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Review

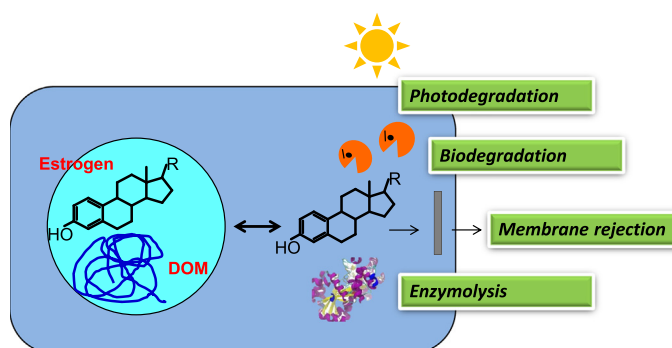
Dissolved organic matter and estrogen interactions regulate estrogen removal in the aqueous environment: A review

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HIGHLIGHTS

- Dissolved organic matter interacts with estrogens via binding or sorption.
- Binding mechanisms include π - π electron donor-acceptor interaction and hydrogen bonding.
- The interactions were primarily associated with dissolved organic carbon quality.
- Methods to characterize and quantify binding or sorption affinity were summarized.
- The regulatory effects of dissolved organic matter on estrogen elimination were discussed.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:

Received 16 April 2018

Received in revised form 23 May 2018

Accepted 24 May 2018

Available online 3 June 2018

Editor: Jay Gan

Keywords:

Estrogens
Dissolved organic carbon
Sorption
Aromaticity
Phenolic group
Removal

ABSTRACT

This review summarizes the characterization and quantification of interactions between dissolved organic matter (DOM) and estrogens as well as the effects of DOM on aquatic estrogen removal. DOM interacts with estrogens via binding or sorption mechanisms like π - π interaction and hydrogen bonding. The binding affinity is evaluated in terms of organic-carbon-normalized sorption coefficient ($\log K_{OC}$) which varies with types and composition of DOM. DOM has been suggested to be a more efficient sorbent compared with other matrices, such as suspended particulate matter, sediment and soil; likely associated with its large surface area and concentrated carbon content. As a photosensitizer, DOM enhanced estrogen photodegradation when the concentration of DOM was below a threshold value, and when above, the acceleration effect was not observed. DOM played a dual role in affecting biodegradation of estrogens depending on the recalcitrance of the DOM and the nutrition status of the degraders. DOM also acted as an electron shuttle (redox mediator) mediating the degradation of estrogens. DOM hindered enzyme-catalyzed removal of estrogens while enhanced their transformation during the simultaneous photo-enzymatic process. Membrane rejection of estrogens was pronounced for hydrophobic DOM with high aromaticity and phenolic moiety content. Elimination of estrogens via photolysis, biodegradation, enzymolysis and membrane rejection in the presence of DOM is initiated by sorption, accentuating the role of DOM as a mediator in regulating aquatic estrogen removal.

Published by Elsevier B.V.

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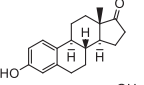
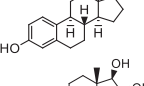
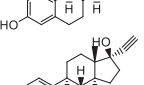
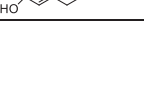
1. Introduction

Endocrine disrupting compounds (EDCs) are chemicals that exert adverse effects on endocrine systems of humans and wildlife. EDCs include but are not limited to pharmaceuticals, pesticides and hormones, natural or synthetic, among which, estrogens stand out due to their negative effects on aquatic organisms at environmentally-relevant (ng L^{-1}) levels. For example, the lowest observed effective concentration for the synthetic estrogen 17 α -ethynylestradiol (EE2) to induce plasma vitellogenin (female yolk precursor protein) in male fathead minnow (*Pimephales promelas*) was 1 ng L^{-1} (Pawlowski et al., 2004; Zhu et al., 2004). The threshold concentration for 17 β -estradiol (E2) to induce vitellogenin on female juvenile rainbow trout was 4.7 and 7.9 ng L^{-1} (Thorpe et al., 2001). Exposure to 10 ng L^{-1} of estrone (E1) induced intersex of male Japanese medaka (*Oryzias latipes*) (Metcalf et al., 2001). The estrogenicity of EDCs evaluated by a yeast estrogen screen (YES) bioassay is expressed in terms of estradiol equivalent factors (EEFs) (Beek et al., 2006). Higher EEF value corresponds to greater estrogenic potency. As shown in Table 1, the most biologically active estrogen is the synthetic estrogen EE2, which displays 1.25-fold higher potency than E2. Generally, estrogens exhibit up to six orders of magnitude higher estrogenicity in the YES than other major pharmaceuticals

and personal care products (PPCPs) (Beek et al., 2006). In the current review, the three natural estrogens E1, E2 and estriol (E3), and a synthetic estrogen (EE2) are considered and the scope is limited to the aquatic ecosystems. The physical and chemical properties together with the structure of the four common estrogens are displayed in Table 1.

Estrogens, naturally produced in living creatures or as medicine administered to humans and livestock, are excreted, either in free form or as their conjugated counterparts, primarily through urine but also in the feces. These estrogens end up in the aquatic environment through discharges of wastewater treatment plants (WWTPs), animal waste disposal and runoff of field applied hormone-bearing materials (manure, sewage sludge and biosolid, etc.). From a global perspective, concentrations of estrogens in the sewage influents ranged $7.3\text{--}197 \text{ ng L}^{-1}$ for E1, $4.9\text{--}48 \text{ ng L}^{-1}$ for E2, and $(<0.2)\text{--}(<11) \text{ ng L}^{-1}$ for EE2, which were eliminated within sewage treatment plant with an average removal rate of 78% (E1), 89% (E2), and 74% (EE2) (reviewed by Xu et al. (2012)). Numerous studies reported the occurrence of estrogens in the aquatic ecosystems worldwide. A recent review by Adeel et al. (2017) summarized in detail the occurrence of estrogens (E1, E2, E3, and EE2) in river and surface waters on a global scale. Generally, the concentrations were extremely variable ranging from below detection limit to hundreds of ng L^{-1} , depending on sampling countries.

Table 1
Physicochemical properties of major estrogens considered in this study.

Estrogens	Molecular weight	Log K_{OW} at pH 7 ^a	Water solubility at 20 °C (mg L^{-1}) ^b	pK _a ^c	EEF ^d	Structure
E1	270.37	3.43	13	10.3	0.25	
E2	272.39	3.94	13	10.6	1	
E3	288.39	2.81	13	10.05	5.9×10^{-3}	
EE2	296.41	4.15	4.8	10.4	1.25	

a,b Ying and Kookana (2005).

c.Yamamoto et al. (2003); Adeel et al. (2017).

d. Estradiol equivalent factor (EEF) (Beek et al., 2006).

Natural waters contain a multitude of dissolved organic matter (DOM), which is defined as the fraction of organic substances that pass by filters (0.1–0.7 μm) (Mostofa et al., 2013). A fraction of DOM that is retained by a ~ 1 kDa ultrafilter is colloidal organic matter (COM) (Holbrook et al., 2003). In river waters, colloidal organic carbon (COC) accounted for approximately 57–89% of total dissolved organic carbon (DOC*) (Sun and Zhou, 2014). Dominant component of DOM in natural waters is humic substances (HS) (mainly humic and fulvic acids) and the concentrations of DOM in natural water span a wide range from 0.5 to 100 mg C L^{-1} (Frimmel, 1998). Because of its high surface area and concentrated organic carbon content, DOM exhibits high capacity to bind with organic contaminants. For example, Nie et al. (2014) reported that up to 72% of estrogens in a drinking water reservoir was bound to COM, suggesting colloids as a significant sink for environmental estrogens. Yang et al. (2011) found that the sorption capacity of colloids in Yangtze River for pharmaceuticals was 2–4 orders of magnitude higher than that of suspended particulate matter (SPM). Sorption and binding mechanisms include hydrogen bonding, ligand exchange and hydrophobic interaction, etc. (Senesi, 1992). These interactions were suggested to cause solubility enhancement (Chiou et al., 1986) and abatement of toxicity of the contaminants (Neale et al., 2015; Tanghe et al., 1999). Notably, the presence of DOM was suggested to influence the removal rate of the pollutants via photolysis, biodegradation and mineral surface catalyzed transformation. The role of DOM as a natural photosensitizer in accelerating the photodegradation has been investigated for a variety of aquatic contaminants (Ren et al., 2017b; Yan et al., 2015b). A review by Polubesova and Chefetz (2014) discussed the role of DOM as mediators regulating the transformation of various contaminants by minerals. The review summarized that DOM influenced the transformation in three ways: 1) competitive adsorption on the mineral surface, 2) dissolution of minerals allowing new surface sites on the mineral surface exposed; and 3) electron shuttling. Therefore, DOM is suggested to play a mediating role in regulating the degradation and transformation of emerging contaminants.

There are a number of studies probing the interactions of estrogens and DOM, and the impact of DOM on degradation and transformation. However, these studies are relatively unsystematic and no uniform trends were generalized. The occurrence, fate, transport and degradation of estrogens, together with the impact of DOM on hydrophobic contaminant behavior have been extensively reviewed (Adeel et al., 2017; Campbell et al., 2006; Haitzer et al., 1998; Khanal et al., 2006), while estrogen-DOM interactions and their impacts on estrogen removal have not been systematically addressed. Studies on fate, transport and transformation of emerging contaminants have been inevitably pointed to the investigation of the interactions between them. In this paper, methodologies to characterize and quantify the interactions between estrogens and water-borne DOM and the incurring removal efficiencies were summarized. The development of a more fundamental understanding of information in this regard will provide far-reaching insights which could assist in potential regulatory controls.

2. Interactions between estrogen hormones and DOM

The octanol-water partitioning coefficient ($\log K_{OW}$) and the organic-carbon-normalized sorption coefficient ($\log K_{OC}$) are commonly used to indicate the partitioning tendency of organic compounds to organic matter (Karickhoff, 1981). The greater the coefficient values are, the greater the tendency of the compounds to partition to organic matter. For highly hydrophobic contaminants such as polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs) and pesticides, a high correlation was usually observed between $\log K_{OC}$ and $\log K_{OW}$, indicative of hydrophobic interaction as major contribution to sorption of those compounds to organic matter (Kopinke et al., 1995). Estrogens, however, which represent moderately hydrophobic compounds, might have different binding mechanisms compared to those highly hydrophobic compounds. Poor correlations between $\log K_{OC}$ and $\log K_{OW}$ for

estrogens have been observed in several studies (Liu et al., 2005; Yamamoto et al., 2003), suggesting that sorption mechanisms other than nonspecific hydrophobic interaction play a key role in estrogen sorption. In aqueous phase, estrogens interact with DOM to form estrogen-DOM complex and the interactions were usually evaluated by $\log K_{OC}$.

2.1. Interaction mechanisms

Holbrook et al. (2003) revealed, via fluorescence quenching (FQ) method, the strong correlation ($r^2 = 0.83$) between the magnitude of $\log K_{OC}$ for E2 and EE2 and the molar extinction coefficient at 280 nm (ϵ_{280} : $\text{L mol}^{-1} \text{cm}^{-1}$). UV absorptivity at the range of 254–280 nm was proposed to be related to the aromaticity of the DOM (Chin et al., 1994). Additionally, K_{OC} values of PAHs were also shown to strongly correlate with the aromaticity of HS (Perminova et al., 1999). It was surmised that the π - π interaction between estrogens and COC governs the binding behavior. In the π - π complex, the sorbate which acts as π -electron donor interacts with SOM which contains abundant π -acceptor groups (e.g., quinones, aromatic rings with electron-withdrawing groups), known as “ π - π stacking”, “ π - π charge-transfer”, or “ π - π electrone donor-acceptor” interactions (Zhu et al., 2004). The formation of π - π complexes (using PAHs and model DOM) was demonstrated using ^1H nuclear magnetic resonance spectroscopy (NMR) and UV/visible spectroscopy (Wijnja et al., 2004; Zhu et al., 2004). Yamamoto et al. (2003), using FQ and solubility enhancement methods, observed a significant positive relationship ($r^2 > 0.97$) between $\log K_{OC}$ of E2 and EE2 and UV absorptivity of DOM surrogates at 272 nm ($\log A_{272}$), as well as between $\log K_{OC}$ and the concentration of phenolic group of DOM. Additionally, Jin et al. (2007) observed that E1 interacted more strongly with hydrophobic acid containing phenolic groups than with HA without phenolic groups although the latter possessed much greater aromaticity than the former. These clearly suggested the involvement of hydrogen bonding in the overall sorption in addition to π - π interaction. The hydrogen bonding can occur between the estrogen —OH group and oxygen- or nitrogen-containing groups on DOM. Sorption was reinforced for tannic acid, for example, which is characterized by the abundance of phenolic groups (Yamamoto et al., 2003) (Fig. 1). Bedard et al. (2014) employed biochemical assays (enzyme-linked immunosorbent assay and YES) to probe binding between HA with E2 and suggested that the hydrogen binding occurs proximal to the hydroxyl group at C-3 position of the estrogen aromatic ring. With the aid of Fourier-transformation infrared spectroscopy, Ren et al. (2017b) also confirmed the binding of EE2 to HS majorly via π - π interactions and hydrogen bonding.

Infusion tandem mass spectrometry has been used to assess the bonding strength and stability of some PPCP-DOM complexes by monitoring their mass signal relative to a DOM-free control (Hernandez-Ruiz et al., 2012; Ruiz et al., 2013). Strong associations between the target compounds (i.e., PPCPs) and matrices (i.e., organic acids) can prevent chromatographic or gas phase separation, leading to reduced signal intensity and ensuing deviated recoveries. It was found in these studies that the recoveries of the PPCPs were close to 100%, suggesting that the majority of interactions which incurred FQ were relatively weak. This implies that these PPCPs which interacted weakly with DOM via hydrophobic interaction, van der Waals and/or hydrogen bonding can be separated chromatographically to become labile in the gas phase during mass analysis. Complexation of estrogens with DOM has not been elaborated by investigators applying infusion tandem mass spectrometry, however, the relative low recoveries of estrogens acquired in the occurrence studies (Ma et al., 2016) are indicative of a stronger affinity between estrogens and DOM compared to affinity of PPCPs to DOM. Nevertheless, using isotope labeled standard or surrogates, the reduction in recovery due to presence of DOM in natural environment can be compensated to obtain valid determination.

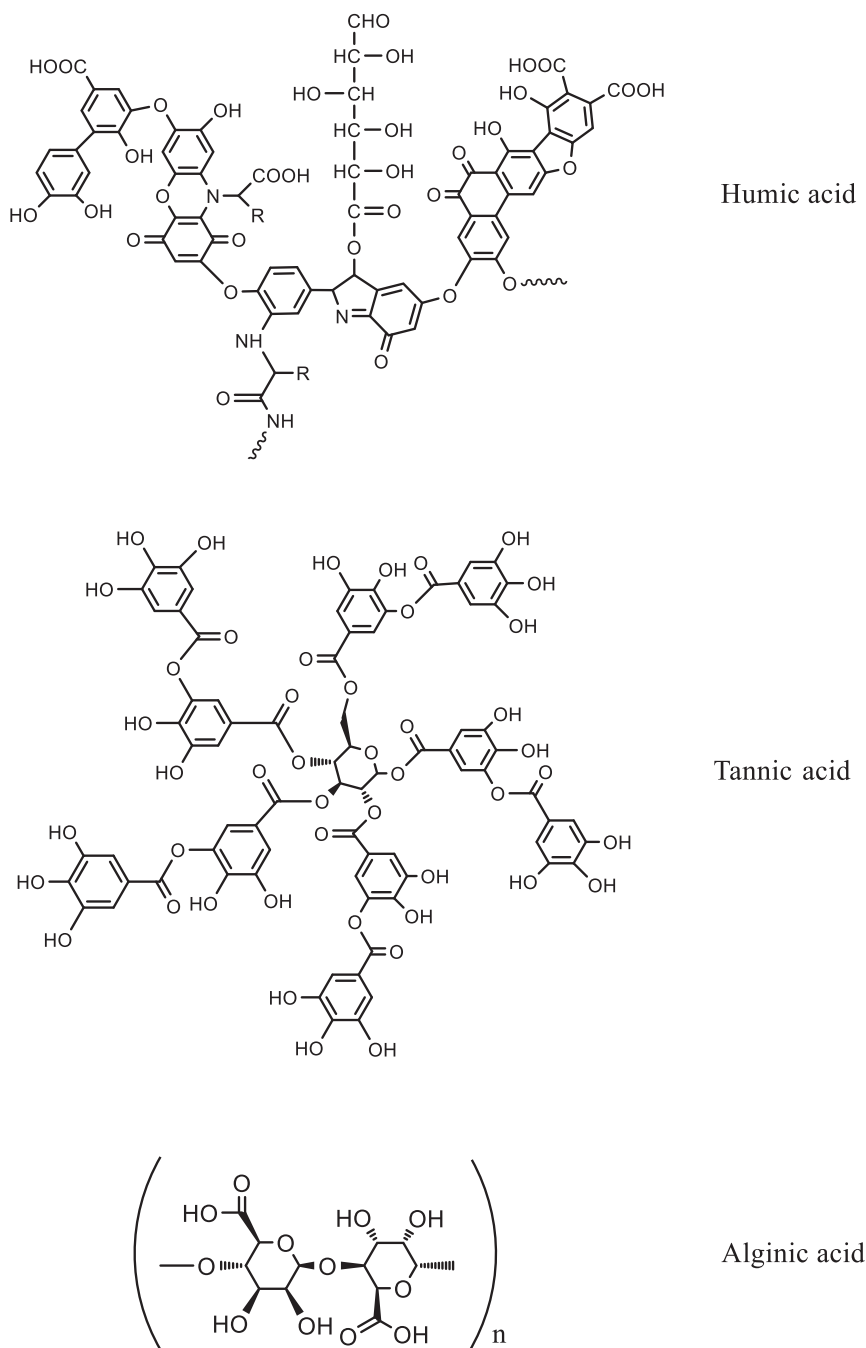


Fig. 1. Chemical structures of humic acid (Stevenson, 1994), tannic acid and alginic acid.

2.2. Log K_{OC} measurement

2.2.1. FQ

The fluorescence intensity of the sorbate decreases proportional to the concentration of DOC, accounting for which static quenching is the dominant mechanism. After background subtraction, the fluorescence of the sorbate in DOC-free solution (F_0) was divided by the fluorescence (F) in DOC-containing solution gradients, and the ratio was plotted against DOC concentration (mg C L^{-1}) in the form of a Stern-Volmer plot. The DOC binding coefficient (K_{OC} with units of L kg^{-1}) was calculated based on the equation:

$$F_0/F = 1 + K_{OC} [\text{DOC}] \quad (1)$$

where [DOC] represents the concentration of DOC (Holbrook et al., 2003). This method is vulnerable to loss of fluorescence intensity by quenchers other than DOM (e.g., dissolved oxygen) (Danielsen et al., 1995) and therefore may overestimate the binding efficiency. Manipulators usually pre-evaluated the demerits to ensure a valid use of the method (Holbrook et al., 2004). Overall, for fluorescent compounds, FQ is still a popular option considering its advantages in time and simplicity over other sorption evaluation methods.

2.2.2. Cross-flow ultrafiltration (CFUF)

Dissolved phase of aquatic organic matter was normally acquired by passing the water through 0.45–1.5 μm filter (Botero et al., 2011; Holbrook et al., 2003; Yan et al., 2015b; Yang et al., 2011). The dissolved

phase (<0.45–1.5 µm filtrate) was then subject to CFUF using a membrane with a 1 kDa cutoff. Consequently, the filtrates (<0.45–1.5 µm) were separated into permeates (<1 kDa, truly dissolved phase) and retentates (1 kDa to 0.45–1.5 µm, the colloidal phase). To perform the CFUF method for Log K_{OC} calculation, estrogens were allowed initially to interact with colloids for a period of time, then colloids were separated from the truly dissolved phase by CFUF, and finally estrogens in filtrate and permeate were extracted and analyzed. Estrogen concentration in retentate was obtained by subtracting its concentration in permeate from filtrate. In general, equilibrium between estrogens and DOM occurs rapidly. The reported complexation equilibrium time was ca. 30 min for EE2 with aquatic HS (Botero et al., 2011), and 5 min for E2 and EE2 with colloids (Holbrook et al., 2004). A value of K_{OC} was calculated using the following equation (Lee et al., 2011b; Zhou et al., 2007):

$$K_{OC} = [\text{estrogen}_{\text{colloids}}] / ([\text{estrogen}_{\text{free}}][\text{COC}]) \quad (2)$$

where $[\text{estrogen}_{\text{colloids}}]$ and $[\text{estrogen}_{\text{free}}]$ represent estrogen concentrations (ng L^{-1}) associated with colloids (retentate) and truly dissolved phase (permeate), respectively; while $[\text{COC}]$ signifies the concentration of COC (mg C L^{-1}) in filtrate.

2.2.3. Solid-phase microextraction (SPME)

SPME can be used to measure freely dissolved contaminants while those bound to COM cannot be extracted by polymer SPME fiber. Polyacrylate manifests its higher extraction capacities than other stationary phases for H-bond donor compounds (e.g., phenols, amides, pesticides and pharmaceuticals) (Endo et al., 2011; Haftka et al., 2013) and is thus an ideal sampling phase for moderately hydrophobic contaminants with polar functionalities, such as hormones. Drawbacks of SPME include the reduced extraction capacity for charged microcontaminants (Escher et al., 2002), as well as the potential of fouling of SPME fiber by organic matter (Zhang et al., 1996). To apply this method, the initial estrogen concentration spiked in solution (C_{total} , $\mu\text{g L}^{-1}$), concentration of estrogens freely dissolved in solution (C_{free} , $\mu\text{g L}^{-1}$), and the concentration extracted by fiber (C_{fiber} , $\mu\text{g L}^{-1}$) are required. A mass-balance approach can be applied to calculate the concentration sorbed to DOC (C_{DOC} , $\mu\text{g kg}^{-1}$). The equation is:

$$C_{\text{total}} V_{\text{water}} = C_{\text{free}} V_{\text{water}} + C_{\text{fiber}} V_{\text{fiber}} + C_{\text{DOC}} M_{\text{DOC}} \quad (3)$$

where V_{water} , V_{fiber} and M_{DOC} are volume of water solution (L), volume of fiber extractant (L) and mass of DOC (kg), respectively. Finally the following equation can be used to calculate K_{OC} (Haftka et al., 2013):

$$K_{OC} \left(\text{L kg}^{-1} \right) = C_{\text{DOC}} / C_{\text{free}} \\ = [(C_{\text{total}} V_{\text{water}} - C_{\text{free}} V_{\text{water}} - C_{\text{fiber}} V_{\text{fiber}}) / M_{\text{DOC}}] / C_{\text{free}} \quad (4)$$

2.3. Log K_{OC}

Table 2 summarizes from different studies the Log K_{OC} values of the four estrogens considered in this paper. Spiking manner, source and concentration of aquatic DOC and COC, measurement method of Log K_{OC} , as well as bound fraction of estrogens (%) are included. The calculated Log K_{OC} values are fairly variable depending on sources of DOC and experimental conditions.

Table 2 shows that most of the studies on Log K_{OC} measurement were based on laboratory spiking experiments with application concentrations of target compounds much higher than the environmentally-realistic levels. Although a few studies applied CFUF method to field samples to probe in-situ Log K_{OC} values, divergent results were obtained compared to spiking experiments. For example, Yan et al. (2015a) and Nie et al. (2014) presented in-situ Log K_{OC} values in Chinese rivers ranging 5.82–7.8 L kg^{-1} for the four estrogens, higher than that of the spiking experiments listed in Table 2. Nevertheless, Zhou et al. (2007)

observed comparable values between two measurement methods performed on an English river. It is postulated that, in real water environment, the sorption coefficient could be lower than much of the reported values in Table 2 because estrogens at environmental-realistic concentrations show decreased chances to contact DOM which weakens their interactions with DOM. More research needs to be focused on the real field conditions for confirmation.

Generally, differences in Log K_{OC} values between E1, E2, E3 and EE2 for the same sorbent are not pronounced, which is reasonable in light of the fact that the four sorbates have an aromatic ring in common attached by a —OH at C-3 position to interact with DOM.

Log K_{OC} values of estrogens were inclined to be independent of DOC quantity (Zhou et al., 2007). Elemental ratios (e.g., C/O and H/C ratios) or carboxylic group content was also suggested to be weakly linked to K_{OC} values (Yamamoto et al., 2003; Zhou et al., 2007). Size of fractionated DOM, Aldrich tannic acid for example, showed insignificant effect on Log K_{OC} values (Lee et al., 2011a). Chemical composition or type of DOM sources, however, has a conspicuous effect on the adsorption affinity. According to Yamamoto et al. (2003), highest Log K_{OC} values were observed for tannic acid (5.22–5.32 L kg^{-1}), moderate for HS (4.55–4.99 L kg^{-1}) and least for polysaccharides (alginic acid and dextran) (2.76–3.75 L kg^{-1}). Similar results were reported by Neale et al. (2009). High affinity of tannic acid arises from the abundance of phenolic groups, whereas HS usually possess fewer phenolic groups and polysaccharides contain fewer aromatic groups (Neale et al., 2009) (Fig. 1). Tannic acid and HS are hydrophobic fraction of DOM closely related to the aromaticity. Collectively, parameters that regulate aromaticity and speciation of phenolic functionalities will play a defining role in influencing sorption. It is noteworthy that solution chemistry, pH in particular, would influence the interactions due to changes in charge, conformation and solubility of both organic matter and hormones in response to variations in pH. For example, in natural waters, pH is generally neutral and estrogens are uncharged (pKa around 10, Table 1), while HA with high content of carboxylic groups (pKa around 4.3) is anionic and tannic acid primarily containing phenolic groups (pKa around 8.5) is not dissociated (Neale et al., 2009). Therefore, the interactions between estrogens and tannic acid are the strongest. When pH is elevated to around 9, estrogens and tannic acid begin dissociation and their interactions tend to decrease.

Approximately one third of studies listed in Table 2 used commercial HS as surrogates for natural aquatic DOM. However, results acquired from commercially available HS should be interpreted with caution since HS only account for about 50–70% of the total DOC (M. Thurman, 1985). HS representing the hydrophobic part of DOM act as a main contributor to the sorption affinity, while the hydrophilic fraction of natural DOM contributes less or little to binding. Therefore, calculating Log K_{OC} values based on HS surrogates may overestimate the correspondent effect of DOM in natural waters.

Table 3 showed the affinity of estrogens to other matrices. Comparatively, the affinity tends to follow this order: aquatic DOM > riverine sediment > soil > SPM. Similar results were also presented by Yang et al. (2011) that the sorption capacity of colloids in Yangtze River for pharmaceuticals was 2–4 orders of magnitude higher than that of SPM. It is assumed that the high sorption affinity was associated with the large surface area and condensed carbon content of smaller size materials. Qi and Zhang Tian (2016) observed that sorption affinity of testosterone for soil colloids were three times stronger compared with bulk soil and increased significantly with decreasing diameter size of colloids; and elsewhere Holthaus et al. (2002) reported greater affinity of E2 and EE2 associated with sediment of smaller particle size, providing cogent proofs for this assumption.

2.4. Interactions influence bioavailability

Lee et al. (2011a) and Holbrook et al. (2005) investigated the effect of size fractionated DOM/COC on estrogenicity of E2 by using

estrogenicity-screen bioassay and YES and pointed out that the estrogenicity for large size fraction bound with E2 was significantly reduced while that for the small size fraction having no binding with E2 was not, compared to that of the DOM-free control. Not surprisingly, the results directed to the pivotal role of sorption affinity on estrogenicity reduction because the mechanism of endocrine disrupting effects is based on binding of endocrine disruptors to human estrogen receptors while DOM-estrogen complex is not recognized by the receptor (Tanghe et al., 1999). That is DOM-contaminant complex lowers the estrogenicity and the bioconcentration of contaminants in aquatic organisms by reducing their bioavailability. A previous review presented

an overall suppression effect of DOM on bioconcentration factor values of hydrophobic contaminants (e.g., PAHs and PCBs) in aquatic animals (Haitzer et al., 1998). Accordingly, Yamamoto et al. (2004) reported that partitioning of E2 to liposome decreased slightly to moderately with the increase of DOM concentration from 0 to approximately 4 mg L⁻¹ due to competition between DOC and liposome for E2. Similarly, Tanghe et al. (1999) and Neale et al. (2015) indicated that application of HS to E2 led to decreasing bioavailability and thus estrogenic response. Also, Holbrook et al. (2005) suggested that COM-E2 mixture at 1–5 mg L⁻¹ of COC led to a reduction in bioavailability of E2. Nevertheless, enhancement of bioconcentration of estrogens or other organic

Table 2

Estrogen K_{OC} (L kg⁻¹) values calculated by different methods in aquatic environment with different parameters.

Estrogens	Spiking or in-situ	Level	DOC source	COC (mg C L ⁻¹)	DOC (mg C L ⁻¹)	Log K_{OC} (L kg ⁻¹)	Method	Bound fraction (%)	Reference
E1	Spiking	0.1–100 µg L ⁻¹	Aldrich HA		12.5	4.82	SPME		(Neale et al., 2009)
	Spiking	100 ng L ⁻¹	Aldrich HA		12.5	4.82	SPME		(Shen et al., 2012)
	Spiking	~1 µg L ⁻¹	Aldrich HA and Leonardite HA		~200	3.98	Dialysis		(Qiao et al., 2011)
	Spiking	600 ng L ⁻¹	River water, UK			4.2	CFUF		(Liu et al., 2005)
	Spiking	600 ng L ⁻¹	River water, UK&France	2.3–3.0		4.67–4.85	CFUF	4–26%	(Zhou et al., 2007)
	Spiking	600 ng L ⁻¹	Seawater	0.4		5.04	CFUF		(Zhou et al., 2007)
	Spiking	600 ng L ⁻¹	STP effluent	9.2		4.3	CFUF		(Zhou et al., 2007)
	Spiking	0.1–100 µg L ⁻¹	Commercial TA		12.5	5.51	SPME		(Neale et al., 2009)
	In-situ	~250 ng L ⁻¹	Domestic wastewater, China			5.4	CFUF	8.12%	(Yan et al., 2015b)
	In-situ	<20.3 ng L ⁻¹	Donggang River, Taiwan	77.7–86.2	~108	4.08	CFUF	7.3–8.5%	(Chen et al., 2014)
	In-situ	0.2–4.5 ng L ⁻¹	Huangpu River, China		3.8–9.6	5.86–7.26	CFUF		(Nie et al., 2014)
	In-situ	26.5 ng L ⁻¹	STP outfall of river water, UK			4.18–4.85	CFUF		(Zhou et al., 2007)
	In-situ	<5.99 ng L ⁻¹	Yangtze Estuary, China	2.8–5.8		7.09	CFUF	~10%	(Yan et al., 2015a; Yang et al., 2011)
									(Neale et al., 2009)
E2	Spiking	0.1–100 µg L ⁻¹	Aldrich HA		12.5	4.21	SPME		(Shen et al., 2012)
	Spiking	100 ng L ⁻¹	Aldrich HA		12.5	4.21	SPME		(Qiao et al., 2011)
	Spiking	~1 µg L ⁻¹	Aldrich HA and Leonardite HA		~200	3.93–4.12	Dialysis		(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Aldrich HA, Suwannee River HA/FA	2.0–10		4.57–4.94	FQ		(Lee et al., 2011a)
	Spiking	<1 m L ⁻¹	Aldrich TA		14.5	4.72–6.15	FQ		(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Commercial AA	2.0–10		3.75	SE		(Neale et al., 2009)
	Spiking	0.1–100 µg L ⁻¹	Commercial AA		12.5	3.96	SPME		(Holbrook et al., 2003)
	Spiking	0.96 m L ⁻¹	Biological wastewater	8.7–16.7	18.6–20.6	4.1–4.7	FQ	20–32%	(Sun and Zhou, 2014)
	Spiking	0.4–2.4 m L ⁻¹	Chinese river water	0.47–26.2	0.63–33.66	3.75–5.26	FQ	0.4–48%	(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Commercial dextran	2.0–10		2.76	SE		(Neale et al., 2008)
	Spiking	0.1–100 µg L ⁻¹	DOM surrogate		12.5	3.95–4.86	SPME		(Haftka et al., 2013)
	Spiking	3–2500 µg L ⁻¹	Natural water in Europe		282	3.23	SPME		(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Nordic FA	2.0–10		4.61	FQ		(Neale et al., 2008)
	Spiking	0.1–100 µg L ⁻¹	Commercial polysaccharides		12.5	3.75–3.96	SPME		(Liu et al., 2005)
	Spiking	600 ng L ⁻¹	River water, UK			3.9	CFUF		(Zhou et al., 2007)
	Spiking	600 ng L ⁻¹	River water, UK&France	2.3–3.0		3.84–3.98	CFUF	15–30%	(Zhou et al., 2007)
	Spiking	600 ng L ⁻¹	Seawater	0.4		4.86	CFUF		(Zhou et al., 2007)
	Spiking	600 ng L ⁻¹	STP effluent	9.2		4.04	CFUF		(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Commercial TA	2.0–10		5.28	FQ		(Neale et al., 2009)
	Spiking	0.1–100 µg L ⁻¹	Commercial TA		12.5	4.86	SPME		(Lee et al., 2011a)
	Spiking	<1 m L ⁻¹	WWTP effluent, Korea			4.63–4.87	FQ	36–46%	(Chen et al., 2014)
	In-situ	<4.8 ng L ⁻¹	Donggang River, Taiwan	77.7–86.2	~108	4.04	CFUF	7.3–8.5%	(Nie et al., 2014)
	In-situ	0.9–27.8 ng L ⁻¹	Huangpu River, China		3.8–9.6	5.85–7.27	CFUF		(Zhou et al., 2007)
	In-situ	22.5 ng L ⁻¹	STP outfall of river water, UK			3.96–4.2	CFUF		(Yan et al., 2015a; Yang et al., 2011)
	In-situ	<5.99 ng L ⁻¹	Yangtze Estuary, China	2.8–5.8		7.58	CFUF	~30%	(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Aldrich HA, Suwannee River HA/FA	2.0–10		4.64–4.99	FQ		(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Commercial TA	2.0–10		5.32	FQ		(Chen et al., 2014)
	In-situ	<6.2 ng L ⁻¹	Donggang River, Taiwan	77.7–86.2	~108	4.11	CFUF	7.3–8.5%	(Nie et al., 2014)
	In-situ	0.1–2.7 ng L ⁻¹	Huangpu River, China		3.8–9.6	5.96–7.72	CFUF		(Yan et al., 2015b)
	In-situ	~25 ng L ⁻¹	Livestock wastewater, China			6.11	CFUF	47.57%	(Yan et al., 2015a; Yang et al., 2011)
	In-situ	<5.99 ng L ⁻¹	Yangtze Estuary, China	2.8–5.8		7.8	CFUF	~40%	(Yamamoto et al., 2003)
EE2	Spiking	700 µg L ⁻¹	Aldrich HA, Suwannee River HA/FA	2.0–10		4.55–4.80	FQ		(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Commercial AA	2.0–10		3.23	SE		(Holbrook et al., 2003)
	Spiking	1 m L ⁻¹	Biological wastewater	8.7–16.7	18.6–20.6	4.3–4.7	FQ	32–72%	(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Commercial dextran	2.0–10		3.04	SE		(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Nordic FA	2.0–10		4.63	FQ		(Liu et al., 2005)
	Spiking	600 ng L ⁻¹	River water, UK			4.7	CFUF		(Zhou et al., 2007)
	Spiking	600 ng L ⁻¹	River water, UK & France	2.3–3.0		4.58–4.85	CFUF	20–29%	(Zhou et al., 2007)
	Spiking	600 ng L ⁻¹	Seawater	0.4		5.48	CFUF		(Zhou et al., 2007)
	Spiking	600 ng L ⁻¹	STP effluent	9.2		4.73	CFUF		(Yamamoto et al., 2003)
	Spiking	700 µg L ⁻¹	Commercial TA	2.0–10		5.22	FQ		(Nie et al., 2014)
	In-situ	0–18.9 ng L ⁻¹	Huangpu River, China		3.8–9.6	5.82–6.26	CFUF		(Yan et al., 2015b)
	In-situ	~300 ng L ⁻¹	Livestock wastewater, China			5.47	CFUF	11.74%	(Zhou et al., 2007)
	In-situ	<1 ng L ⁻¹	STP outfall of river water, UK			4.0–4.63	CFUF		

HA: humic acid; TA: tannic acid; FA: fulvic acid; AA: alginic acid; DOM: dissolved organic matter; DOC: dissolved organic carbon; COC: colloidal organic carbon; STP: sewage treatment plant; WWTP: wastewater treatment plant; FQ: fluorescence quenching; SPME: solid-phase microextraction; SE: solubility enhancement; CFUF: cross-flow ultrafiltration. Bound fraction of estrogens (%) = $K_{OC} \cdot [DOC] / (1 + K_{OC} \cdot [DOC])$.

Table 3
Estrogen K_{OC} ($L\ kg^{-1}$) values in different matrix.

	E1	E2	E3	EE2	Reference
River suspended particulate matter					
(Huangpu River, China)	1.67–3.46	2.27–2.46	3.53–4.07	2.3	(Nie et al., 2014)
(Yangtze Estuary, China)	2.01–3.88	1.91–3.45	2.08–4.08		(Nie et al., 2015)
(English rivers)		1.32–2.09		1.28–2.41	(Holthaus et al., 2002)
Artificial suspended particles	1.05	1.56		1.77	(Ra et al., 2008)
Riverine sediment					
(Songhua River, China)	~4		~3.8		(Zhang et al., 2014)
(Baitang River, Dagu River and Yongding New River, China)	4.02–4.60	4.22–4.57	3.64–4.39	4.21–4.80	(Lei et al., 2009)
(Blackwater Estuary/Thames River, UK)	3.1	3.6	2.5	3.8	(Lai et al., 2000)
Sludge					
(STP, Spain)	3.00–4.18	3.13–3.69	2.23	2.90–4.16	(Carballa et al., 2008)
(WWTP)		3.3		3.31	(Clara et al., 2004)
Soil					
(Agriculture soils, Ohio)	2.77	2.83			(Card et al., 2012)
(Four soils from Colorado, Nevada, and North Dakota)	3.5	3.23		3.25	(Roberts et al., 2014)
(Top soil, Michigan)	3.30–3.81	3.14–3.71		3.35–3.55	(Yu et al., 2004)
(Natural soils, Texas/Nebraska)	3.63–3.72	3.58–3.95	2.82–3.34	3.02–4.13	(Karnjanapiboonwong et al., 2010)

STP: sewage treatment plant; WWTP: wastewater treatment plant.

compounds due to DOM was also reported by a number of studies (Chen et al., 2012; Haitzer et al., 1998). Haitzer et al. (1998) summarized that the advancement in bioconcentration factors was pronounced at low DOC concentrations, up to $10\ mg\ L^{-1}$. One possible mechanism provided by Chen et al. (2012) for the enhancement effect of DOC at low concentrations was that the direct interaction of DOC with organisms blocked and inhibited the multixenobiotic resistance transporter in organisms, causing the intracellular accumulation of E2 and the ensuing estrogenic effects.

3. Effect of DOC on estrogen removal

3.1. Photodegradation

Estrogens in environmental waters undergo both direct and indirect photodegradation. For direct photodegradation, light is absorbed directly by the pollutants followed by a chemical reaction, and for indirect photodegradation, a sensitizer (e.g., DOM, nitrate and ion complexes) mediates the reaction (Lin and Reinhard, 2005). DOM as photosensitizers could bind with pollutants and induce photodegradation through reactive oxygen species (ROS) (Fig. 2), such as hydroxyl radical ($HO\cdot$), singlet oxygen (1O_2), superoxide radical ($O_2\cdot^-/HO_2\cdot$), hydrogen peroxide (H_2O_2), solvated electron (e_{aq}^-) and peroxy radical ($ROO\cdot$), as well as triplet dissolved organic carbon ($^3DOC^*$) (Aguer et al., 1999; Blough and Zepp, 1995; Boule et al., 1999; Liang et al., 2015). During this process, the binding role of DOM was underlined in facilitating estrogen photodegradation. For example, Ren et al. (2017b) observed a significant positive relationship between the percentage of bound EE2 and its photodegradation rates, which demonstrated that the bound EE2 was directly oxidized by ROS and $^3DOC^*$. Additionally, existing work shows that photodegradation of estrogens, under sunlight or simulated sunlight, generally followed the pseudo first-order kinetics, and DOM accelerated the indirect photodegradation of estrogens when the concentration of DOC was below a threshold value, for which degradation plateaued. Acceleration efficiency (AE) can be calculated as the ratio of estrogen photodegradation rate constants in the presence and absence of DOM (Ren et al., 2017a). Reported AE values were 3.74–4.35 for EE2 (Ren et al., 2017a), 1.56–2.73 for E1 (Silva et al., 2016a) and 1.55 for E2 photodegradation (Leech et al., 2009) in the presence of $5\ mg\ C\ L^{-1}$ HS, $20\ mg\ C\ L^{-1}$ DOC and $10\ mg\ C\ L^{-1}$ DOC, respectively. Overall, the plateau concentrations varied based on experimental conditions such as fortification concentrations, time of photodegradation and HS sources. Leech et al. (2009) reported that a plateau was reached for $5.0\ mg\ L^{-1}$ of Suwannee River HA when $0.27\ mg\ L^{-1}$ of E2 was investigated. Silva et al. (2016a), in studying the degradation of $500\ \mu g\ L^{-1}$ E1 in the presence of HS, for 2-h irradiation, found that the degradation

was enhanced at a maximum concentration of $30\ mg\ L^{-1}$ of HS. Elsewhere, in the case of E1 degradation for 30 min of irradiation, a plateau concentration of HA was reported at $8\ mg\ L^{-1}$ (Chowdhury et al., 2010). For EE2 (initial $1.46\ mg\ L^{-1}$), a threshold of $10\ mg\ L^{-1}$ HS was reported (Ren et al., 2017a). Despite the variations in reported plateau concentrations, given the average DOC concentration in lakes, streams and rivers is between 5 and $10\ mg\ L^{-1}$ (Wetzel, 2001), estrogen photodegradation is likely occurring to a high degree in surface waters. Above the maximum concentration, the scavenging effect of ROS (Chowdhury et al., 2010), self-quenching reactions of increased radicals, as well as elevated light attenuation (Chowdhury et al., 2011) prevents further increase in degradation with increasing DOC concentration. Another finding is that HA exerted an inhibition effect on photodegradation under high irradiation light intensity. For example, photodegradation of E3 was inhibited by HA under intense simulated sunlight (Chen et al., 2013). It was speculated in the study that the intense light irradiation could alter the HS characteristics, converting its role as an accelerator or inhibitor. The effects of HS on photodegradation of pollutants are complicated due to its versatile roles as photosensitizers, light screening agents and radical quenchers. The photodegradation rates of estrogens in DOC-free water and sampled environmental surface waters are summarized in Table 4. Due to differences in the experimental conditions, it is hard to make a lateral comparison. Overall, under simulated solar radiation, photodegradation rates are higher in environmental surface waters than that in ultrapure water, suggesting that DOC photosensitizing effects are, at least partially, responsible for the higher photolysis degree in different water compartments. In fact, Silva et al. (2016b) reported 91–98% contribution of HS to overall photodegradation of E2 and EE2. Caupos et al. (2011) presented ~60% of overall photodegradation of E1 due to DOC photosensitized reactions. Oliveira et al. (2016) reported that dissolved aqueous matrix contributed up to 97% to the overall E3 photodegradation.

Not only the concentration of DOC but also the type and quality of DOC are important factors for the photodegradation increase. Fulvic acids and XAD-4 fraction were shown to have greater enhancement effect than HA in EE2 and E2 photolysis (Silva et al., 2016b). One explanation for this is that XAD-4 fraction which features low aromaticity seems to produce high amount of ROS while HA, rich in aromatic and chromophoric groups, tends to have high inner filter effect by reducing the available energy for DOM and the ensuing photodegradation rate (Silva et al., 2016b). Estuarine water was shown to have higher photodegradation rate than freshwater and wastewater, although estuarine water has lower DOC content than wastewater (DOC $16.7\ mg\ C\ L^{-1}$ for estuarine water and 45.5 – $48.6\ mg\ C\ L^{-1}$ for wastewater) (Silva et al., 2016a; Silva et al., 2016b). This may be due to the enrichment of fulvic acid and XAD-4 and the low content of HA in

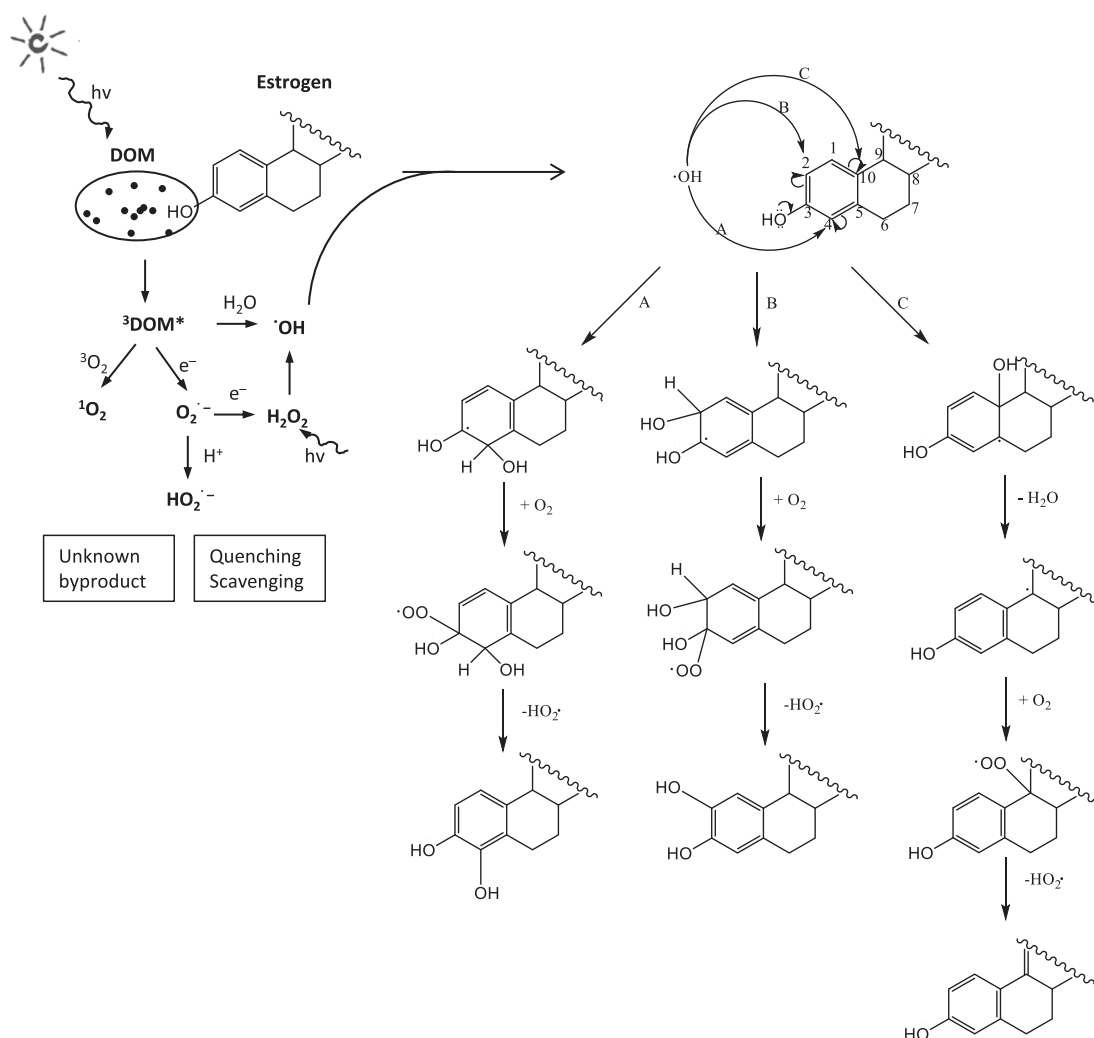


Fig. 2. Proposed pathways of photochemical generation of reactive oxygen species (ROS) and reactions between estrogens and hydroxyl radicals (modified based on [Chen et al. \(2013\)](#); ([Gmurek et al., 2015](#))).

estuarine water. Chromophoric and quinone-like fraction of DOM tends to generate more $^3\text{DOM}^*$, which has been reported to be more effective in EE2 photolysis compared with DOM of low quinone content provided that the contents of phenolic hydroxyl and carboxyl groups are similar ([He et al., 2018](#)).

ROS and $^3\text{DOC}^*$ scavenging experiments were conducted to probe the contribution of the photogenerated reactive species to estrogen degradation. To perform this, azide ions, isopropanol, sorbic acid and 1,4-benzoquinone were added primarily as $\text{HO}\cdot/{}^1\text{O}_2$ ([Ge et al., 2010](#)), $\text{HO}\cdot$ ([Buxton et al., 1988](#)), $^3\text{DOC}^*$ as well as $\text{O}_2\cdot^-/\text{HO}_2\cdot$ scavengers ([Caupos et al., 2011](#)), respectively. [Ren et al. \(2017a\)](#) indicated that the promotion effect of dissolved HS on EE2 photodegradation was mainly induced by the reaction species $\text{HO}\cdot$ (35–50%), $^3\text{DOC}^*$ (22–34%) and ${}^1\text{O}_2$ (<10%). In another study, [Ren et al. \(2017b\)](#) also reported that $\text{HO}\cdot$ and $^3\text{DOC}^*$ were responsible for about 60% of the overall EE2 photodegradation. Analogous results were reported for other pollutants in sunlit natural waters ([Boule et al., 1999](#); [Liang et al., 2015](#); [Song et al., 2012](#)). $\text{HO}\cdot$ photogenerated by DOC was also found to be the main contributor to the photodegradation of E1 ([Caupos et al., 2011](#)) and E2 ([Leech et al., 2009](#)). $\text{HO}\cdot$ is an electrophile which readily attacks the aromatic ring of estrogens at 2,4,10-position carbons that bear relatively high electron density due to the conjugated effect incurred by the electron-donating substituent ($-\text{OH}$) at C3-position. The general reaction pathways between $\text{HO}\cdot$ and primary estrogens

are summarized in [Fig. 2](#) based on existing references. As proposed by [Ren et al. \(2017a\)](#) for EE2 photodegradation, attack of $\text{HO}\cdot$ at C-10 position led to a loss of H_2O to form an unsaturated byproduct; while attack at 2- and 4-position involved a reaction of the EE2 radicals with oxygen and a subsequent elimination of $\text{HO}_2\cdot$ to yield hydroxylated byproducts. Such $\text{HO}\cdot$ oxidation processes were also proposed for E3 photodegradation ([Chen et al., 2013](#)). Similarly, DOC photoinduced monohydroxylations at C-2 and C-4 positions of the aromatic ring have been observed for E1 ([Caupos et al., 2011](#)) and E2 ([Mazellier et al., 2008](#)). However, there are conflicting reports on the contribution of ROS involved in estrogen photolysis. For instance, [Silva et al. \(2016b\)](#) indicated that $\text{HO}\cdot$ played a minor role in indirect photodegradation of EE2 and E2 in wastewater effluent. This disparity remains unexplained. So far, information on effect of DOC on in-depth water photodegradation and photolysis pathways of estrogens is scarce.

The aforementioned content highlights the paramount role of photogenerated ROS in inducing estrogen photodegradation, while estrogens can be photo-transformed, which is mediated by metals, not by ROS, in the presence of DOM. [Wang et al. \(2018\)](#), for example, reported that soluble Mn (III) was responsible for estrogen removal in the presence of HA under visible light irradiation. In this reaction system, HA underwent photo-chemical reaction to generate excited DOM^* , which reacted with oxygen to form superoxide radicals. The superoxide radicals oxidized Mn (II) to Mn (III), which deprived estrogens

Table 4Degradation rate constant (*k*) and half-life for estrogen photolysis under different experimental conditions.

Estrogens	Level	Water matrix	DOC (mg C L ⁻¹)	<i>k</i> (h ⁻¹)/half-life time	Irradiation	Reference
E1	500 ng L ⁻¹	Distilled water	0	0.208 ± 0.019/3 h	Fluorescent lamp UVB = 133 μW cm ⁻²	(Atkinson et al., 2011)
	500 ng L ⁻¹	Ottawa River	6.76	0.085 ± 0.016/8 h		
	500 ng L ⁻¹	Lake Cromwell	6.85	0.087 ± 0.016/8 h		
	500 ng L ⁻¹	Raw sewage	10.78	0.065/11 h		(Lin and Reinhard, 2005)
	500 ng L ⁻¹	Raisin River	23.9	0.004 ± 0.013/173 h		
	1–2 μg L ⁻¹	Milli-Q water	4.6	0.15 ± 0.005/5 h	Sunlight simulator (765 W m ⁻² ; 290–700 nm)	
	1–2 μg L ⁻¹	Santa Ana River	4.6	0.31 ± 0.009/2 h		(Silva et al., 2016a)
	500 μg L ⁻¹	Milli-Q water	0	0.1137 ± 0.005/6 h ^a	Simulated solar radiation (55 W m ⁻² ; 290–400 nm)	
	500 μg L ⁻¹	Fresh water	4.8			
	500 μg L ⁻¹	Estuarine water	16.7			
	500 μg L ⁻¹	Wastewater primary	48.6			
	500 μg L ⁻¹	Wastewater effluent	45.2			
E2	1–2 μg L ⁻¹	Milli-Q water	4.6	0.02 ± 0.002/35 h	Sunlight simulator (765 W m ⁻² ; 290–700 nm)	(Lin and Reinhard, 2005)
	1–2 μg L ⁻¹	Santa Ana River	4.6	0.35 ± 0.024/2 h		
	50 μg L ⁻¹	Milli-Q water	0	0.0073 ± 0.0003/94 h ^a	Simulated solar radiation (55 W m ⁻² ; 290–400 nm)	(Silva et al., 2016b)
	50 μg L ⁻¹	Fresh water	4.8			
	50 μg L ⁻¹	Estuarine water	16.7			
	50 μg L ⁻¹	Wastewater primary	48.6			
E3	50 μg L ⁻¹	Wastewater effluent	45.2			
	1–2 μg L ⁻¹	Milli-Q water	4.6	0.02 ± 0.003/35 h	Sunlight simulator (765 W m ⁻² ; 290–700 nm)	(Lin and Reinhard, 2005)
	1–2 μg L ⁻¹	Santa Ana River	4.6	0.24 ± 0.013/3 h		
	100 μg L ⁻¹	Ultrapure water	0	0.0138 ± 0.0004/50 h	Sunlight simulator (55 W m ⁻² ; 290–400 nm)	(Oliveira et al., 2016)
	100 μg L ⁻¹	Wastewater	32.9	0.17 ± 0.02/4 h		
	100 μg L ⁻¹	Estuarine water	14.6	0.45 ± 0.04/1.6 h		
EE2	100 μg L ⁻¹	Freshwater	6.2	0.073 ± 0.003/9.5 h		
	300 ng L ⁻¹	Distilled water	0	0.04 ± 0.02/17 h	Solar simulator, UVB = 2.0 W m ⁻² , UVA = 31.2 W m ⁻²	(Grzybowski and Szydlowski, 2014)
EE2	300 ng L ⁻¹	Baltic Sea	4.9 ± 0.2	0.06 ± 0.02/12 h		
	300 ng L ⁻¹	Vistula River	10.8 ± 0.3	0.11 ± 0.03/6 h		
EE2	500 ng L ⁻¹	Distilled water	0	0.013 ± 0.006/53 h	Fluorescent lamp UVB = 133 μW cm ⁻²	(Atkinson et al., 2011)
	500 ng L ⁻¹	Ottawa River	6.76	0.001 ± 0.004/693 h		
	500 ng L ⁻¹	Lake Cromwell	6.85	0.021 ± 0.014/33 h		
	500 ng L ⁻¹	Raisin River	23.9	0.007 ± 0.003/69 h		(Lin and Reinhard, 2005)
	1–2 μg L ⁻¹	Milli-Q water	4.6	0.02 ± 0.002/28 h	Sunlight simulator (765 W m ⁻² ; 290–700 nm)	
	1–2 μg L ⁻¹	Santa Ana River	4.6	0.30 ± 0.015/2 h		
	10–40 mg L ⁻¹	Milli-Q water	0	0.61/1 h	Solar simulator (507.5 W m ⁻² ; 300–800 nm)	(Matamoros et al., 2009)
	10–40 mg L ⁻¹	Ebre River	2.85 ± 0.02	0.69/1 h		
	10–40 mg L ⁻¹	Besos River	11.2 ± 0.04	0.73/1 h		
	10–40 mg L ⁻¹	Mediterranean Sea	1.14 ± 0.01	0.62/1 h		(Silva et al., 2016b)
	10–40 mg L ⁻¹	Besos River	11.2 ± 0.04	0.007/106 h	Sunlight, May, 41 °N	
	50 μg L ⁻¹	Milli-Q water	0	0.0151 ± 0.0002/46 h ^a	Simulated solar radiation (55 W m ⁻² ; 290–400 nm)	
	50 μg L ⁻¹	Fresh water	4.8			
	50 μg L ⁻¹	Estuarine water	16.7			
	50 μg L ⁻¹	Wastewater primary	48.6			
	50 μg L ⁻¹	Wastewater effluent	45.2			

^a Photodegradation rate follows the order: Milli-Q water < freshwater < wastewater < estuarine river water.

of one electron, leading to the formation of phenoxyl radicals and a recovery of Mn (II). Further degradation proceeded with self- and cross-coupling of phenoxyl radicals to form oligomers. So far, studies regarding this light/DOM/metal ions and/or more complicated systems are definitely lacking. Other materials such as Cu (II), Fe (III) and Fe (III)-modified minerals are assumed to function similar to Mn (II)/Mn (III) for photochemical transformation of estrogens in the presence of DOM, a hypothesis need testing.

3.2. Biodegradation

Theoretically, the effect of DOC on estrogen biodegradation should be two-fold. On one hand, a suppressive effect could be expected due to enhanced sorption of estrogens to DOC; on the other hand, an enhancement effect might occur considering DOM itself might act as a carbon source for bacterial flourish. DOM and estrogens can serve as substrates for microbes aerobically where oxygen is a major electron acceptor (Fig. 3a). There is a variety of bacteria responsible for degradation of estrogens in aqueous environment (Zhang et al., 2016). The degraders can be specific to certain estrogens or versatile, and can degrade the estrogens quickly and completely or transform them to multiple unknown metabolites stepwise. Biodegradation of estrogens generally obeys first-order degradation kinetics. Estrogens could be good

competitors to DOM for microbes in natural aquatic environment. For example, Ma and Yates (2018) demonstrated that estrogens conjugates and their degradation products can be bio-degraded in river water even at the concentration as low as 25 ng L⁻¹. While laboratory studies suggested that factors like the recalcitrance of fortified DOM, the availability of substrate and the source of the DOM may influence the biodegradation. Lee et al. (2012) found that, due to enhanced sorption of E2 to DOM, biodegradation of E2, its subsequent maximum transformation to E1, and total removal rate of E2 decreased noticeably as the DOC concentrations in the lake or river were adjusted to a high level with DOC of the same source. Lee et al. (2011b) observed that E2 biodegradation and transformation to E1 were significantly decreased as the concentration of HA amended increased (0–50 mg C L⁻¹). The author hypothesized that HA, representing a recalcitrant part of DOM that could not be readily used by microbes, exhibited inhibitory effect on bacterial activity, as evidenced by the dramatic drop of bacterial cell number in the presence of nutrients. Unfortunately, the author failed to monitor the change of HA and/or total DOC concentration in the time course, making the hypothesis inadequately tested. On the contrary, Lim et al. (2008) indicated that, for the same biodegradable DOC (from WWTP), biodegradation rates of PPCPs generally increased as the initial concentration of biodegradable DOC rose. One explanation for the disparity was that the microbial communities in the WWTP

could be substrate limited and the addition of labile DOC enriched the degraders. Possible evidence for this is that the biodegradable DOC from WWTP effluent was inclined to deplete in the biotic samples but not in the abiotic controls. Comparably, Tan et al. (2015) and Tan et al. (2013) demonstrated that the addition of organic carbon promoted E1 biodegradation under starvation conditions (substrate limited conditions). Moreover, Z.T. Li et al. (2017) found that substituting HA (recalcitrant carbon source) with acetic acid (labile carbon source) in a biologically active carbon reactor facilitated E2 biodegradation. Lake water, though it usually contains lower level of DOC than WWTP, tended to have higher degree of biodegradation of E2 into E1 than the WWTP effluent because of more labile DOC in lake than in WWTPs (Lee et al., 2012).

DOM could serve as a redox mediator or electron shuttle, which transforms between their oxidation and reduction forms, in mediating anaerobic biodegradation of contaminants (Meng et al., 2014). The catalytic effects of different organic redox mediators or electron shuttles on the anaerobic (bio)transformation of various contaminants, organic and inorganic, have been reviewed elsewhere (Van der Zee and Cervantes, 2009). DOM's redox activity is primarily determined by the quinone-type structure in DOM (Wolf et al., 2009). Quinone-reducing bacteria, widely distributed in diverse environment, have been potentially applied in pollution remediation through biodegradation. So far, a few studies addressed quinones as electron shuttles mediating biodegradation of estrogens by quinone-reducing bacteria. Gu et al. (2016) found that, under anaerobic conditions, a model quinone compound acted as terminal electron acceptors and couple with microbial growth to promote the oxidation of E2 which served as electron donors. He et al. (2018) found that the joint photodegradation and biodegradation of EE2 in the presence of DOM and quinone-reducing bacteria were much faster than either alone. The coupling removal of EE2 in this study arose from the role of DOM as an electron shuttle to promote

the EE2 biodegradation together with the $^3\text{DOM}^*$ induced photolysis. In the aforementioned studies, quinone-structure of DOM components served as terminal electron acceptors while estrogens electron donors. A most recent work disclosed the role of quinone as an electronic shuttle mediating the biodegradation of E2 with Fe (III) as an terminal electron acceptor (Gu et al., 2018). In the DOM/Fe (III)/bacteria system, E2 as an electron donor was oxidized to E1, while quinone in DOM was reduced to hydroquinone by quinone-reducing bacteria. Hydroquinone is a strong reducing agent and can reduce Fe (III) to Fe (II) with itself oxidized back to quinone. Generally, anaerobic biodegradation of estrogens followed pseudo-first order kinetics. Gu et al. (2016) reported an AE (ratio of estrogen biodegradation rate constants in the presence and absence of DOM) value of 1.5 for E2 with 0.5 mM quinone model compound added. Gu et al. (2018) also presented an AE value of 1.67 for E2 in the presence of quinone model compound and the addition of both quinone model compound (<2 mM) and Fe (III) elevated the value to 1.97. The results suggested the coupled action of quinone and Fe (III) can enhance estrogen biotransformation and a schematic illustration was depicted in Fig. 3b.

3.3. Enzymatic transformation

Estrogens were known to undergo enzyme-catalyzed oxidative coupling reactions, during which, enzymes converted estrogens into free radicals which then self-oligomerized to form insoluble oligomers or polymers (Auriol et al., 2007; Lloret et al., 2013; Mao et al., 2009; Mao et al., 2010b; Suzuki et al., 2003). Enzymatic removal of parent compounds generally followed a pseudo first-order rate equation and the addition of DOM was reported in a few studies to lower the degradation rates significantly (Huang et al., 2013; Sun et al., 2016) (Fig. 4). Huang et al. (2013) tested the effect of DOM on E2 removal by horseradish peroxidase (HRP) and found that the presence of DOM not only impaired the degradation of E2 but also the formation of self-coupling products (e.g., dimer and trimer of E2). The inhibitory efficiencies (0–25.1%) on degradation of parent compound increased with DOC quantity ($0\text{--}14\text{ mg L}^{-1}$), which was attributable to the ability of DOM to compete with E2 for active sites on HRP surface or to bind with E2 to reduce its reactivity with enzymes (Sun et al., 2016). Meanwhile, nearly all the self-coupling products of E2 were suppressed in the presence 5 mg L^{-1} of DOM, which, as suggested by the author, was due to the nonselective coupling of DOM radicals with E2 radicals, or itself, to form cross-coupling species. Elsewhere, Sun et al. (2016) also found that the inhibitory effect of DOM on E2 removal by laccase was dependent on the HA concentration ($0\text{--}60\text{ mg L}^{-1}$); HA hampered E2 self-coupling while fostered cross-coupling between E2 and HA. Likewise, Mao et al. (2010a) also found a concentration dependent inhibitory effect of DOM on E2 removal in the ligninase-catalyzed system as well as a cross-coupling reaction which suppressed the polymerization of parent compound. Nevertheless, the inhibitory efficiencies varied depending on experimental conditions. It is not surprising that DOM radicals formed and coupled with each other in the enzymatic systems since a substantial fraction of DOM is composed of phenol groups. Potentially, the phenolic functionality is susceptible to oxidation via an electron loss at the hydroxyl group to form a radical, which could form covalent bonds with another radical with two hydrogen atoms eliminated, one from each radical (Lu et al., 2009). This is of great significance since, in natural environment, the concentrations of DOM (e.g., mg C L^{-1}) are much higher than that of estrogens (e.g., ng L^{-1}), incorporation of the microcontaminants into DOM might be an important way of their sequestration under certain circumstances.

In contrast to the aforementioned inhibitory effect, a promoting effect of DOM on enzyme-catalyzed degradation of estrogens in light- and enzyme-combined systems has been reported. J.H. Li et al. (2017) noticed appreciable degradation of E2 by HRP ($0.01\text{--}0.1\text{ U mL}^{-1}$) in the presence of Suwannee River HA ($1\text{--}5\text{ mg C L}^{-1}$) and simulated solar light. Such enzyme-catalyzed oxidation of E2 was driven by

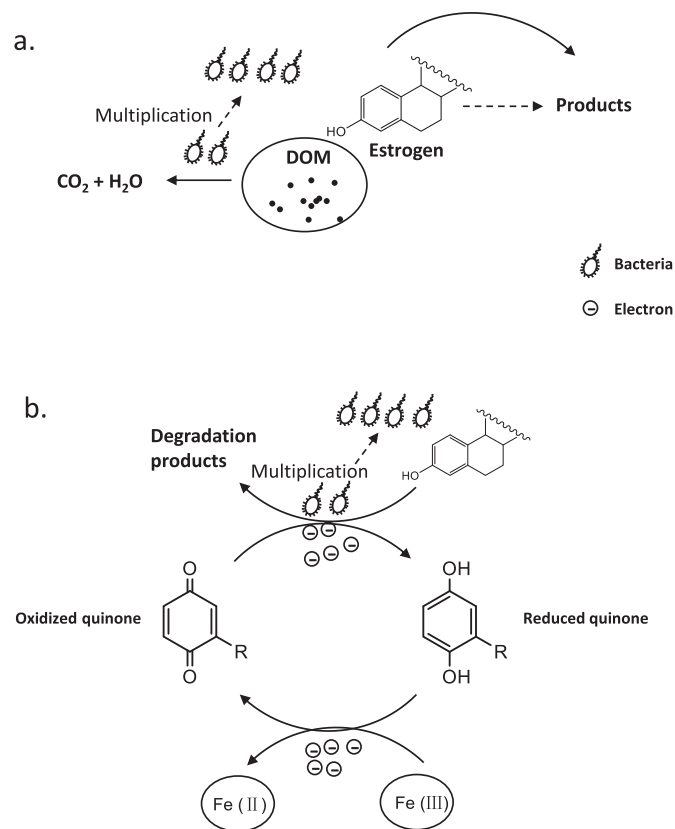


Fig. 3. Proposed biodegradation pathways of estrogens in the presence of dissolved organic matter (DOM) (a) aerobically and (b) anaerobically.

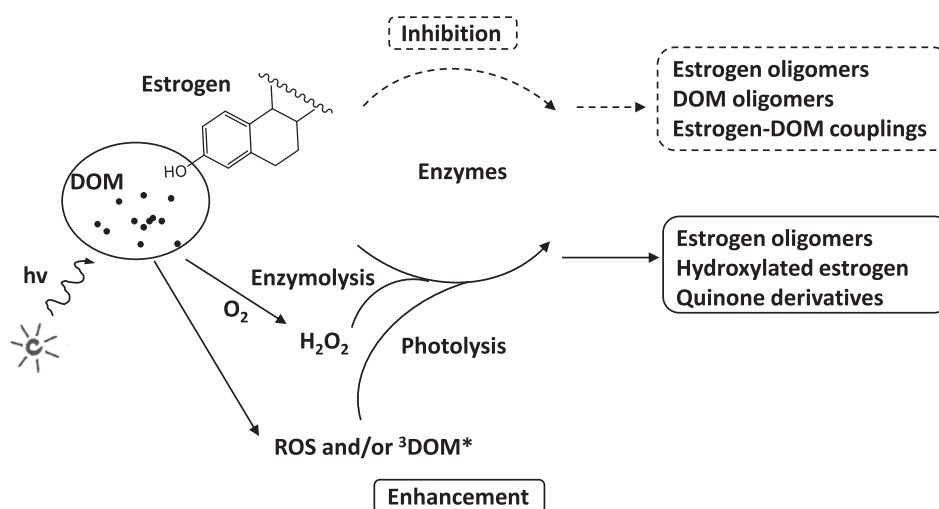


Fig. 4. Proposed inhibition (dash line) and enhancement (solid line) effects of dissolved organic matter (DOM) on enzymatic degradation of estrogens.

photogenerated H_2O_2 which originated from irradiated DOM (Fig. 4). E2 was catalyzed to oligomers, E1, hydroxylated E2 and some quinone derivatives in the presence of H_2O_2 . Yang et al. (2017) also observed, upon solar irradiation, enhanced degradation of EE2 by HRP at the co-existence of DOM compared to that in solution with DOM alone. Such enzymatic transformation was inhibited as the DOM concentration increased due to the deactivation of the enzyme activity by accelerating photoproduced ROS; while the acceleration effect of DOM on EE2 photodegradation compensated for the former effect, overall rate of photo-enzymatic transformation was maintained across a range ($2\text{--}20\text{ mg C L}^{-1}$) of DOM level.

It is speculated that both the two contrasting effects exist in natural waters. It is likely that the inhibitory effect of water-borne enzymes occurs at deep water with little sunlight penetration while the enhancement effect occurs at surface water with adequate solar irradiation. Nonetheless, no matter which effect dominates, DOM might play an overall positive role in microcontaminant removal via coupling and/or oxidative reactions.

3.4. Estrogen removal via membrane rejection

Membrane filtration, particularly nanofiltration and reverse osmosis, is a promising technology for EDC removal in wastewater. Major mechanisms in which target micropollutants are rejected are charge repulsion, steric hindrance and adsorption. In neutral filtration environment, charge repulsion should be ruled out for estrogen rejection given their high pKa value (Table 1); hence, steric hindrance and adsorption should be responsible for their high removal efficiency, if there is any. However, the removal behavior could be altered by the co-present DOM. Generally, one of the primary mechanisms by which DOM is supposed to influence rejection is via the sorption of DOM to membrane to form the hybrid layers to which the partition of the contaminants take place. The other important mechanism is via their binding to DOM to form complexes that are larger in sizes and possess more negative charges to interact with the membrane than the microcontaminant alone. Two extra interactions are included in the filtration systems, namely, the interaction between DOM and membrane and interaction between DOM and estrogens, with the first case taking place on membrane while the second in solution. Hu et al. (2007) and Jin et al. (2007) found that the presence of Aldrich HA significantly encouraged sorption of E1 from feed solution to membrane while the “enhancement effect” on rejection was limited. The results suggested that most of interactions between DOM and estrogens took place on membrane rather than in solution. In contrast, Jin et al. (2007) also found that the hydrophobic acid isolated from sewage effluents only slightly decreased the E1 concentration in the feed solution while greatly

enhanced E1 rejection. The author envisaged the phenomena to result from the formation of E1-hydrophobic acid complexes in solution which were electronegative and retained by negatively charged membranes based on the mechanisms of size exclusion and charge repulsion. Additionally, the hydrophilic compound dextran without aromaticity had negligible effects on E1 removal compared to control (Jin et al., 2007). These results suggested that estrogen rejection efficiencies were likely to be linked to type of DOM, among which, the hydrophobic fraction which features aromaticity and phenolic functionalities is the major driver.

4. Conclusions

Two major mechanisms i.e., $\pi\text{--}\pi$ interaction and hydrogen bonding are characterized for describing DOM and estrogen interactions. The sorption affinity of estrogens to DOM was quantified in terms of organic-carbon-normalized sorption coefficient ($\log K_{OC}$) values which are influenced by types and composition of DOM. DOM plays a vital role in governing estrogen removal (photodegradation, biodegradation, enzymolysis and membrane rejection) likely via sorption with estrogens or third-party participants to form a complex with which to mediate the subsequent reactions or re-partition of estrogens.

Collectively, the existing work provided, at least partially, experimental proofs why estrogens don't accumulate in the aquatic environment; herein DOM plays an important role. Majority of the available work has focused on the binding and sorption of estrogens at fortified concentrations much higher than environmentally-relevant levels, additional field experiments involving desorption process thus need to be addressed. Furthermore, gaps on DOM-affected transformation of estrogens on mineral surfaces need to be filled considering the wide application of heterogeneous photocatalytic degradation on aquatic contaminant remediation. Given DOM surrogates do not adequately represent natural DOM, it is advised to use DOM extracted from aquatic matrix for the sorption experiment to obtain unbiased results. Notably, in the aquatic environment, there would be a synergistic degradation of the microcontaminants by light, microorganisms, inorganic metals, oxides, enzymes and DOM. Most of previous work dealt with only one factor, and the latest research began to investigate the combined effects of photolysis and biodegradation, and/or with enzymatic catalysis, while the joint effects of multiple factors and their interplay remain to be further addressed. Roles of DOM as redox mediators need to be exploited more. Finally, the DOM-estrogen interactions investigated in this work could be extrapolated to nano-size materials such as engineered nanomaterials, organic

and inorganic in the 1–100 nm size range, a scope deserving future research attention.

Acronyms

AE	acceleration efficiency
CFUF	cross-flow ultrafiltration
COC	colloidal organic carbon
COM	colloidal organic matter
DOC	dissolved organic carbon
DOM	dissolved organic matter
E1	estrone
E2	17 β -estradiol
E3	estriol
EDCs	endocrine disrupting compounds
EE2	17 α -ethynylestradiol
EEFs	estradiol equivalent factors
FQ	fluorescence quenching
HA	humic acid
HRP	horseradish peroxidase
HS	humic substances
NMR	nuclear magnetic resonance spectroscopy
PAHs	polycyclic aromatic hydrocarbons
PCBs	polychlorinated biphenyls
PPCPs	pharmaceuticals and personal care products
ROS	reactive oxygen species
SPM	suspended particulate matter
SPME	solid-phase microextraction
WWTPs	wastewater treatment plants
YES	yeast estrogen screen

Acknowledgement

This work was supported by the United States Department of Agriculture (USDA) under Project No: 2036-12130-011-00D.

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