Environmentally persistent free radicals: Occurrence, formation mechanisms and implications☆

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ABSTRACT

Environmentally persistent free radicals (EPFRs) are defined as organic free radicals stabilized on or inside particles. They are persistent because of the protection by the particles and show significant toxicity to organisms. Increasing research interests have been attracted to study the potential environmental implications of EPFRs. Because of their different physical forms from conventional contaminants, it is not applicable to use the commonly used technique and strategy to predict and assess the behavior and risks of EPFRs. Current studies on EPFRs are scattered and not systematic enough to draw clear conclusions. Therefore, this review is organized to critically discuss the current research progress on EPFRs, highlighting their occurrence and transport, generation mechanisms, as well as their environmental implications (including both toxicity and reactivity). EPFR formation and stabilization as affected by the precursors and environmental factors are useful breakthrough to understand their formation mechanisms. To better understand the major differences between EPFRs and common contaminants, we identified the unique processes and/or mechanisms related to EPFRs. The knowledge gaps will be also addressed to highlight the future research while summarizing the research progress. Quantitative analysis of the interactions between organic contaminants and EPFRs will greatly improve the predictive accuracy of the multimedia environmental fate models. In addition, the health risks will be better evaluated when considering the toxicity contributed by EFPRs.

1. Introduction

A free radical is a kind of atom or molecule that contains at least one unpaired electron. Because of this unpaired electron, a free radical is highly reactive. For instance, the OH radical ($\cdot$OH) is one of the most active species ever found. It can oxidize almost all types of organic compounds quickly and effectively. The generation of free radicals is often the key process controlling chemical reactions (Castranova, 2004). In living organisms, free radicals are involved in immunity, killing bacteria and viruses. However, free radicals generated from external sources (such as smoking or pollutants), or misfunctioning of catalase in eliminating excessive free radicals may easily cause oxidative stress and cell damage (Balakrishna et al., 2009). Therefore, knowledge of the generation and activity

of free radicals is fundamental in understanding all the biological, physiological and chemical processes. However, the small molecular free radicals have lifetimes typically about several picosecond ($\cdot$OH has a lifetime of ~10^{-9} s), and thus no technique is currently available to detect free radicals in situ. Investigators have used chemical reagents to trap specific free radicals, or quantum chemistry calculations to reveal the role of free radicals.

Ingram and coworkers initially discovered a paramagnetic resonance absorption of high intensity and narrow width in charcoals, coal, and carbonized coal samples (Ingram et al., 1954). Although the following studies reported stabilized or persistent free radicals during the reactions between organic chemicals (Heimer, 1977) and the nitrogen-centered free radicals (Miura et al., 1985), no systematic work was conducted to focus on the environmental roles of these long-lasting free radicals. Since the proposed term of environmentally persistent free radicals (EPFRs) in 2007 by Dellinger and coworkers (Dellinger et al., 2007), the toxicity as well as environmental implications of EPFRs have attracted a great deal of research attention (Fig. 1). This review thus

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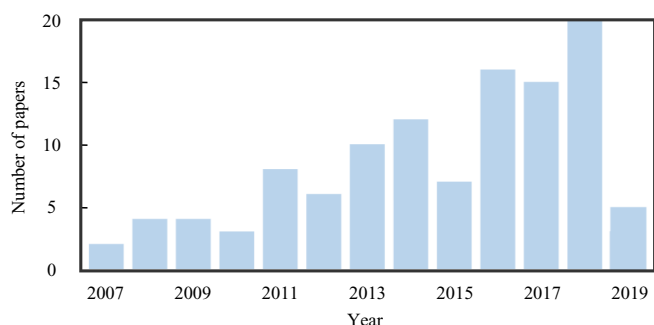
Fig. 1. Number of papers indexed by Web of Science with the key word of "environmentally persistent free radicals". Altogether, 117 papers are summarized up to date of February 7, 2019.

mostly focuses on the research closely related to EPFRs. In the past decade, investigators have reported that EPFRs could be stabilized on/in solid particles, and last for hours (Lomnicki et al., 2008), days (Li et al., 2014), or even months (Liao et al., 2014). Generally, these EPFRs are associated with solid particles, and surely will behave differently from the generally studied reactive species, such as reactive oxygen species (ROS) (Khachatryan and Dellinger, 2011). Also, EPFRs are different from common contaminants, such as polyaromatic hydrocarbons, for which Henry's law and sorption theories apply when modeling their environmental fate. The concepts of multimedia behavior and toxicity evaluation for these common contaminants could not be simply applied for EPFRs, again because of their association with solid particles (Chen et al., 2018a; Chen et al., 2018b). Considering their high reactivity (Yang et al., 2016), significantly higher toxic impacts than common contaminants (Liu et al., 2018), and wide occurrence in the environment (dela Cruz et al., 2011a), it is important to systematically explore the geochemical behavior as well as the risk assessment of EPFRs. However, research in this area is rare and discrete, even with some puzzling and opposite explanations and concepts. A review is thus urgently needed to summarize the current understanding and knowledge on EPFRs and more importantly, provide guidance to the future research.

Recently, Qin et al. (2018) reviewed the roles of EPFRs in carbon-based materials for eliminating organic contaminants. They mainly focused on the potential application of EPFRs in wastewater treatment. Environmental implication was not discussed. Vejerano et al. (2018) summarized the potential of EPFR formation on the surfaces of engineered nanomaterials (ENMs), again without any focus on the environmental processes. Different from these reviews, this current one intended to critically discuss the current research progress on EPFRs, specifically on their occurrence, generation mechanisms and environmental implications (including both application and toxicity).

2. Occurrence and transport of EPFRs in the environment

The stabilized free radicals were initially reported in coal (Ingram et al., 1954 Green et al., 2012; Liu et al., 2014; Petrakis and Grandy, 1978) and humic substances (Jezierski et al., 2000; Polak et al., 2005). The appreciable concentration of stable free radicals existed in coal were presumably formed in the "coalification" process, and altered greatly during its weathering after excavation (Green et al., 2012). These studies primarily examined the health risks of the stabilized free radicals in combination with the generated reactive oxygen species (Dalal et al., 1995) and the coexisted organic chemicals (Schulz, 1997) to coal workers. However, it should be noted that EPFRs in coals may be disturbed and mixed with dust during mining and transport, and thus have wider health impacts. The fly ashes produced from coal combustion also contain EPFRs signals (Tian et al., 2009). According to Wang et al. (2018), the g factors and band widths were different between coal and soot collected from the outlet of a chimney. In addition, PAH fingerprints were different in fly ash or soot compared to those in coal, suggesting PAH volatilization and degradation were involved in coal combustion. Therefore, abundant EPFRs were generated during coal combustion. Most of the original EPFRs in coal may not survive through combustion.

The literature has reported that the organic free radical concentrations in soil humic substances ranged from 0.3×10^{16} to 2.4×10^{18} unpaired spins per gram. The g-values of these free radicals were in the range of 2.0028–2.0047, corresponding to oxygen-centered radical species such as semiquinones and methoxybenzenes (Martin-Neto et al., 1998; Rivero et al., 1998; Watanabe et al., 2005). These free radicals were formed during and increased with humification (Watanabe et al., 2005; Yabuta et al., 2008) or the interactions between humic substances and the mineral particles (Saab and Martin-Neto, 2004). Previous study has demonstrated that the free radicals in humic substance are stabilized by aromatic ring systems because the free electrons can be partially delocalized (Senesi, 1990). The electron-conjugated systems are more developed in the humic substances with higher aromatic C content, which facilitates the stabilization of free radicals (Watanabe et al., 2005).

Investigators also detected electron paramagnetic resonance (EPR) signals in the humic substances extracted from waters (Chen et al., 2002; Paul et al., 2006). With the light irradiation, the concentrations of free radicals were further increased (Paul et al., 2006). Hence, the free radical-related structures may be protected in the macromolecular structures or aggregated form of humic substances even in their dissolved form. EPFRs from humic substances may be transported with suspended particles or even with water. However, how these free radicals were stabilized in relation to the 3-D structural characteristics of humic substances? Will these free radical-related structures be preferentially adsorbed by a certain type of particles? Would the persistence or activity change during their transport? These questions still remain unanswered.

In the past decade, investigators highlighted similar long-lasting free radicals being related with anthropogenic sources. Dellinger and coworkers (Dellinger et al., 2007) suggested that EPFRs are formed in the post-flame cool zone of the combustion during garbage incineration. Briefly, an electron was transferred from a degrading chemical to a transition metal, and the complexes formed between free radicals and reduced transition metal made the free radicals stable. These EPFRs have characteristics similar to semiquinone radicals and can make their way to airborne particulate matter (Gehling et al., 2014; Valavanidis et al., 2010; Yang et al., 2017c) and soils (dela Cruz et al., 2014; dela Cruz et al., 2011b).

Research data also suggested that EPFRs could form at ambient conditions. For instance, Li et al. found that catechol could form EPFRs on hematite under UV irradiation (Li et al., 2014) or even in dark (Li et al., 2016). Phenol (Nwosu et al., 2016a) and PAH (Jia et al., 2016; Jia et al., 2018) could form EPFRs in iron(III)-exchanged smectite clay under ambient conditions. These processes may occur in the environmental matrices such as soil and suspended particles, and thus the generated EPFRs may be involved in many environmental processes.

EPFRs originated from engineering sources also attracted wide research attention. Very strong EPFR signals were detected in biochars (Liao et al., 2014; Fang et al., 2014) and tar balls (Kiruri et al., 2013). For example, EPFR concentrations in biochars were generally around 10^{18} unpaired spins per gram (Fang et al., 2015; Liao et al., 2014). During their production and massive application, these

EPFRs will be widely involved in environmental processes.

It should be noted that the detected free radicals signal in different environmental matrices or EPFRs of different sources may mix together (Fig. 2). For example, the EPFRs in soil may contain an exogenous portion from atmospheric particulates, which deposited into soil via atmospheric dust fall. At the same time, the EPFRs originally generated in soil may be blown by wind, contributing to atmospheric particulates. Identifying the sources and transport routes are an important research area for the environmental behavior of EPFRs. Some preliminary work was conducted in this line of research. For example, dela Cruz et al. (2011b) observed that the EPFR concentration in contaminated soils at superfund sites in Georgia, USA were around 20.2×10^{17} unpaired spins per gram, which was about 30 folds higher than those in non-contaminated soils. This result suggested that over 90% of the EPFR signals in the contaminated soils were originated from the interactions between the contaminant (pentachlorophenol) and soil mineral particles. Although the analysis may be affected by the heterogeneous properties of soil samples, this is the first research that intended to identify the sources of EPFRs. Wang et al. (2018) compared the EPR signal properties in environmental samples and lab simulated PAH degraded products, and concluded that the EPFR signals in soot and total suspended particulate most likely originated from coal combustion, not coal itself. Clearly, it is extremely challenging to identify the sources of EPFRs. Currently, limited studies only used g values and band width to recognize the type of free radicals (oxygen- or carbon-centered). Techniques are demanded to quantify the contribution of or simply identify EPFRs from different sources, which is essential for the geochemical behavior prediction and risk assessment of EPFRs.

3. Mechanisms of EPFR formation

The breaking of covalent bond is crucial for forming free radicals. To break a covalent bond in organic compounds, a certain amount of energy is required in the form of heat, light, electric or chemical energy. Up to now, two types of EPFRs were discussed in the literature. One is transition metal-mediated EPFRs. Another type may not be dependent on transition metals, but is inside organic matrices, such as the ones formed during biomass pyrolysis

or humification. These two types of EPFRs will be discussed in detail in the following contexts. In addition, EPFR precursors and the environmental factors to control EPFR formation will also be presented to further illustrate EPFR formation mechanisms.

3.1. EPFR formation mediated by transition metals

Transition metals have been demonstrated to be a key component enabling the formation of EPFRs according to various laboratory studies (Lomnicki et al., 2008; Vejerano et al., 2012b). EPFRs generated as the byproducts of substituted benzene degradation, may interact with transition metals at $150\,°C–400\,°C$ through electron transfer (Lomnicki et al., 2008). EPFRs were compared among different transition metal oxides, such as ZnO, NiO, CuO, Fe_2O_3, and TiO_2, as listed in Table 1 for their lifetimes and EPFR concentrations (Patterson et al., 2013; Vejerano et al., 2012a; Vejerano et al., 2012b). For example, the half-lives of EPFRs formed on ZnO were relatively long, lasting for days (Vejerano et al., 2012a) or even months, which have significant health concern if they are ambient air particles. Generally, the half-life of EPFRs was found to positively correlate with the standard reduction potential of the associated metals (Vejerano et al., 2012a). Previous researchers also compared the tendency of EPFR formation on different types of metals oxides, and proposed that the catalytic ability of the metal oxides to promote EPFR formation were in accordance with the oxidizing strengths of the metal cations (Yang et al., 2017b) or redox potentials of the metal ions (Jia et al., 2018). However, other particle characteristics, such as their particulate sizes, shapes, and surface areas were not controlled. Yang et al. (2017c) reported that the airborne particulate matter with aerodynamic diameters lower than 1 μm possessed the highest levels of EPFRs, but they did not analyze their chemical compositions and properties of different sized particles as discussed in the aforementioned studies. More work systematically considering these particle properties is needed.

It should also be noted that the-above mentioned investigations were carried out in extreme conditions with high temperatures. Theoretically, the formation of EPFRs is possible in the ambient environment as long as free radicals are generated during organic chemical decomposition. Li et al. (2014) observed EPFRs on
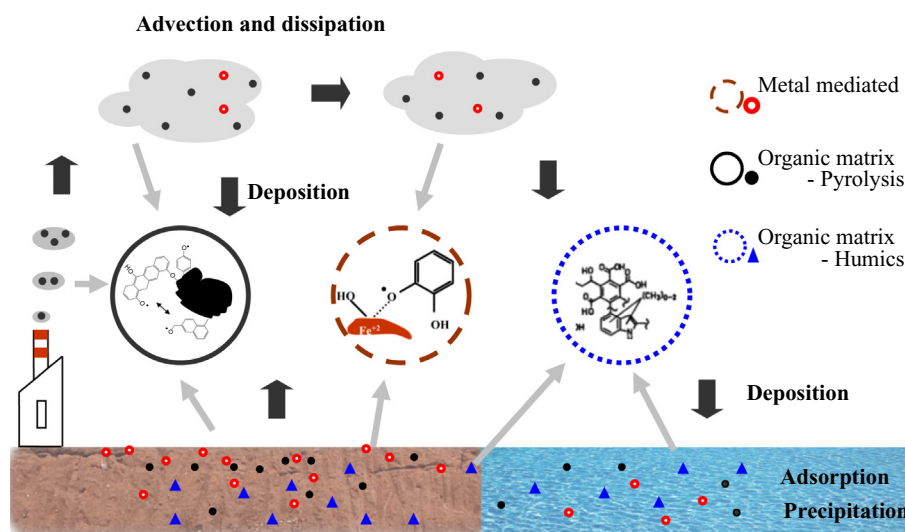
Fig. 2. The formation and multimedia transfer of environmentally persistent free radicals (EPFRs). Three types of EPFRs are summarized, namely, EPFRs mediated by transition metals (⊙) or inside organic matrix (including both pyrolyzed particles (●) and humic substances(▲)). EPFRs may be generated during pyrolysis of biomass, the interactions between organic contaminants and mineral particles, or inside humic substances. Different processes need to be considered when describing the environmental fate of EPFRs, such as advection, deposition, adsorption and precipitation.

Table 1
The EPFRs generated on different transition metal surfaces.

Particles	g Value	Conditions	Stability	Reference
α-Fe$_2$O$_3$/SiO$_2$	2.0043—2.0046	UV irradiation		Li et al., (2014)
NiO/SiO$_2$	2.0029—2.0044	423 K - 673 K	1.5—5.2 days (half-lives)	Vejerano et al. (2012b)
ZnO/SiO$_2$	~2.003—2.004	503 K	› 73 days	Vejerano et al. (2012a)
Fe$_2$O$_3$/SiO$_2$	2.0024—2.0040	423 K - 673 K	24—111 h (half-lives)	Vejerano et al., (2011)
	2.0050—2.0065			
CuO/SiO$_2$	2.0013—2.0070	423 K - 673 K	27—74 min	Lomnicki et al., (2008)
CuO/MMT	2.0034	505 K	~20 h	Nwosu et al. (2016b)
γ-Al$_2$O$_3$	2.0043	505 K	57.4 days (half-lives)	Patterson et al., (2013)
TiO$_2$	2.0032	505 K	4.3 days (half-lives)	Patterson et al., (2013)

hematite-silica surface during catechol degradation under ambient conditions with UV-light irradiation and in dark. This research provided an important insight that the formation of EPFRs may be ubiquitous in the environment because of the abundance of transition metals. Jia et al. (2015) later reported that EPFRs were formed during degradation of PAHs through photolysis or chemical oxidation on clay minerals under natural conditions.

Based on the above studies, EPFR formation mediated by transition metals generally has the following three steps involving a one-electron reduction (Fig. 3). The first step is the physical sorption of an aromatic molecule or its degradation intermediate product onto the transition metal oxides or transition metal ions. For hydrophilic compounds, the hydroxyl and/or chlorine substituents interact with the surface hydroxyl of the transition metal

oxide surface. For some apolar aromatic compounds, such as PAHs, adsorption with metal ions-modified minerals is accompanied by cation-π interaction at the active sites (Jia et al., 2018). The second step involves the chemisorption of the precursor molecule or its degradation byproducts via the formation of a chemical bond and elimination of water, hydrogen chloride or both. Fourier transform infrared study validated the second step as the OH stretching frequency at $3600 \, cm^{-1}$ disappears when the substituted benzene chemically binds on the surface (Alderman et al., 2005). These chemisorption and radical formation were also confirmed with the aid of the vibrational electron energy loss spectroscopy (EELS) measurements of phenol on Al$_2$O$_3$ (Patterson et al., 2013).

The third step involves electron transfer between the organic compounds and transition metals. This unique electron-sharing
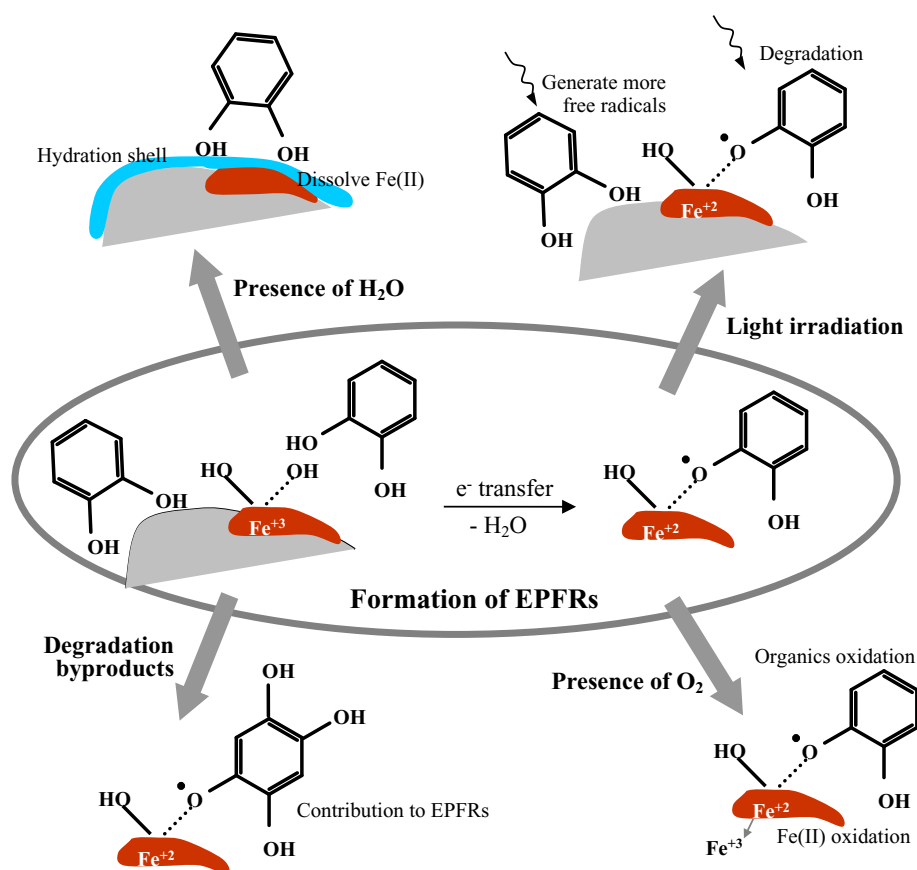
Fig. 3. Prevailing conceptual process for EPFR formation on transition metals. Fe is illustrated here to represent transition metals. The impacts of O$_2$, H$_2$O, light irradiation, as well as the presence of degradation byproducts are highlighted. O$_2$ may oxidize Fe(II) or directly react with EPFRs. H$_2$O could form a surface hydration shell on particle surface, compete with organic chemicals for the active sites, or dissolve the reduced transition metals. These processes may decrease the persistence of EPFRs. Light irradiation promotes the degradation of organic chemicals and thus the generation of organic byproducts, including organic free radicals, which may contribute to the additional EPFR signals. On the other hand, direct light irradiation on EPFRs may facilitate their decay.

system in resonance with the delocalization effect by the π orbits in the aromatic ring enabled a rather stable structure. Clearly, this electron transfer between the organic compound and transition metal is a key step in forming EPFRs. However, the detailed mechanism is still unclear, and the discussions on the electron transfer are even controversial in the literature. Most time, transition metals act as electron-accepting sites and the negative charge transfers from the electron-rich oxygen atom to the metal cations, which results in the oxidation of the chemicals and the formation of intermediate or free radicals (Patterson et al., 2015). The reduction of transition metals during the formation of EPFRs was evidenced using X-ray absorption near-edge structure (XANES) spectroscopy (Nwosu et al., 2016a), XPS (Deng et al., 2018), density functional theory (DFT) calculation (Assaf et al., 2017) or the trapping-detection of the reduced metals (Li et al., 2014). However, in a study of single crystal ZnO (1010, 0001) and phenol, the formation of EPFRs was accompanied by the electron transfer from the ZnO surface toward phenol, as directly evidenced by ultraviolet photoelectron spectroscopy (UPS) (Thibodeaux et al., 2015). This electron donating ability was attributed to the band bending of ZnO which depends on its intrinsic semiconductor property (Thibodeaux et al., 2015). The negative charge seems more easily moving from the ZnO surface by upward (toward the Fermi level) band bending to the closest energy levels of the orbits of an acceptor molecule (Patterson et al., 2017; Thibodeaux et al., 2015; Zhang and Yates, 2012). No conclusion has been reached on which type of metals accepts electron, which donates electron. Thus, more types of particles with semiconducting properties should be included to evaluate the formation EPFRs. Fig. 3 presents only a prevailing conceptual process for EPFR formation, which may neither be generally applied to all the transition metals, nor transition metals only. Besides the electron transfer properties of the particles, some other properties in relation to their redox-activities, such as vacancies, defects, and photogenerated charges, should also be systematically evaluated for their roles in the formation and stabilization of EPFRs.

3.2. EPFR formation inside the matrix of organic moieties

EPFRs have been reported in large organic moieties, such as coal (Tian et al., 2009) and humic substances (HS) (Pandey et al., 1999) as discussed in Section 2. Recently, researchers noticed the generation of EPFRs during the production of engineered carbon-based materials, mainly biochars (Qin et al., 2018). Anthropogenic carbons involved with high-temperature treatment (higher than 700 °C) generally do not possess significant amount of EPFRs. Different from EPFRs discussed in the previous section, EPFRs formed inside the matrix of organic moieties are not related to transition metals. Liao et al. (2014) prepared biochars from biopolymers without any transition metals, and detected EPR signals comparable to those in biochars produced from common biomass. Chen et al. (2018a) referred the EPFRs signals in PM 2.5 to the solvent-resistant organic matter (88%), which likely consisted of graphene oxide analogues. They observed that EPFR concentration was significantly and positively correlated with the elemental carbon content, but poorly correlated with the contents of the 24 metal elements (Chen et al., 2018a). Thus, EPFRs generated inside the matrices of organic moieties is highly dependent on the organic structure.

The generation of EPFRs in the thermally treated particles is relatively complicated and the breaking of chemical bonds in the precursors during pyrolysis is the primary reason. Previous studies have suggested the processes of EPFR generation during the pyrolysis of feedstocks (Liao et al., 2014). At the initial pyrolysis stage, the cleavage of some weak linkage bonds resulted in the formation of free radicals in biochar, such as the homolytic cleavage of the α- and β-alkylaryl ether bonds, C-C and C-O linkage. The outer-surface free radicals would rapidly react and dissipate, resulting in the decrease of EPR signals. The free radical concentrations then increased with the extended pyrolysis, resulted in the accumulation of a large quantity of free radicals on the surface. The authors also pointed out a special free radical formation process during the cooling stage (Liao et al., 2014). Briefly, the EPR signals increased dramatically during the cooling process. The shrinkage of macro-molecule structures at different directions during the cooling of biochars resulted in the cleavage of chemical bonds and thus the formation of additional free radicals. The free radicals formed in the matrix of the produced biochars are probably protected from reacting with each other or other chemicals, and thus stabilized.

Biochars produced from different types of feedstocks showed EPR signals with various g-factors and intensities at the same pyrolysis conditions (Liao et al., 2014; Fang et al., 2017). A certain chemical composition in the feedstock has its specific decomposition temperature and consequently the energy needed for bond rupture. For example, the EPFR intensity in a biochar produced from lignin was 5 times higher than that from cellulose (Fig. 4). However, how are the EPFR intensities related to the pyrolysis temperature and chemical compositions (such as lignin and cellulose) in the feedstock? How does the organization of chemical compositions in the feedstock control the 3-dimensional structure of the formed carbonaceous particles, and thus the formation of EPFRs? How would the precursors of coal and HS determine their EPFR characteristics? These questions remain unanswered.

3.3. Precursors for EPFR formation

Molecules that can form EPFRs through thermal cracking or electron transfer are known as free radical precursors. Dated back to the 1950's, investigators suggested that the long-lived carbon-centered radicals in solid matrices were associated with delocalized electrons in a polyaromatic organic polymer (g ~2.002–2.003) (Ingram et al., 1954; Lyons et al., 1958). Recent studies also emphasized EPFRs formation from aromatic structures including benzene (D'Arienzo et al., 2017) and polycyclic aromatic hydrocarbons (PAHs) (Wang et al., 2018; Jia et al., 2018). Based on DFT calculations, the benzene ring structure could donate electrons to transition metals (D'Arienzo et al., 2017), which facilitated the formation of carbon-centered EPFRs. At the same time, PAHs may be firstly oxidized to phenols or quinones, resulting in the formation of semiquinone-type EPFRs or phenoxyl radical species, as supported in part by the g-factors of the EPFRs (Wang et al., 2018).

Some functional groups associated with the benzene ring are beneficial to the formation of EPFRs. The hydrogen atoms on benzene are less likely to react with transition metals, because such a reaction will perturb and diminish the aromatic structure of the benzene. However, the hydroxyl and chlorine functional groups substituted on phenol can form a chemisorbed species on solid surface by eliminating H_2O and/or HCl, which is essential for the formation of EPFRs. Thus, to facilitate EPFR formation, the aromatic precursor requires an easily donatable proton, such as those in phenol (Nwosu et al., 2016a), or contains an electronegative atom, such as chlorine (Patterson et al., 2017; Patterson et al., 2015; Thibodeaux et al., 2015).

The frequently reported precursor molecules of EPFRs include quinone, phenolics, chlorinated/hydroxylated benzenes, as well as PAHs. A general relationship between the properties of precursors and EPFRs will greatly facilitate the prediction of EPFR occurrence and thus their behavior in the environment. Current studies often use g-factors to approximately classify EPFRs as oxygen-centered or carbon-centered. It is commonly proposed the coexistence of
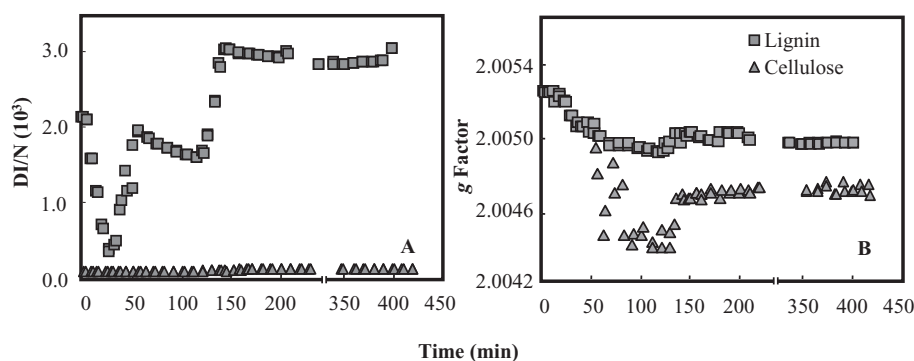
Fig. 4. An in situ observation of EPR signal intensity (A) and *g* factor (B) during biochar production when using lignin and cellulose at 200 °C under N₂ protection. The grey area indicates the charring process and the white background is the cooling process. EPR signal intensity was calculated by dividing the double-integrated (DI) intensity of the EPR spectrum with the normalization constant N (Liao et al., 2014). EPR signals showed obvious difference from different feedstocks, indicating the importance of knowing the chemical structures of the precursor when evaluating EPFR properties. Reprinted with permission from American Chemical Society (2018).

various free radicals (Vejerano et al., 2012b) and supported only by mathematical peak differentiating and deconvolution. No practical in situ measurement is available to examine the types and structures of the stabilized free radicals, let alone to predict EPFR properties based on the structure of the precursors. Accurate discrimination of the type and structure of EPFRs needs well-designed and subtle experiments, such as EPR signal superfine splitting or even super hyperfine splitting observed in liquid nitrogen, and stable isotope labeling in combination with DFT calculations.

Besides the apparent generation of EPFRs, their characteristics, such as the life times and activities, in relation to the properties of precursors deserve more detailed study. Song et al. (2008) studied biphenyls with different chlorine atom numbers, and found that the increase in the number of chlorine atoms in polychlorinated biphenyls can improve the stability and persistence of the corresponding semiquinone free radicals. Currently, literature information is too limited to have meaningful discussions on this research topic.

3.4. The environmental factors controlling EPFR formation and stability

Although the EPFRs exhibit relatively long-lasting stability, its resonance structure and lifetime are affected by external factors, such as temperature, humidity, presence of oxygen, pH, and light irradiation. Oxygen content was reported to be a very influential parameter to control EPFR formation and stability. For example, the EPFR lifetimes were 151.8 days (with 72 h of radical generation) under vacuum compared to 12.4 days (with 48 h of radical growth) in air (Nwosu et al., 2016a). Oxygen may directly react with some less persistent EPFRs formed on particle surface, such as cyclopentadienyl radical (Vejerano et al., 2011), or oxidize the reduced transition metals (Li et al., 2016). Investigators also compared the apparent characteristics of EPFRs, such as g-factors and band width, as affected by oxygen. However, the results were not consistent. For example, some investigators proposed that oxygen diminished the oxygen centered EPFRs and thus carbon-centered EPFRs were enriched, which resulted in the decreased g-factors and signal width (ΔH_{p-p}) (Jia et al., 2017; Nwosu et al., 2016a). However, it is noted that carbon-centered free radicals are generally more reactive than oxygen-centered ones (Dellinger et al., 2007). The presence of oxygen may preferentially react with carbon-center EPFRs, resulting in increased g-factors (Li et al., 2016). Depending on the specific chemical structures and locations of EPFRs, the above two reactions may occur simultaneously. Again, the current

experimental results are not abundant enough to draw any clear conclusion.

Water content, measured as humidity in most conditions, is another determining environmental factor controlling EPFR formation. A generally reported phenomenon is that EPFR concentrations decreased in the presence of water. For example, EPFR decay at humidity of 75% was 5 times faster than that in humidity of 22–38%, and was 71 times faster than that in vacuum (Nwosu et al., 2016a). The aging of soil samples under relatively dry conditions (humidity of ~7%) showed rather stable EPFR signals in two months (Jia et al., 2017). When humidity increase to ~100%, the spin densities of the soil samples exhibit a "fast" decay when the peak area decreased by more than 95% within 7.5 days (Jia et al., 2017). Several explanations are provided: (1) It is well-know that metal oxides are easily surface hydrated in the presence of water molecules (Tamamura et al., 2006), which will decrease the direct interactions between organic chemicals and the particle surface, and consequently decrease the generation of EPFRs or eliminate already existing EPFRs. (2) The presence of water on the particle surface may result in competition with the chemicals, such as competing with arene for the Lewis acid site (Jia et al., 2016). (3) The reduced transition metal is unstable or dissolvable in water, which breaks the electron sharing system (Li et al., 2016).

Light irradiation is a universal energy source for the degradation of organic chemicals. On one hand, light provides energy for the production of EPFRs (Jia et al., 2019). This is because the degradation byproducts, organic free radicals, were widely generated, which enhanced the possibilities of electron transfer with transition metals. On the other hand, direct light irradiation on EPFRs may facilitate their decay. It is shown that under light irradiation, transition metals may promote the generation of ROS, such as ·OH and $\cdot O^{2-}$ (Jia et al., 2019), which facilitated the transformation from radical cations to oxygenic EPFRs. Therefore, special research efforts should be put on photosensitive organic compounds and particles with semiconductor properties.

Humic substances (HS) are ubiquitous in the environment, and it is likely that HS coexist with transition metals and organic contaminants. It has been well documented that HS have electron shuttle properties and promote the electron transfer between chemicals and organisms (Stern et al., 2018). Nwosu et al. (2016b) established a model system to simulate HS-coated clays. They used poly-p-phenylene to modify copper-loaded montmorillonite, and observed a unique two-step decay pattern for the simulated soil system. The authors attributed the slow decay of EPFRs to possible electron shuttling between the dosed chemical, phenol, and the poly-p-phenylene polymer chain. It is therefore easy to

speculate that HS-mediated electron transfer between chemicals and transition metals is ubiquitous in the environment. In other words, a metal atom does not need to be in direct contact with an organic pollutant to have an electron sharing system. After covered by HS, the transition metals may have a better chance to interact with organic contaminants because of sorption by HS.

4. Toxicity of EPFRs

As summarized in Table 2, EPFRs stabilized by transition metals exhibited significant cellular oxidative stress and cytotoxicity to human bronchial epithelial cells, which decreased the cellular antioxidants and then resulted in cell death (Balakrishna et al., 2009). Exposure of EPFRs associated PM to neonatal rats has been shown to cause cardiac and pulmonary diseases, such as decreased cardiac function, increased pulmonary artery pressure and airway hyper-responsiveness in lungs (Balakrishna et al., 2011; Lord et al., 2011; Mahne et al., 2012). EPFRs containing PM could also enhance severity of influenza virus infection and inhibit the activity and metabolism by cytochrome P450 purified from the livers of rabbits and rats (Lee et al., 2014; Reed et al., 2014; Reed et al., 2015a, b). Saravia et al. (2013) reviewed that the particulate matter containing EPFRs exhibited adverse effects to infant respiratory health.

EPFRs in organic matrices also showed significant toxic impacts (Fig. 5). Studies have investigated that the stable free radicals present in coal may be possibly related to coal workers' pneumoconiosis (CWP) (Dalal et al., 1991; Dalal et al., 1995; Dalal et al., 1989b; Huang et al., 1999). The EPFRs in biochar could trigger neurotoxicity in *Caenorhabditis elegans*, indicating that EPFRs in biochars may be neurotoxins to soil organisms (Lieke et al., 2018). EPFRs showed toxicity not only to animals, but also to plants. Significant toxicity of EPFRs in biochars to crops was observed, such as inhibition of germination, retardation of root and shoot growth and plasma membrane damage (Liao et al., 2014).

It is easy to understand that the generation mechanisms of the above two types of EPFRs were different, and thus most likely, the location of EPFRs were different. For example, the transition metal stabilized EPFRs are mostly on particle surface, while EPFRs in organic matrices may be distributed inside the 3-D structure of the
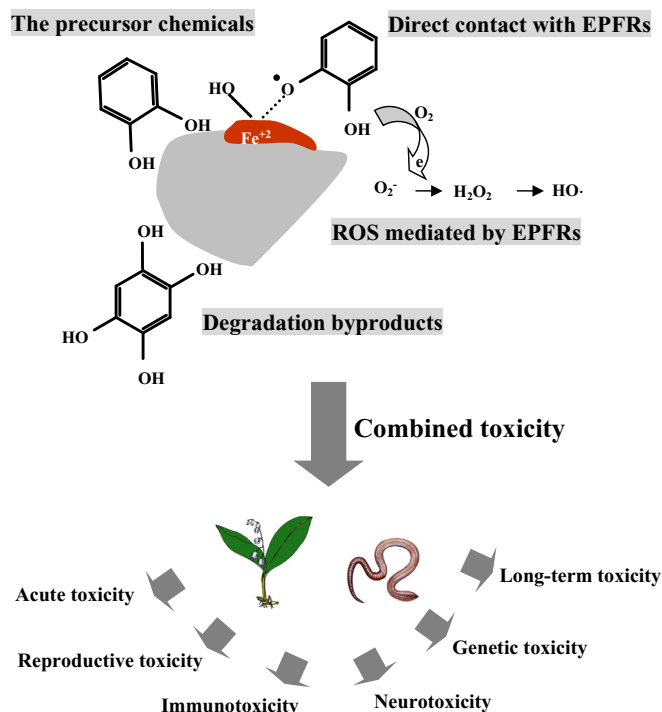

Fig. 5. The toxicity of EPFR-laden particles to organisms. The particles may have combined toxicity to organisms originated from the direct contact with EPFRs, ROS mediated by EPFRs, the precursor chemicals as well as the degradation byproducts.

organic matrices. It is still unclear how these differences related to their toxicity. Early studies showed that ROS generated by EPFRs were the key process for their toxicity (Dellinger et al., 2000; Dellinger et al., 2001; Kelley et al., 2013; Valavanidis et al., 2005; Valavanidis et al., 2011). Various ROS species including hydroxyl radical ($\bullet$OH), superoxide anion radical ($O_2\bullet^-$), and hydrogen peroxide (H_2O_2) were detected in EPFR systems (Khachatryan and Dellinger, 2011; Khachatryan et al., 2014; Khachatryan et al., 2011).

If ROS is the major mechanism for EPFR toxicity, one may easily

Table 2
Evidence of toxic impacts posed by EPFRs.

Type	Particle name	Toxic effects	Reference
Organic chemicals degradation	MCP230	Enhance cellular oxidative stress and cytotoxicity	Balakrishna et al., (2009)
	DCB230	Increase proteins associated with steroid-resistant asthma	Lomnicki et al., (2010)
	DCB230	Decrease cardiac function	Lord et al., (2011)
	DCB230	Caused apoptosis in HL-1 cardiomyocytes	Chuang et al., (2017)
	DCB230	Caused the phenotypic switching of macrophages	Raman et al., (2011)
	DCB230	Induce airway hyperresponsiveness in neonatal rat lungs	Balakrishna et al., (2011)
	MCP230	Activate dendritic cells and enhance Th17 inflammation	Wang et al., (2011)
	MCP230	Enhance pulmonary Th17 inflammation	Jaligama et al., (2018)
	DCB230	Initiate epithelial-to-mesenchymal transitions in airway epithelial cells	Thevenot et al., (2013)
	DCB230	Decrease cardiac function and increase pulmonary artery pressure	Mahne et al., (2012)
	DCB230	Enhance severity of influenza virus infection	Lee et al., (2014)
	MCP230 and DCB230	Inhibit cytochrome P450 activity	Reed et al., (2014)
	MCP230	Inhibit cytochrome P450 2B4 activity	Reed et al. (2015b)
	MCP230	Inhibit metabolism by cytochrome P450 1A2	Reed et al. (2015a)
Pyrolytic carbon-based material	Biochar	Inhibit germination, retardate root and shoot growth and plasma membrane damage	Liao et al. (2014)
	Biochar	Trigger neurotoxicity in caenorhabditis elegans	Lieke et al. (2018)
Nature substance	Coal dust	Caused pneumoconiosis, progressive massive fibrosis, chronic bronchitis, lung function loss and emphysema.	Schins and Borm, (1999)
	Fresh coal mine dust	Caused pulmonary injury	Dalal et al. (1989a)
	Coal fly ashes	Caused DNA damage in rat lung epithelial cells	van Maanen et al., (1999)

[a]: MCP230 and DCB230 are EPFRs contained particles generated through exposure of silica containing copper oxide to 2-monochlorophenol (MCP230) and 1,2-dichlorobenzene (DCB230) at $\geq 230\,°C$.

measure ROS in EPFRs-driven systems and predict their negative impacts. However, it is not always the case. The generated ROS, such hydroxyl radicals, may remain associated with the surface of the particles (Khachatryan and Dellinger, 2011). In addition, the major activity of EPFRs was not passivated in the presence of excessive ROS scavengers (Yang et al., 2016), suggesting the activity of the particles themselves.

To make the situation more complicated, the coexistence of the parent chemicals (in the system of EPFRs stabilized by transition metals) and the generated byproducts may have combined toxic impacts to organisms. For example, the residual chemicals of 2-monochlorophenol or dicholorobenzene on the particles may have some interfering toxicity as summarized in Table 2. A previous study used MCP50 (heated at 50 °C without detectable EPFRs) as a reference to exclude the negative impacts from the original chemicals (Reed et al., 2015a). Clearly, MCP concentrations in this reference system were different from those in the 230 °C reaction systems. In addition, some toxic products such as dioxins and furans may be generated during the formation of EPFRs (Nganai et al., 2010; Potter et al., 2016). Reference experiments thus should be carefully designed and carried out to identify and separate the toxicities from EPFRs and the coexistent chemicals.

Different from common pollutants, EPFRs are associated with solid particles, and they will not be taken into consideration if common solvent extraction or digestion was involved in the sample pretreatment. EPFRs were either not extractable (when they are inside the matrix of organic structures), or altered to other chemicals (Truong et al., 2010). Therefore, the traditional methods to assess the environmental risks of contaminants based on their concentrations are likely not appropriate for EPFRs. Currently how EPFR signal intensities relate to their activity is unclear. Because of the various types of free radicals and locations of EPFRs in the 3-dimensional particles, it may not be practical to quantitatively correlate EPR signal intensities to EPFR activities. Thus, it is unknown if there is any indirect measurement to determine the activity or toxicity of EPFRs.

## 5. EPFRs-participated processes in organic contaminant fate

Because of their preserved activities, EPFRs may be involved in the reactions with different chemicals. For the parent chemicals that interact with transition metals, the generation of EPFRs may alter their degradation pathways, which consequently alters their environmental behavior. Most of the previous studies were focused on the generation mechanisms, detection and toxicity of EPFRs. Li et al. (2014) established a first experiment to investigate the impact of EPFR formation on the fate of a contaminant, catchol. They observed that when EPFRs were generated, catchol degradation was simultaneously decreased. Different degradation pathways were then proposed. Their follow-up study confirmed similar results in a dark reaction situation (Li et al., 2016). Jia et al. (2018) observed PAH decay on transition metal-loaded montmorillonite, but not on Na^+ saturated montmorillonite, inferring that the presence of transition metals practically increased PAH degradation. Although the authors did not focus on the impact of EPFR formation on PAH degradation pathways, they did propose that the hydroxylized PAHs interact with transition metals during the formation of EPFRs. It is reasonable to speculate that PAH degradation pathways are altered because of the formation of EPFRs, with extended life times for the hydroxylized PAHs. Because of the significant activities and thus toxic impacts of these hydroxylized PAHs, special efforts should be given to PAH degradation pathways as well as the life times of their degradation byproducts.

Because of the limited information, the chemical degradation as affected by EPFR formation is not included in organic pollutant multimedia environmental fate modeling. This probably is one of the missing puzzles in the whole picture. For this eventual purpose, more quantitative research is required. For example, how is the extent of the impact on degradation determined by the types and lattice structures of the transition metals? How is the EPFR signal intensity related to the extent of degradation inhibition? In addition, extended study is required to incorporate more experiments on the impacts of environmental chemistry conditions, such as the cation exchange capacity, organic content, pH, size or even shape of the particles.

For EPFRs in organic matrixes, the adsorbed organic chemicals may have interactions with EPFRs or their activated species. A significant degradation of these organic chemicals will be expected. Special efforts were devoted to confirm the degradation of organic chemicals, because of the possible low recoveries of the solvent extraction of the original chemicals from the carbonaceous particles. Combining both solvent extraction and degradation byproduct analysis, Yang et al. (2016) confirmed that p-nitrophenol (PNP) was degraded significantly in biochar sorption systems. Importantly, considering that NO_3^- is the typical degradation product of PNP, the authors used NO_3^- as a conservative parameter to estimate PNP degradation. Based on their calculation, the authors concluded that if the degradation was neglected, the sorption will be overestimated two times higher. Clearly, this process will play an important role in the environmental fate of organic contaminants, especially considering the massive production and application of biochars in the environment, particularly in soils.

The mechanisms with which organic contaminants degraded in biochar system are discussed in the following three aspects. The first and readily accepted mechanism is the ROS driven processes (Fig. 6). Most studies proposed that EPFR-containing carbonaceous particles mediate ROS generation, which is the primary driving force for organic chemicals degradation (Qin et al., 2018). With the light irradiation, biochar could generate much more ROS than in dark, leading to the enhanced degradation of sulfadimidine (Chen et al., 2017). Oxidation and thermal treatment of biochar combined with the characterization results demonstrated that the oxygen-containing group (especially for surface carboxyl group) on biochar were attributed to the enhanced generation of ROS with light irradiation. However the underlying mechanisms for photochemical activity of biochar were still unclear. This mechanism is quickly accepted by the investigators because the previous studies have widely shown the role of ROS in organic chemical degradation,
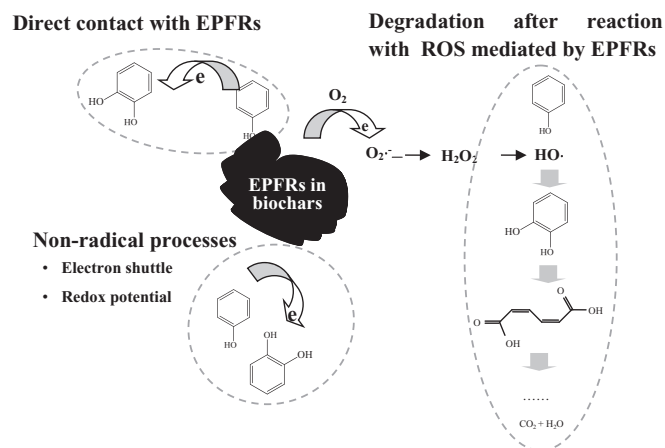
Fig. 6. The chemical reaction mechanisms of organic contaminants in biochar systems. Three major reaction mechanisms presented include direct contact with EPFRs, degradation by ROS mediated by EPFRs as well as none radical processes related with electron shuttle and redox potential of biochar particles.

such as in Fenton reaction and photodegradation systems.

However, researchers did not observe a quantitative or even a monotonous relationship between ROS generation and organic chemical degradation. Yang et al. (2016) detected HO· in the system, but most of the degradation of p-nitrophenol was not affected when the HO· was quenched by the overdosed scavenger. The authors observed that the slightly decreased degradation correlated to the slightly inhibited sorption. They thus proposed another mechanism to explain organic chemical degradation in biochar sorption system, i.e., the direct contact between EPFRs in the solid phase and organic contaminants.

After a careful examination of EPR signals before and after the degradation reaction, these EPR signals were hardly consumed after the reaction. They thus composed the third mechanism, non-radical reaction mechanism (Yang et al., 2017a). Because currently no relationship between the reactivity and EPR signal was proposed, the analysis of EPR signal intensities without referring to their free radical compositions may not provide solid evidence on the reactivity of free radicals. Nevertheless, the proposed non-radical reactions enlightened the investigators to examine biochar properties more extensively.

The above three mechanisms may occur simultaneously for the degradation of organic contaminants. Although the exact contribution of a certain mechanism is unknown yet, it can be speculated that their contributions vary with biochar properties, such as the aromaticity and the composition of functional groups. Focusing on the engineering application of biochars, it is proposed that the reactivity of carbonaceous materials (biochars) may be further strengthened when catalyzing the decomposition of the applied H_2O_2 or persulfate to produce HO· or SO_4^-·, respectively, which were efficient reactants for polychlorinated biphenyls (PCBs) degradation (Fang et al., 2014; Fang et al., 2015). This line of research is out of the scope of this current review, and the readers are recommended to refer to another recent review paper on the role of EPFRs in biochars on degradation of refractory organic contaminants in water (Qin et al., 2018).

6. Research perspectives

EPFRs are contaminants with emerging concern and ubiquitous in the environment and they have significant toxic impacts. Systematic work is thus needed for assessing and predicting their fate and risks. Because of the mixing of various EPFRs in the environment, the first challenge is to identify their sources when investigating the fate of EPFRs (Fig. 7). More parameters other than the apparent g-value and band width should be included for this purpose. Therefore, the first challenge is the analytical methods that need to be incorporated in EPFR research. Combining the EPR signal superfine and DFT calculation may be helpful to reveal EPFR structures and compositions. Unlike common contaminants that the multimedia behavior could be described by their physiochemical properties, no theory is currently available to quantify the interfacial and kinetic behavior of EPFRs. Combination of certain colloidal-based techniques or theories may greatly facilitate the study on the fate of these particle-associated EPFRs.

According to the current studies, EPFRs may be formed with or without the aid of transition metals. It has not been concluded yet on what property of transition metals determines the formation of EPFRs (both intensity and stability). At this stage of EPFR research, we suggest to systematically consider both particle (such as particle size and surface area) and transition metal (such as electron transfer and redox activities) properties. The generation of EPFRs in biomass pyrolysis is independent of transition metals and the breaking of chemical bonds in the precursors during the pyrolysis is the primary reason. Extended study is required to clarify the relationship between the generated EPFRs and the chemical compositions as well as the 3-D structure of the feedstock.

The frequently reported precursor molecules of EPFRs include quinone, phenolics, chlorinated/hydroxylated benzenes, as well as PAHs. However, no relationship is proposed to correlate the properties of the precursors and EPFRs. It is common that various free radicals coexist in a system. But no in situ measurement is conducted to examine the types and structures of the stabilized free radicals, except mathematical peak differentiating and deconvolution. Besides the EPR intensity, the life times and activities of EPFRs in relation to the properties of the precursors are not studied yet. The environmental factors, such as oxygen, light irradiation, humidity as well as humic substances, play important roles in the generation and stabilization of EPFRs. All these factors are environmentally relevant and thus this line of research will provide

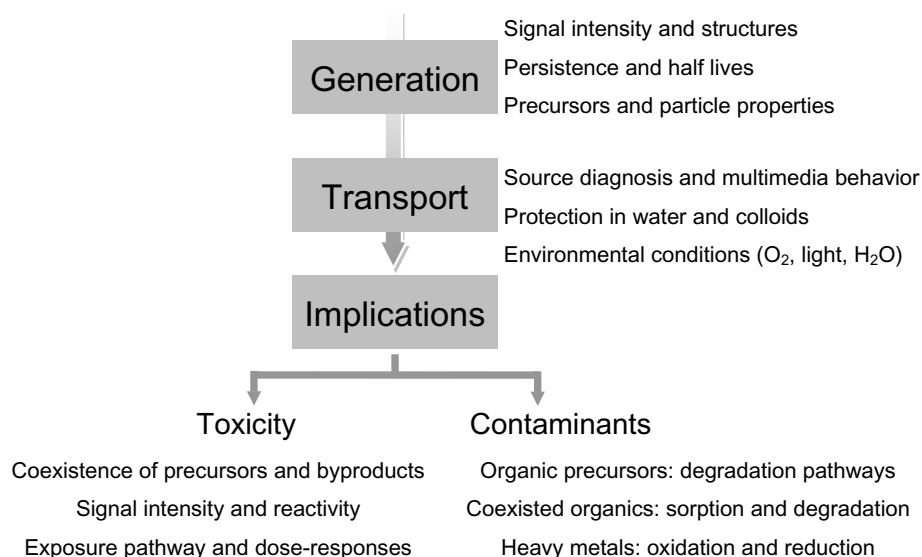## Environmentally persistent free radicals

Fig. 7. Research needed for environmental persistent free radicals (EPFRs). The research areas on their geochemical behavior and environmental implications are highlighted.

valuable information for understanding EPFRs generation mechanisms and their fate.

Significant toxicity of EPFR-embedded particles has been reported. However, no well-designed experiment was conducted to separate the toxicity contributed by the precursor chemicals, their degradation byproducts and EPFRs. More importantly, how EPFR signal intensities relate to their activity is unclear. Any indirect measurement of EPFR activity and thus their toxicity will be helpful for their risk assessment.

For the precursor chemicals that interact with transition metals, the generation of EPFRs may alter their degradation pathways. In addition, other coexisted organic contaminants may interact with EPFRs or their activated species. Both processes are important in the behavior of organic contaminants, but not properly considered in previous studies on their multimedia environmental fate.

Acknowledgement

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