). In addition to the toxicity of microplastics, their bioaccumulative properties make them reside in the bodies of organisms for a prolonged period of time. Although there are currently no regulations on microplastic pollution in the drinking water system, the Safe Drinking Water Act (SDWA) released by the California State Water Resources Control Board has defined microplastics and started testing them in the drinking water systems under Health and Safety Code section 116376 due to the ubiquity of microplastics.

Many recent studies have been devoted to rapid and reliable SERS detection and quantification of microplastics in different environmental water matrices, including tap water, rainwater, snow water, river water, and sea water (Yin et al., 2021; Zhou et al., 2021; Yang et al., 2022). Different sizes and types of plastic particles, i.e., polystyrene (PS), polymethyl methacrylate (PMMA), polyethylene (PE), polyvinyl chloride (PVC), polypropylene (PP), polycarbonates (PC), and polyethylene terephthalate (PET), have been analyzed using Au or Ag-based SERS substrates (Fig. 6). Xu et al. utilized Klarite, an array of inverted pyramid nanostructures coated with a gold layer, as the SERS substrate to detect individual PS and PMMA microplastic particles down to 360 nm in diameter (Xu et al., 2020a). The single particle detection is enabled by the high-resolution SERS mapping capacity combined with the strong SERS hot spots generated from the pyramid pits of Klarite. Yang et al., on the other hand, used a silver nanowire membrane as the SERS substrate to simultaneously concentrate and detect PS nanoplastics (Yang et al., 2022). The dual functions of silver nanowire membranes allowed the direct SERS analysis of nanoplastics on the membrane surfaces without the need for washing them off and adding them to an SERS substrate. This method achieved the detection of PS nanoplastic particles down to 50 nm.

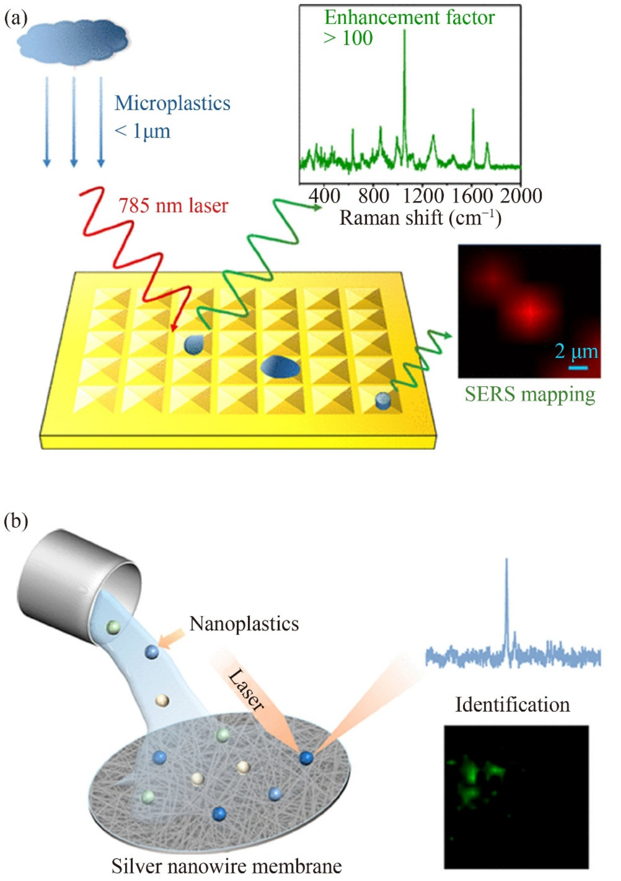

Fig. 6 Schematics of (a) Klarite and (b) a bifunctional silver nanowire membrane. Reprinted (adapted) with permission from Yang Q, Zhang S, Su J, Li S, Lv X, Chen J, Lai Y, Zhan J (2022). Identification of Trace Polystyrene Nanoplastics Down to 50 nm by the Hyphenated Method of Filtration and Surface-Enhanced Raman Spectroscopy Based on Silver Nanowire Membranes. Environmental Science & Technology, 56(15): 10818–10828. Copyright 2022 American Chemical Society. Reprinted (adapted) with permission from Xu G, Cheng H, Jones R, Feng Y, Gong K, Li K, Fang X, Tahir M A, Valev V K, Zhang L (2020). Surface-Enhanced Raman Spectroscopy Facilitates the Detection of Microplastics < 1 μm in the Environment. Environmental Science & Technology, 54(24): 15594–15603. Copyright 2020 American Chemical Society.

4 Conclusions and perspectives

This review article summarizes the latest progress on the development of SERS sensors targeting five groups of emerging contaminants (ECs) — per- and polyfluoroalkyl substances (PFAS), novel pesticides, pharmaceuticals, endocrine-disrupting chemicals (EDCs), and microplastics. ECs in drinking water are first defined based on their ubiquitous occurrence and uncertain health effects after long-term human exposure. The routes of ECs to drinking water supplies are briefly summarized. Following introduction of the advantages and disadvantages of SERS compared with standard EC analytical methods, recent research progress on SERS sensor design for EC analysis is discussed in terms of not only technological advancements but also drinking water regulatory policies.

While SERS allows inexpensive and rapid detection of ECs, most of the studies were performed in DI water and the reported LOD values were based on the extrapolations from the experimental data. Although the insights in sensor design provided by these studies can be easily translated to other water matrices, further research is needed to evaluate the performance of these SERS sensors in drinking water and validate the LOD values experimentally. There is no "one-fit-for-all" strategy for EC analysis using SERS. Physicochemical properties of ECs, such as charges, sizes, functional groups, and hydrophobicity, determine their affinity towards plasmonic nanoparticle surfaces, thus significantly affecting the sensitivity of SERS analysis. Therefore, SERS substrates should be tailored to accommodate different targeting analytes based on their chemical structures. It is relatively easy to achieve a low LOD for ECs with moieties that can either bind strongly with plasmonic nanoparticle surfaces or exhibit high Raman cross-sections. While for the ECs with either low Raman cross-sections or low affinity to sensor surfaces, i.e., PFAS and steroid estrogens, SERS labels are usually needed to achieve a high detection sensitivity.

In addition to the efforts to maximize SERS hot spot density, strategies to place the targeting ECs into the hot spots are highly desired. The orientational variation of ECs on SERS sensor surfaces as a function of their concentrations impedes their quantitative analysis. It is important to further improve the reproducibility of SERS analysis, especially when the concentrations of ECs are low. So far, the sensitivity and precision of direct SERS sensors for EC analysis are still not on par with the standard analytical methods, such as LC-MS/MS. As the EC regulations become more and more stringent, further improvement of LOD is required to meet the contemporary drinking water guidelines via optimization of the affinity between ECs and plasmonic nanoparticle surfaces and development of indirect SERS sensors with high selectivity. From the perspective of quality assurance and quality control, reproducibility of SERS measurement at different times and across different laboratories should be further improved by standardizing the procedures for SERS substrate synthesis, analysis implementation, and instrument operation. The precision of the acquired results should be validated using standard analytical methods. In addition, the performance of SERS sensors can be further improved by integrating SERS with sample pretreatment steps, e.g., liquid chromatography and microfluidic device, and advanced data analytics, e.g., multivariate statistics and machine learning. In summary, the low cost, (near) real-time data collection, and potential for onsite analysis make SERS a promising tool for EC monitoring in drinking water.

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