Molecular and Integrative Toxicology

Kavindra Kumar Kesari
Niraj Kumar Jha *Editors*

# Free Radical Biology and Environmental Toxicity

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Editors

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*Editors*
Kavindra Kumar Kesari
Department of Applied Physics and
Department of Bioproducts and Biosystems
School of Science
Aalto University
Espoo, Finland

Niraj Kumar Jha
Department of Biotechnology
School of Engineering and Technology
Sharda University
Greater Noida, Uttar Pradesh, India

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# Foreword

The edited book, *Free Radical Biology and Environmental Toxicity*, by Kavindra Kumar Kesari and Niraj Kumar Jha represents an interdisciplinary literature by integrating the basic principles of physics, chemistry, and biology. The title itself defines the theme of the book, wherein the authors have considered relevant environmental issues impacting human and animal health. This book contains 17 chapters which cover most of the environmental issues. The arrangement of the chapters is orchestrated, synchronized, and coherently connect to each other with suitable schematic presentation of mechanisms and pathways to comprehend the subject in a better way. It would be appropriate to say that this book is a good recipe for the readers and researchers in the field of environmental toxicology. Though the major focus of the book is on nanotoxicity, fine particle contaminants, heavy metals, and radiation toxicity, including a chapter on COVID-19 makes it more pertinent with the impact of environmental toxicity on the worsening of the COVID-19 pandemic. One of the most important components of this book is elucidating mechanisms and presenting evidence-based studies, which is an occasional combination in available environmental toxicology books. In the majority of the chapters, the connection of free radical biology, a complement of oxidative stress with environmental toxicity, represents the mechanistic clues of environmental toxicants induced oxidative damage. The chapters in this book are relevant with the theme of the book as it begins with introductory chapters on the environment persistent free radicals, followed by causative factors, and ends with protective measures including numerous therapeutic strategies. To discuss a few of the chapters, Chapter "Reactive Oxygen Species Producing Photoactivatable Molecules and Their Biological Application" showcases the free radicals–induced photoactivated molecules that may work as photosensitizers and pave the way for therapeutic opportunities in biomedical sciences. Arsenic is one of the carcinogens which may cause severe health issues, and Chapter "Role of Arsenic in Carcinogenesis" presents the health hazards of arsenic and provides evidence-based information for better understanding. Chapter "Regulation of Glucose Transporters in Cancer Progression" deals with glucose transporters in cancer progression that open new doors for future research. Several other chapters are dedicated to toxic metal contaminations and radiation-induced toxicity, which are

leading health hazards. The role of environmental toxicants in neurological diseases is well covered in the book.

This book may serve as a reference book for academic programs and represents an update for environmental toxicology researchers. The book will also be useful for general readers as it covers many public issues. The editors of this book deserve special thanks for editing such an important book on an important topical issue.

Professor, Department of Applied Physics, School of Science, Aalto University, Espoo, Finland
e-mail: janne.ruokolainen@aalto.fi

Janne Ruokolainen

Associate Professor of Pharmacology and Therapeutics, College of Medicine and Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates
e-mail: shreeshojha@uaeu.ac.ae

Shreesh Ojha

# Preface and Acknowledgements

In the present scenario, the major concerns to our environment and its toxicity have raised a great interest globally, especially for the younger generation. With spreading networking of mutagenic factors in the environment, every individual is exposed to different chemicals and fine particles, which may react with our genetic material and may cause myriad health issues. The fundamental questions on the effects of environmental toxicants and pollutants mainly focus on the multidisciplinary field of science by applying the basic principles of physics, chemistry, and biology. We are all surrounded with various natural and man-made environmental toxicants, mutagens, and infectants, which may present significant risk to human health. The global industrialization together with the development of our health system has led to an exponential growth in the number of toxic chemicals used for different purposes. There are varieties of chemical, physical, and biological contaminants that are present in the environment. These toxicants are mainly heavy metals, toxic chemicals, compounds, tobacco smoke, nanoparticles, pesticides, viruses, radiations (ionizing and non-ionizing), and several others (fine particles, pollutions, climate change). These toxicants are highly associated with our daily life and affect our health. In principle, any exposure to these toxicants may induce oxidative stress and start producing free radicals within the cells and may eventually cause severe diseases such as neurological disorders and cancer. It would not be entirely incorrect to assume that the oxidative stress is the root cause of most of the severe health conditions.

This book is a value-added collection of 17 chapters which discuss the multidisciplinary approaches with a focus on the environmental toxicity and free radical formation. Chapter "Environment Persistent Free Radicals – Long Lived Particles" discusses the significant role of long-lasting environment persistent free radicals (EPFRs) on human health. Study also highlights a set of potential risk factors, which are associated with the EPFRs in bioremediation of organic pollutants and human health. Although, in Chapter "Reactive Oxygen Species Producing Photoactivatable Molecules and Their Biological Application", photosensitizers have been reported as reactive oxygen species (ROS) producing molecules and found exclusive for site-specific targeting. Photosensitizers prove to be the emerging therapeutic molecules

for tumor treatment and cancer cell destruction with high specificity. This chapter describes the mechanisms, types, and the therapeutic applications of photosensitizers. Chapter "Effects of Transformation of Metallic Nanoparticles in the Environment and its Toxicity on the Aquatic and Terrestrial Life Forms" discusses the toxicity of nanomaterials that may raise serious concern to human health, as these are potentially used in several research fields. Similar to EPFRs (Chapter "Environment Persistent Free Radicals – Long Lived Particles"), living organisms in the environment may experience a long-lasting unwanted effect due to the release of nanomaterials to the environment. Therefore, this chapter describes the various sources of the unwanted release of nanomaterials in the environment, their mechanism of actions, and associated side-effects on the living system. Along with nanomaterials, nanodrugs or drug compounds may also induce oxidative stress which may induce cellular toxicity as reported in Chapter "Drug Induced Oxidative Stress and Cellular Toxicity". In this chapter, the role of ROS and reactive nitrogen species (RNS) in response to various drugs and further retrieval effects after co-supplementation of the antioxidants have been discussed. Evidences show that any kind of drug supplementation either nanoparticle and/or drug compounds may affect majorly the elderly populations. Therefore, Chapter "Adversities of Nanoparticles in Elderly Populations" discusses the pros and cons of the nanoparticles in the elderly populations. Study highlights the association of nanotoxicity with the phenomenon of ageing and possible link of various organs-related diseases. The major sources of nanoparticles or nanodrugs are being used in food and other commonly used products at the large scale. Therefore, Chapter "Toxicity of Titanium Dioxide Nanoparticles and Oxidative Stress" discusses the role of titanium dioxide ($TiO_2$) nanoparticles-induced oxidative stress which may cause oxidative damage and genotoxicity in the human system. Study mainly focuses on exploring the role of nanotoxicity based on the nanoparticle size, shape, route of administration, and various other sources. In this chapter, study highlights the applications of $TiO_2$ nanoparticles and their toxic potential to cause severe diseases in humans. The sources of contamination through the consumption of various modes such as food, air, water, and waste irrigated crops may play an important role in cell cycle progression and severe disease development, especially water has raised serious health issues due to chemical and heavy metal contaminations. Chapter "Role of Arsenic in Carcinogenesis" discusses the arsenic contamination in drinking water leading to poisoning in the healthy living population. Evidences reported in this chapter suggest that the arsenic has potential to lead many conditions such as diabetes, hearing loss, portal fibrosis, cardiovascular and peripheral vascular diseases, as well as various cancer types, such as skin, bladder, kidney, prostate, liver, and lung cancer. These diseases may be caused due to oxidative stress induced by arsenic, which may alter the DNA structure by insertion, deletion, and by several other mutations like gene amplification and suppression of p53 leading to the manifestation of cancer. One of the important mechanisms of arsenic poisoning-induced oxidative stress is lipid peroxidation, which may increase the arsenic-induced mutations up to fivefold. Cancer is one of the leading diseases globally. Until now, from first chapter to seventh chapter, there is one thing in common, i.e., nanotoxicity and chemical

toxicity raising serious health concerns. The reported toxicants mostly alter mitochondrial functions, where mitochondria have been found a key player in maintaining the metabolism, bioenergetics, biosynthesis, and cell. In connection to this, Chapter "Role of Mitochondrial Oxidative Stress in Pathophysiology of Lung Cancer" discusses the role of ROS in regulating the molecular signaling pathway alterations, which may lead to lung cancer progression. Besides the mitochondrial metabolic changes, mitochondrial dynamics such as fission and fusion events are also affected in cancer cells. Study also focuses on the various redox-sensitive miRNAs and their roles in pathophysiology of lung cancer progression. After detailed discussions on the mutagenic factors and cancer, Chapter "Regulation of Glucose Transporters in Cancer Progression" shows great impact towards the regulation of glucose transporters in cancer progression. Study discusses glycolysis, which is often the preferred metabolic pathway for cancer cells that enables them to acquire energy and other metabolites for their growth and survival. After going through Chapter "Role of Mitochondrial Oxidative Stress in Pathophysiology of Lung Cancer", it provides a better understanding of regulatory pathways where glucose transporters are rate-limiting checkpoints, abnormally regulated in cancer. The regulation of glucose transporters (GLUTs) by key proliferation and pro-survival pathways including the phosphatidylinositol 3-kinase (PI3K)-Akt, hypoxia-inducible factor-1, and HIF-1 pathways provide pioneering ways for future research. GLUTs can be targeted in a relatively tumor cell-specific manner to block glucose-regulated processes more comprehensively for cancer therapy which has been discussed in detail in this chapter.

In the follow-up studies, chemical contamination has raised severe health concerns since past few decades. The previous chapters of this book have already discussed the pros and cons after consuming contaminated crops, food, and water, which has causative impact on our biological system. In the continuation, Chapter "Oxidative Stress: A Potential Link Between Pesticide Exposure and Early-Life Neurological Disorders" elaborates different classes of pesticides and their effects on the oxidative stress parameters. This chapter highlights the association between pesticide exposure and the development of different neurological disorders. In Chapter "Sleep Disturbance Induced Free Radical Formation in Gut May Blocked by Melatonin", the oxidative stress has been recognized as a responsible factor to cause sleep disturbances and produces free radicals in the gut. The inhibitory effect of oxidative stress by melatonin has been reported to improve the sleep/wake cycle. Melatonin is an antioxidant which has the potential to cure the sleep-related complications. Therefore, this chapter introduces the natural products and their ability to produce novel secondary metabolites which may act as potential drug candidate in future research. In the follow-up, Chapter "Initiation of Neurodegenerative Disorders (NDDs) Through Metal Toxicity Generated Oxidative Stress" discusses the metal-induced toxicity which may initiate the neurodegeneration. Heavy metal toxicity is the most common contamination in our daily life and could be consumed easily through various sources. In this chapter, the authors depict various unwanted effects of metal toxicity in human brain and its favorable antidotal strategies in treating the intoxication. In this chapter, study mainly aims to explore the pros and cons of metal

toxicity in the brain and associated neurodegenerative diseases, i.e., Alzheimer's and Parkinson's diseases.

Until now, after reviewing first chapter to twelfth chapter, it could be concluded that oxidative stress is the factor responsible for increase in the level of ROS, and as resultant, it has been considered to be a hallmark for diabetes-induced pressure ulcers, which has been reported in Chapter "Reactive Oxygen Species and Oxidative Stress on the Formation of Diabetic Ulcer". For better understanding of the underlying signaling cascades, which may lead to diabetic wounds could facilitate pharmacological intervention and thereby helping to combat with this debilitating disease conditions. Diabetes-induced pressure ulcers are a growing burden for any healthcare system, and it has been observed that wound healing is delayed by hyperglycemia, excess levels of ROS, and the resulting imbalance at the wound site. In Chapter "Role of Mitochondrial Oxidative Stress in Pathophysiology of Lung Cancer", it has been reported that mitochondria are major targets to ROS, which is also reported in Chapter "Chronic Oxidative Stress Leads to Genomic Instability in the Pathogenesis of Fanconi Anemia". In this chapter, role of mitochondria in cellular oxidative stress regulation along with altered mitochondrial dynamics in relation with the clinical symptoms of Fanconi Anemia (FA) has been discussed. Study also reports the first human disease evidence where mitochondrial role in genomic instability is depicted. Studying mitochondrial dysfunction in this chapter would offer deeper insights as well as diagnostic and therapeutic solutions to FA.

In the environment, both ionizing and non-ionizing radiations play a major role in biological toxicity, where these radiations produce the free radicals and cause severe health concerns, i.e., cancer and neurological disorders. In this connection, Chapter "Toxicity with Waste Generated Ionizing Radiations: Blunders Behind the Scenes" discusses the various sources of ionizing radiations and their effects on human health. Evidences suggest that the radiation may affect the cellular system by producing higher number of free radicals which may start inducing health detriments as discussed in this chapter. Furthermore, provoking biotechnological implications from radiation-tolerant life forms have been sufficed and discussed in detail. The networking of environmental toxicants may also responsible to cause infectious diseases, e.g., COVID-19 detected as biggest tragedy in the twenty-first century. Therefore, Chapter "The Antioxidant Arsenal Against COVID-19" addresses the role of free radicals in post-coronavirus infections in the human biological system. In this chapter, a compelling view of the various mechanistic networks within which COVID-19-led oxidative stress could deter the homeostatic harmony and how antioxidants would emerge as a highly sought therapy is discussed. Chapter "Synergistic Effects of Heavy Water in Health Prospects", the final chapter, provides an insight of heavy water/deuterium use in the medicinal chemistry and biotechnology, due to its physico-chemical characteristics that are reported to have potential applications in applied research. Study discussed in this chapter is on the synergistic effects of heavy water, and health prospects are vividly sketched to understand its explorable properties. Further, few case studies on various pharmaceuticals employing the active isotopes in the drugs that are under clinical trials have been discussed in this

chapter. This is a very interesting chapter which addresses environmental toxicity perspectives.

All the chapters presented in this book have follow-up links from each other and conclude that oxidative stress-induced free radical formation is the responsible factor for all types of serious health concerns. This book focuses on molecular and integrative toxicology in understanding the mechanisms of toxicity associated with free radical generation. One who can read all the chapters, from first chapter to seventeenth chapter, will inculcate a better understanding of environmental challenges and be able to measure the mutagenic factors in the environment and understand how they are impacting human and animal health. Moreover, a brief discussion on the other challenges such as changing environment, climate, and lifestyle factors are growing concerns in the twenty-first century. I hope this book will serve as both an excellent review and a valuable reference for formulating suitable measures against environmental toxicology and for promoting the science involved in this area of research.

Finally, we would like to dedicate this book to all the frontline workers globally, who are fighting 24/7 against COVID-19 to save our lives, and also COVID-19 warriors who lost their lives in saving humanity. We would like to thank all authors who have contributed to this book. Last but not least, our special thanks go to series editors (Jamie C. Dewitt and Sarah Blossom), publisher, and entire Springer editorial team for their sincere assistance and support. Our special thanks go to Carolyn Spence (Senior Publishing Editor) for her continuous support and suggestions throughout the book editing.

Espoo, Finland — Kavindra Kumar Kesari
Greater Noida, India — Niraj Kumar Jha

# Contents

# Environment Persistent Free Radicals: Long-Lived Particles

**Ankita Vinayak, Gaurav Mudgal, and Gajendra B. Singh**

## Contents



**Abstract** Environment persistent free radicals (EPFRs) are emerging environmental pollutants that have longer lifetime than other free radicals. EPFRs are more stable in ambient environment because they are protected by surrogate particles like particulate matter. They are primarily emitted during thermal processes such as pyrolysis and organic material combustion. The byproducts formed from these processes provide breeding ground to the radicals for EPFR generation. Such surface bound free radicals become more persistent and resistant to atmospheric oxidation. They are also found in contaminated soil, tar ball, and cigarette smoke. The stabilization and formation of EPFR are significantly affected by elemental precursor composition and environmental factors. EPFRs are capable of producing reactive oxygen species like hydroxyl radicals, responsible for inducing oxidative stress in living organisms thereby posing adverse environmental and human health effects.

A. Vinayak · G. Mudgal · G. B. Singh (✉)
University Institute of Biotechnology, Chandigarh University, Mohali, Punjab, India



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Despite acting as persistent environment pollutant, recent research investigations have shown EPFRs to be potentially active candidate for degradation of organic environmental contaminants. Consequently, research studies regarding occurrence, formation, toxicity, and environmental application of EPFRs have attracted global attention in the past few years. However, the existing data and investigations in this field are discrete and limited. Hence, this chapter is organized to discuss research studies and important finding on persistent free radicals, highlighting sources, occurrences, generation mechanism, exogenous factors for formation, as well as environmental implication. Moreover, role of EPFRs in the degradation of organic pollutants for environmental remediation is also being discussed.

**Keywords** Environment persistent free radical · Organic pollutants · Pyrolysis · Particulate matter · Degradation

## 1 Introduction

Free radicals are simply defined as atoms or molecules having unpaired electron and is very unstable. It includes alkoxyl radicals, hydroxyl radicals, intermediate molecules, transition metal species, and also excited state molecules. The formation of radical species occurs through redox reactions and ionizing radiations (Chaudhuri et al. 2010). The multiplicity of chemical reactions increases the chances of generation of free radical species. As redox reactions occur normally in all biological systems, likely is the generation of free radicals. They are basically involved in providing immunity and in eliminating pathogenic viruses. However, introduction of new chemicals into environment through industrial, medicinal, or agricultural use has added excessive number of radicals into the surrounding. The presence of unpaired electron makes them highly reactive. They have the tendency to react with proteins, lipids, and nucleic acids of living cells, thereby causing oxidative stress and ultimately cell damage (Alkadi 2020; Bartolomei et al. 2015).

Free radicals are also emitted in thermal treatments such as waste incineration and combustion systems, but those produced species are more stable and persistent. They are also known as "long-lived particles" because they have longer life span ranging from hours to months in comparison to free radicals which have lifetime of picoseconds only (Lomnicki et al. 2008; Pan et al. 2019). In the combustion system like in pyrolysis they are primarily formed in cooling zones of processors (Wang et al. 2019). When particles emitted in the system leave the high temperature flame, they tend to attach to the surface of fine particles. The combination or chemisorption of radical species onto the surface of some other particle like metal oxide and coarse particle imparts extra stability to radicals. It results in the generation of bio-stable free radical, which is a newly formed particle pollutant system, highly stable and persistent termed as – "environment persistent free radicals" (EPRFs) (Dugas et al. 2016). These resonance and surface stabilized radicals include cyclopentadienyls, phenoxyls, and semiquinones formed during thermal decomposition of catechol, phenols, and hydroquinone. They are mainly detected in particulate matter,

combustion system, organic compound contaminated soil, plastic generation, during pyrolysis (biochar/biodiesel), coal combustion, and cigarette tar (Gao et al. 2018). EPFRs have the tendency to carry out prolonged oxidation–reduction reactions, thus forming large number of radical species. This property confers high level of toxicity to EPFRs which is more pronounced than either pollutant or particle. EPFRs are considered as emerging pollutants because they display toxic effects not only on plant and human health but also on ecological health. The EPRFs require special chemical reactions for their removal and treatment (Xu et al. 2020). In spite of being a new bio-stable environmental pollutant posing adverse toxic effects, EPFRs mediate degradation of organic contaminants also. They have the tendency to activate persulfate for the formation of reactive oxygen species like superoxide and hydroxyl ion. The formation and activation of intrinsic radicals induce the transformation and degradation of organic pollutants without catalyst and additional energy source (Qin et al. 2018). Therefore, we aim to discuss knowledge and research on EPFRs to date, focusing particularly on possible sources, environmental occurrences, formation, lifetime, toxicity, and their environmental implications as well as potential application of EPFRs for the wide-ranging remediation application of EPFRs.

## 2 Occurrence of EPFRs

EFRFs are ubiquitous environmental pollutant as it is easily generated in combustion systems and in cooling regions of thermal processes such as pyrolysis and waste incineration (Fig. 1). Recently, EPFRs are also found in the matrix of ultrafine and airborne fine particulate matter. Particulate matter (PM) is emitted into the environment by both natural and anthropogenic processes. The five major source PMs in the atmosphere are coal combustion emissions, (16.8%), vehicular emission (32.1%), industrial processes (11.7%), dust storm (27.2%), and nitrates (3.4%). It is a mixture of organic, inorganic species, solid and liquid components of metals which have the tendency to form radicals (Saravia et al. 2013). Based on aerodynamic size, PM is classified into three categories: ultrafine particles (<0.1 μm), smaller fine particles (0.1–2.5 μm), and coarse particles (2.5–10 μm). The EPRFs are primarily associated with ultrafine and coarse airborne PM particles (Runberg et al. 2020). Studies have demonstrated that organic pollutants like aromatic hydrocarbons bind and chemisorb onto the surface of PM, resulting in surface stabilized radical species. The resultant complex formed are weakly reactive toward atmospheric oxygen, enhancing its persistence in air for hours to months. The strong chemical bond between them makes their removal difficult. The persistence of radical species is due to cyclic regeneration of ROS species whereas stability is because of surface bound particles (Gehling and Dellinger 2013). Mostly semiquinones and its similar type radicals are found to be chemisorbed on PM surface. The studies have reported the ambient 24 hrs concentration of EPFRs in PM ranging from $10^{19}$ to $10^{22}$ spins $g^{-1}$. The environmental samples collected from densely populated and industrialized sites have been reported with approximately 10-fold concentrations

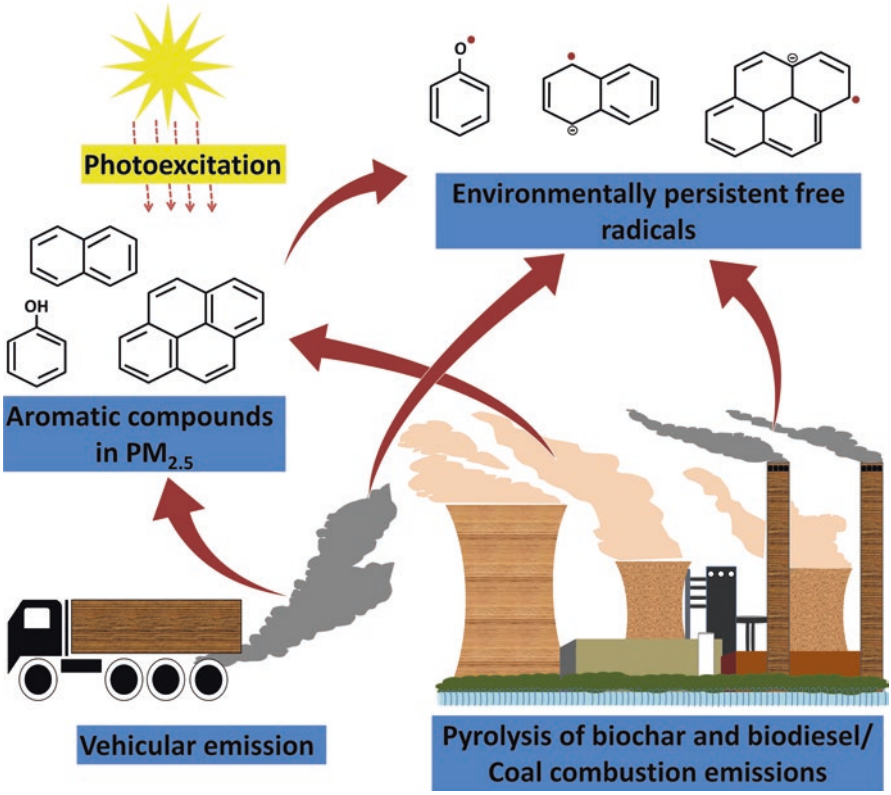


**Fig. 1** Potential sources, occurrence, and transport of EPFRs

of EPFRs compared to less populated areas (Yang et al. 2017; Guo et al. 2020). The inhalation of EPFR-PM complex is implicated in various human health-related complications like cardiovascular, neurodegenerative, and respiratory system.

EPFRs are also widely detected in soil contaminated with organic compounds. Various studies have demonstrated the presence of free radicals in soil since soil is a reservoir of various complex molecules such as industrial organic pollutants and soil organics. The animal and plant residues in soil form antioxidant phenolics like tannins and vitamin C. These phenolics get adsorbed on the surface of metals in soil and form the aromatic radical cations. Organic pollutants are also formed during coal mining, coke production, and in soil contaminated with petrochemical and crude oil (Singh et al. 2013). Being hydrophobic in nature, organic pollutants like polycyclic aromatic hydrocarbons (PAHs) get deposited in soil sediment. The chemical stability and soil conditions inhibiting physical sequestration of PAHs makes them stable and slows down their degradation and leads to sorption of PAHs onto surface of clay minerals forming undesirable dioxins (Eom et al. 2007). The various remediation methods like photodegradation, chemical oxidation, and thermal processing are employed for their removal. Among all, volatilization of organic pollutants by thermal processing is a major phenomenon. The products,

intermediates, and byproducts of thermal treatment of PAHs are detrimental to environment. During such remediation processes, they get transformed into surface stabilized radical species. Jia et al. reported that during the treatment of soil contaminated with anthracene, it gets prone to mineral transformation reactions and readily generates EPFRs (Jia et al. 2018). Similarly, thermal oxidation of catechol contaminated soil favors persistent radical formation. The studies have further demonstrated that soil contaminated with phenolics compounds and oxygen rich environment have higher concentration of EPFRs. The superfund soil containing polychlorinated substituted compound, pentachlorophenol, and PAHs contains 2–30 times higher concentrations of EPFRs as compared to original soil (dela Cruz et al. 2014). In addition to this, atmospheric oxidation of PAHs also forms persistent radicals. The photoexcitation of organic matter and humus like substances during visible light illumination favored the formation of PAHs like EPFRs (Chen et al. 2019). The results suggest that EPFRs' formation occurs via electron transfer mechanism in mixture matrix of biological, organic, and inorganic constituents.

## 3 Sources of EPFRs

### *3.1 Pyrolysis of Biochar and Biodiesel*

Biochar is a stable, carboniferous byproduct derived from pyrolysis of low-cost biomass such as animal or plant at temperatures over 250 °C. Recently, biochar has captured attention because of its promising application in environment remediation, agricultural crop production, and bio-refinery activities. Biochar is considered as organic substituent in environment and agricultural areas because of its potential for contaminant adsorbent, pH buffer, water and nutrient retention, catalyst, and energy production. It can also increase soil fertility through stimulation of microbial community, retention of fertilizers, and reduction of greenhouse gases (Beesley et al. 2011). Being formed from thermal processing of organic biomass residues in oxygen limited conditions, the biochar synthesis forms bio-stable radicals in environment. The thermal decomposition of organic biomass under carbonization conditions at charring temperature facilitates EPFRs' formation. The organic molecules of biomass residues like cellulose, lignin, and hemicellulose are major precursors for EPFRs generation. During decomposition process they form oligosaccharides which is further cleaved at glycosidic linkage to form monomers of radical species (Liao et al. 2014). The various abiotic factors such as pH, temperature, electrical conductivity, elemental composition, calcium carbonate content, electrical charge density, and volatile/nonvolatile molecules influence the EPFRs' formation in pyrolysis process. Among all, the high temperature (250 °C) is a crucial determinant for EPFR generation in biochar pyrolysis. For example, EPFRs' generation was reported in biochar residues produced during thermal processing of maize straw, pine needle, and wheat straw at temperature range of 300–500 °C (Fang et al. 2014). In the biochar residues, the commonly found stable radicals are phenyl radical, hydrogen peroxide, superoxide, hydroxyl, and catechol type radicals and

semiquinones types. In terms of stability, semiquinones type radicals viz. benzosemiquinone and o-semiquinones which are oxygen centered are most stable species, whereas carbon centered radicals like cyclopentadienyls are least stable and are vulnerable to atmospheric oxidation (Khachatryan et al. 2006; Tian et al. 2009). Similarly, the pyrolysis of vegetable oil and animal fats biomass at high temperature for biodiesel formation favors the formation of stable and transient radical species which get adsorbed on particulate matter (Kibet et al. 2018). In 2018, Mosonik and coworkers reported the formation of EPFRs during thermal processing of *Croton megalocarpus* for biodiesel. The pyrolysis of *Croton megalocarpus* at 600 °C facilitated emission of particulate matter and free radical generation having half-life of 431 days, making them EPFR. Further characterization of free radicals revealed that species were carbon-centered with a low decay constant ($1.86 \times 10^{-8}$ $s^{-1}$) and resembled radical species of that in coal (Mosonik et al. 2018). Thus, the formation and persistence of EPFRs formed during pyrolysis of biochar and biodiesel contaminate the environment and have detrimental implications on the environment and human health, such as oxidative stress, cancer, and cardiac abnormalities.

## 3.2 Transition Metals–Mediated Generation of EPFRs

Transition metals are considered as key precursors favoring EPFRs' formation under various environmental conditions. The zinc, vanadium, iron, nickel, and copper are considered as most favorable metals for EPFRs' generation. The hydroxyl- and chlorine-substituted benzenes when decomposed at 150–400 °C chemisorb onto the surface of metal oxide with subsequent electron transfer. It results in metal reduction and simultaneous persistent free radical generation (Yang et al. 2017). Various metal oxides like $Al_2O_3$ and ZnO are emitted during combustion processes. They enhance the stabilization and formation of EPFR. The catalytic ability of metal oxide–generated EPFR generally depends on the standard reduction potential of transition metals. Studies indicated that series of chemical reaction, physisorption, chemisorption, and finally electron transfer from metal surface to adsorbed organic molecules lead to stable radical formation. The EPFRs formed from different metal oxides such as $Fe_2O_3$, NiO, $Cu_2O$, and ZnO were compared, and it was observed that ZnO EPFRs were most stable and long lasting (Vejerano et al. 2012a).

## 3.3 Other Sources of EPFRs

Plastics are used for various purposes in day-to-day life. Huge amounts of plastics are produced, utilized, and disposed into environment. Approximately 10% of plastics used are dumped into surrounding environment. With time, effects from photoaging, chemicals, and microbial actions corroborate the break down of macroplastics into much smaller versions (less than 5 mm) known as microplastics (MPs). MPs

are widespread in natural environment, found in soil, sewage, sediments, and rivers (Andrady 2011). They may induce adverse effects on living forms such as significantly affecting feeding capacity, reproductivity and other system also. Most importantly, MPs can form reactive oxygen species leading to oxidative stress in living organisms. When MPs are released into the environment, they undergo both biotic and abiotic transformations (Zhu et al. 2020a). During these transformations, organic pollutants lead to formation of free radical species. Many MPs such as phenol formaldehyde resin and polystyrene contain substituted benzene rings. During photoaging they undergo oxidation leading to cleavage of C–H and C–C bond and ultimately forming stable radical species (Zhu et al. 2020b). Similarly, other plastic materials like polyvinyl chloride and polyethylene are also subjected to photooxidation in natural environment and form reactive oxygen species (Cai et al. 2018).

Tar balls and oil mineral aggregates are formed from weathering of spilled crude oil. These aromatic molecules tend to chemisorb on the surface of transition metals and suspended minerals in sediments. The metal and crude chemical interactions result in the formation of stable free radicals. Kiruri et al. reported the presence of two semiquinone type organic radicals in the tar ball collected samples. One is asphaltene radical species (g value – 2.0035) occurring in crude oil and the other one is new radical species formed from partial oxidation and interaction of crude components (g value 2.0041–2.0047) (Kiruri et al. 2013).

## 4 Mechanism of EPFR Formation

The resonance stabilized EPFRs are formed by association of substituted aromatic compounds with fine particle or transition metal center. Metals and organic compounds act as model particles for persistent free radical generation. With the adsorption of organic compounds on metals, EPFFRs are formed at transition metal center through metal reduction. The general mechanism for the formation of EPFRs involves initial physisorption, involving weak bonding between organic molecule and transition metal. It is followed by chemisorption of organic compound via removal of water and subsequent electron transfer from adsorbed species to the metal oxide center, resulting in metal reduction and EPFRs' formation (Fig. 2) (Qin et al. 2018). The metal center interaction imparts stability to the formed radical, providing it a resistance to degradation, oxidation, and recombination. The resonance of formed organic radicals allows formation of either carbon centered or oxygen centered EPFRs. Generation of such discreet EPFRs is mediated by transition metals or organic moieties such as those formed after incomplete combustion events like pyrolysis of biochar (Gehling and Dellinger 2013). The possible mechanism of EPFRs' formation in both includes these mentioned steps, while only the precursors such as aromatics, metal oxides, and exogenous factors differ. Various model studies have demonstrated that thermal processes such as pyrolysis and metal smelting processes generate abundant transition metal oxides which mediate the formation of bio-stable free radicals in the cooling zone of smelter. Vejerano et al. investigated

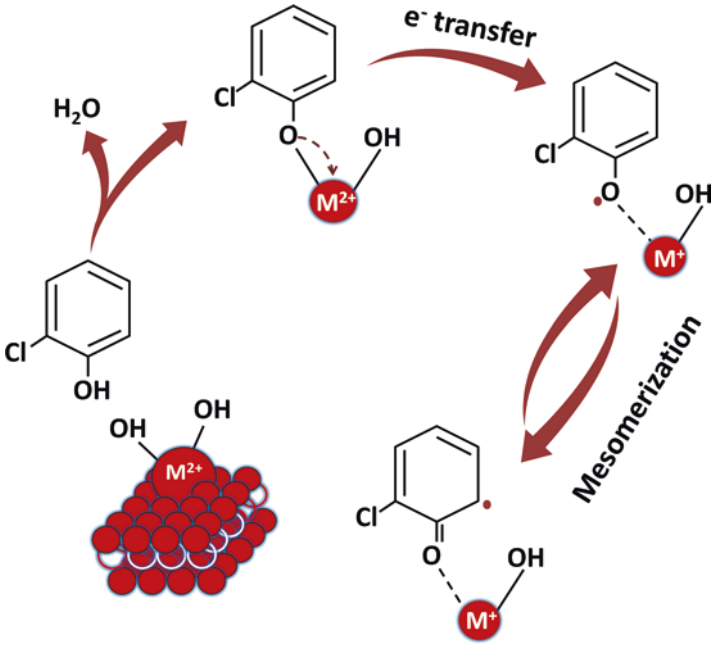


**Fig. 2** Diagrammatic representation of M(II)O mediated EPFR generation from chlorinated benzene (M-Cu, Ni, Zn, Fe, Ti)

the formation and stabilization of persistent free radicals on NiO surface. The results showed that aromatic molecular adsorbates like monochlorobenzene, catechol, and 1,2-dichloronezene gets adsorbed on the surface of NiO/silica particles (5%) at 150–400 °C. The electron transfer occurs from the adsorbate to the center of metal, thereby reducing NiO and resulting in various types of formation of EPFRs. Depending on exogenous conditions such as nature of adsorbate and temperature, different types of radicals were formed, such as semiquinone type radical (g value – 2.0050–2.0080) and phenoxyl type radical (2.0029–2.0044) (Vejerano et al. 2012b). EPFRs formed from different metal oxides such as ZnO, $Fe_2O_3$, $Ti_2O$, and NiO were studied and compared for concentration and half-life. It was found that lifetime of EPFR formed strongly depend upon the standard reduction potential and catalytic oxidizing strength of metal (Yang et al. 2017). The amount and type of EPFR formed depend on different factors such as type of precursors, process time, temperature, and concentration of metal oxides.

The pyrolysis of biomass constituents such as lignin, cellulose, and hemicellulose occurs at high temperature (300–400 °C) for synthesis of biochar (Nzihou et al. 2013). The homolytic cleavage of C–O, C=O, and alpha/beta alkyl bond instigates formation of monomer and free radical. The formed radical then couples with the incomplete combustion by products like hydroquinone, phenol, and polyaromatic compounds for the generation of surface bound EPFR. The extended pyrolysis time

can even increase the accumulation of free radical in residue (Collard and Blin 2014). The cooling zones of thermal processors favor more formation of EPFR. The radical species formed in the matrix of organic moieties are protected from reacting with chemicals and with each other, providing them extra stability. Biochar synthesized from different biomass feedstock showed electron paramagnetic resonance spectra with varying intensity and g factor. The chemical composition of biomass determines the decomposition temperature and also the energy requirement for bond cleavage (Fang et al. 2015a). Thus, EPFR generation mediated by organic molecules significantly depends on carbon content of feedstock and poorly on metal element concentration. In 2014, Liao and colleagues studied the formation of EPFRs during the pyrolysis of biochar from wheat straw, rice, and corns at 200 °C. The results showed that cleavage of bond and decomposition of biomass structure promoted the formation of stable free radicals (Liao et al. 2014). Studies have shown that biochar residues mainly form oxygen centered, carbon centered, and oxygenated carbon centered radicals. Among all, oxygen centered (semiquinone type species) are more stable while carbon centered (cyclopentadienyls) are least stable as they are prone to atmospheric oxidation (Khachatryan et al. 2006; Tian et al. 2009).

## 5 Factors Affecting EPFRs' Formation

Although EPFRs are long-lived and stable radical species, its lifetime and formation are affected by various abiotic factors like light irradiation, precursors, presence of metals, temperature, pH, humidity, thermal processing time, and oxygen (Gao et al. 2018; Liu et al. 2015). The compounds that can form stable radicals through electron transfer or thermal decomposition are known as precursors. They are considered as important factors influencing the EPFRs' formation. The organic components of precursor molecules undergo different reactions thereby producing different radical species under same process conditions. The investigations have also reported that different types of raw material for biochar synthesis under same conditions form EPFRs that vary in their concentration and g value. Liao and his coworkers compared the concentration and nature of radicals in biochar synthesized from cellulose and lignin at 200 °C. It was found that radical species formed from lignin was more stable and five times higher in concentration as compared to cellulose. The loading of biomass with organic components also rapidly increases the EPFRs' concentration in biochar because of significant effect on g value of EPFRs (Liao et al. 2014; Fang et al. 2015a). Also, the presence of functional groups such as chlorine and hydroxyl groups in benzene ring favors the formation of stable radical species. The relationship between the nature of precursors and radical species will greatly determine the occurrence and behavior of EPFRs (Nwosu et al. 2016a). The various types of EPFRs commonly found in environment with their g values are summarized in Table 1.

The presence of metals is an influential parameter controlling the stable free radical formation. The transition metals significantly affect the yield and type of EPFRs

**Table 1** Common types of EPFRs with g values

| Type of EPFRs | Characteristics | Examples | g value | References |
|---|---|---|---|---|
| Oxygen centered radicals | Includes semiquinone and quinone type radicals, Formed from reaction of radical and phenolic compound, More stable in environment | 1,4-Benzosemiquinone | 2.0046–2.0049 | Xu et al. (2020), Segal et al. (1965), Chen et al. (2018), Pryor et al. (1983), and Neta and Fessenden (1974) |
| | | 1,4-Benzoquinone | 2.0050 | |
| | | Benzoquinone | 2.0039 | |
| | | 1,4-Naphthoquinone | 2.0044 | |
| | | Poly-1,4-Naphthoquinone | 2.0035 | |
| | | Poly-1,7-Naphthoquinone | 2.0035 | |
| | | 1,4-Benzosemiquinone anion | 2.0046 | |
| | | Phenanthrene quinone | 2.0039 | |
| Carbon centered radicals | Consists of aromatic, alkyl and aryl radicals, Formed at high temperature of pyrolysis, vulnerable to atmospheric oxidation, induce formation of reactive oxygen species | Pyrene anion | 2.0027 | Xu et al. (2020), Segal et al. (1965), and Odinga et al. (2020) |
| | | Benzene anion | 2.0029 | |
| | | Perylene anion | 2.0027 | |
| | | Perylene cation | 2.0026 | |
| | | Graphitic carbon | 2.0028 | |
| | | Anthracene anion | 2.0027 | |
| | | Anthracene cation | 2.0026 | |
| | | Naphthalene anion | 2.0028 | |
| | | Polyaromatic hydrocarbon radicals | 2.0026 | |
| | | Fluoranthene anion | 2.0027 | |
| Oxygenated carbon centered radicals | Stable radicals, inhibits autooxidation of organic substances | Phenoxyl | 2.0046–2.0053 | Xu et al. (2020), Neta and Fessenden (1974), Odinga et al. (2020), Graf et al. (1977), and Barclay et al. (1994) |
| | | 2-Chloro-phenoxyl | 2.0062 | |
| | | 4-Chloro-phenoxyl | 2.0063 | |
| | | 2-Carboxyphenoxyl | 2.0046 | |
| | | 2,6-Dichloro-phenoxyl | 2.0065 | |
| | | 3,5-Dichloro-phenoxyl | 2.0049 | |
| | | Phenyl radical | 2.0030–2.0040 | |
| | | 3,4-Dimethoxylphenacyl | 2.0036 | |
| | | 2,4,6-Trichloro-phenoxyl | 2.0076 | |

formed. The oxidizing ability of metal oxides largely affects the formation of EPFRs. The copper and zinc catalyze the formation of semiquinone and phenoxyl type radicals only, whereas iron and nickel have potential to form mixture of radicals with different g factor (Yang et al. 2017). g factor is basically the ratio of magnetic moment of electron to its angular moment, considered as unique property of electron in specific environment. For instance, NiO formed two types of radical species: semiquinone type (g value – 2.0050–2.0081) and phenoxyl type (g value – 2.0029–2.0044) radicals. Similarly, $Fe_2O_3$ produces phenoxyl type and semiquinone type radicals but with slightly different g values (Vejerano et al. 2011). The oxidation potential of metal oxides also determines the yield of EPFRs. Among metal

oxides of Ni, Fe, Cu, and Zn, NiO has the highest oxidizing strength and thus maximum EPFRs' formation ability. The amount of metal ions also affects the formation of EPFRs. The increased concentration of metals has negative impact on the yield of radical formation. Fang and coworkers assessed the effect of increasing number of metals on EPFRs' formation in biochar. It was found that EPFRs' concentration was higher at 0.1 mmol $L^{-1}$of metal as compared to 0.2 mmol $L^{-1}$ of metal. It is due to the fact that excess amount of metal ions consumes free radicals because EPFRs can mediate electron transfer thereby reducing metals ions such as $Cr^{6+}$ and $Fe^{3+}$ (Fang et al. 2015a).

Sunlight represents the only exogenous light source for the formation of radicals in environment. Light energy enhances the electron transfer process generating degradation products and free radicals. Chen et al. studied the EPFRs' formation by visible light illumination of PM of organic matter. The formed radicals were similar to PAHs and phenol derived radicals and have lifetime of 30 min to 1 day (Chen et al. 2019). However, direct photo-irradiation of radicals facilitates their decay. It is found that light irradiation promotes transformation of radical cations into oxygenic radicals such as $O^{2-}$ and OH (Jia et al. 2019). Therefore, in-depth investigations are required for photosensitive organic molecules. Oxygen content is another significant factor catalyzing EPFRs generation and stability. Oxygen may reduce the transition metal EPFRs and can also directly interact with less stable radical species like cyclopentadienyl radicals (Vejerano et al. 2011). The oxygen centered radicals are less stable and persistent as compared to carbon centered radicals. For instance, in air EPFRs have lifetime of only 12.4 days whereas under vacuum conditions EPFRs have 151.8 days of lifetime (Nwosu et al. 2016b). The EPFRs' formation is also controlled by water content during process. A general hypothesis is that humidity has determinantal negative effect on EPFR concentration (Pan et al. 2019). Jia et al. studied the effect of increased humidity and decay values of EPFRs. It was found that radicals were stable for 2 months at 7% humidity whereas they exhibit fast decay at nearly 100% humid conditions. This is because of hydration of metal oxides and also the competition of water molecules with radicals for Lewis acid site, thereby decreasing the formation of radicals or elimination of already existing stable radicals (Jia et al. 2017).

Other abiotic factors like temperature and time of process also determine the type and amount of EPFRS formed. For example, the concentration of EPFRs increased rapidly when pyrolysis temperature is increased from 300 to 600 °C. But any further increase in pyrolysis temperature decreased markedly the formation of free radicals because of reorganization and breakdown of organic structures resulting in decay of free radicals. Similarly, the time of different stages of pyrolysis process influences the formation and type of EPFRs (Gao et al. 2018; Qiu et al. 2007).

The different trends on free radical concentration were observed with the increase in time of pyrolysis process. For example, Fang reported that EPFRs' concentration significantly increased when pyrolysis time prolonged from 1 to 12 h (Fang et al. 2015b).

## 6 Lifetime and Persistence of EPFRs

The lifetime of persistence free radicals is generally longer in comparison to free radicals, as EPFRs are surface stabilized by particles making them more stable. Their half-lives range from hours to months depending on environmental conditions. The half-lives of EPFRs are usually associated with redox potential of metals and also the chemical reaction of radical with metal oxides. Thus, the EPFRs associated metals determine the persistence as well as stability of radical species. For example, the half-lives of EPFRs formed on $Cu_2O$ are less than that of EPFRs formed on $Fe_2O_3$. The half-lives of EPFRs generated on $Fe_2O_3$ and NiO are same nearly 1–5 days. However, out of all transition metal studied, the EPFRs formed on ZnO have longest half-life ranging from nearly 3 to 73 days. The EPFRs associated with ZnO can even persist for a year. It is due to increased interaction of metals with free radicals owing to the closed shell structure, small ionic size, and lack of crystal field lattice energy (Vejerano et al. 2012a) . Thus, the stability of radical species, redox potential, and ability to accept electrons significantly affect the lifetime of EPFRs. In addition to reducibility of metal, the concentration of metal also significantly affects the lifetime of radical species. Kiruri et al. in 2014 reported that chlorophenoxyl radical on CuO/silica at 0.75% concentration and phenoxyl radicals on CuO/silica at 0.5% concentration have longer time span (Kiruri et al. 2014).

Being stable molecule, EPFRs are less prone to chemical reactions. The atmospheric oxygen is the only sink for stable free radicals converting them into molecular species. The EPFRs decay in atmosphere depends on reaction of EPFRs with molecular oxygen. Depending on reaction, EPFRs display no decay, low decay, and fast decay. The *no decay* character of EFFRs is attributed to restriction or entrapment of radical species in the bulk of particulate matter. In the matrix of PM, the unpaired electrons of EPFRs are delocalized over aromatic bonds. On the other hand, phenoxyl radicals undergo fast decay and semiquinone radicals are subjected to slow decay (Xu et al. 2020).

## 7 Potential Risks of EPFRs

The stability, persistence, and redox recycling of EPFRs confer them biological toxic properties. The prolonged cycling of persistent free radicals forms large number of radical species which enhances their toxicity. The potential risks of EPFRs are more pronounced than either of pollutant or particle because of its surrogate association. The adverse effects of EPFRs are due to oxidative stress induced through the generation of reactive oxygen species (ROS) such as hydroxyl radicals and superoxide anion radicals, thereby inducing cellular oxidative stress, cytotoxicity, and DNA damage (Dugas et al. 2016). They lower the levels of cellular antioxidants and ultimately lead to cell death. The EPFRs have shown to affect the biotic and abiotic components of environment, viz. humans, animals, plants, microbes, and soil (Fig. 3). The natural and industrial process tends to transport EPFRs into

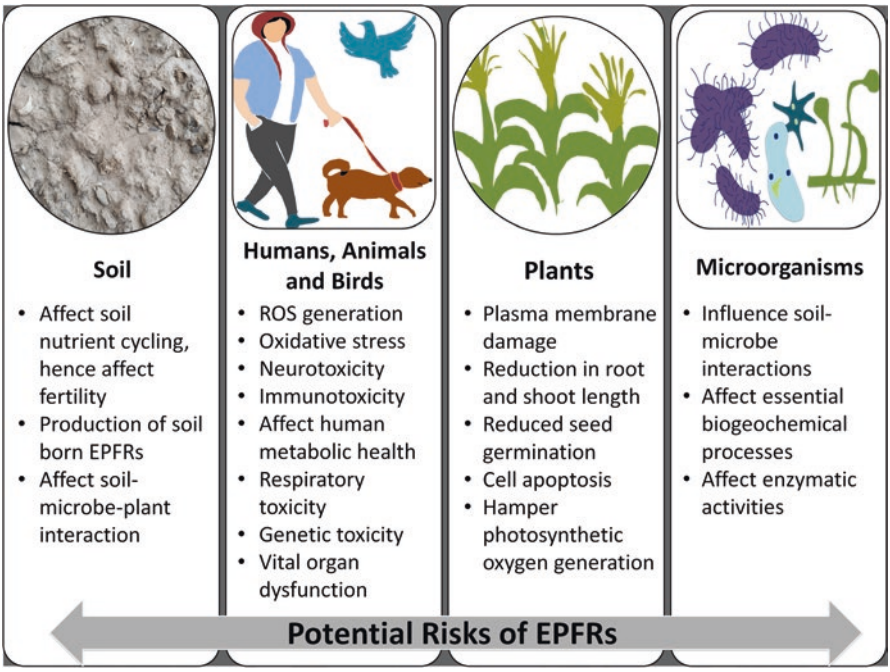


**Fig. 3** Toxic effects of EPFRs on biotic and abiotic components of environment

the soil matrix such as through weathering, runoff, and decomposition. Once in the soil and rhizosphere, free radicals take part in metal complexation and chemical redox reactions. They influence the soil–microbe interaction and essential biogeochemical processes. For example, the biochar derived EPFRs alter the soil microbe community and microbial and enzymatic activity. It directly affects the nutrient cycling (N, P, S) soil–microbe–plant relationship, soil organic matter turnover, and radical scavenging (Spokas et al. 2011). Other than these, pyrolysis and remediation processes are known to induce EPFRs' formation in soil, which might confer internalization led toxicity to soil microbes. Similarly, EPFRs may much easily and variously disseminate into the atmosphere resulting in their easy exposure to human and other lifeforms.

The stable free radicals are widespread in environment and are associated with various human diseases. The presence of phenoxyl type and semiquinone type species in PM induces the generation of activated species which cause human health risks through oxidative stress. Continued aerial persistence of EPFRs may variously lead to serious health complications. Numerous investigation have demonstrated that combustion derived stable radicals are responsible for declining human metabolic health (Xu et al. 2020). EPFRs are correlated with acute infections like respiratory toxicity and influenza virus infection and also chronic risks like pneumonia, DNA damage, and liver dysfunction. They are also reported to be causative agents

of cardiac arrest, cancer, aging, and escalated pulmonary pressure. The exposure of PM related radicals to humans have showed cardiovascular disease, respiratory dysfunction, and type II diabetes (Lord et al. 2011; Mahne et al. 2012). Chuang et al. observed the effect of bio-stable free radicals on mouse cardiomyocytes and found that radicals cause cell mortality by inducing oxidative stress and resulted in cell death. It showed that radical species in experimental animals leads to cellular stress and cardiac toxicity (Chuang et al. 2017). In another experiment, combustion derived radicals led to mitochondrial breakdown of muscles and reduced the energy expenditure. EPFRs also restrict the activity of native proteins in cells, cytochrome 450 – well known for breakdown of foreign bodies. The inhibition of cytochrome 450 will hinder the metabolism of extracellular substances (Reed et al. 2015). Like combustion-derived stable radicals, biochar-associated EPFRs produce the ROS species and reduce the levels of cellular enzymes such as superoxide dismutase and glutathione peroxidase, ultimately decreasing the cell membrane integrity.

The bio-stable radicals are not only toxic to humans and animals but also significantly affect the plants. They are linked with inhibitive traits like plasma membrane damage, reduction in root and shoot length, and reduced germination of seeds. Liao et al. performed experimental study to assess the effect of free radicals produced during biochar pyrolysis of rice straw, wheat, and corns on plant growth and germination. The electromagnetic paramagnetic resonance (EPR) spectra were obtained for original raw material and biomass formed biochar. EPR signal and intensity were only observed in biochar biomass, which even increased by increasing pyrolysis temperature. The root length, shoot length, and growth of test plants were evaluated on corn seedling. Significant retardation in root and shoot length, reduced seed germination, and plant growth was observed in plants exposed to biochar free radicals. In addition, ROS generated from EPFRs also reacted with membrane glycoproteins causing destabilization of cellular integrity and membrane thereby inducing cell apoptosis (Liao et al. 2014). The semiquinone type radical species were also reported to inhibit photosynthesis in plants. The mechanism of photosynthesis inhibition by EPFRs is mainly observed in major components of biochar, such as humic acid and lignin. They act as electron scavengers, altering electron transfer process and hampering photosynthetic oxygen generation in plants (Pflugmacher et al. 2006).

## 8 Role of EPFRs for Remediation of Organic Contaminants

The particle associated EPFRs are active oxidizing agents catalyzing various oxidants. They have potential to generate reactive oxygen species, which are active against organic contaminants. The free radicals effectively activate hydrogen peroxide or persulfate to produce ROS species such as superoxide, singlet oxygen, or $OH^-$. The activation of small intrinsic radical species induces the degradation of environmental organic pollutants (Fang et al. 2014; Yi et al. 2019). Fang and his colleagues studied the role of hydroxyl radical in biochar suspension for the degradation of diethyl phthalate in the presence of oxygen. The persistent free radicals

catalyze the electron transfer to oxygen producing $O^{2-}$and $OH^{-}$, which further induced the formation of hydroxyl radical for diethyl phthalate degradation. The results showed that in the presence of oxygen nearly 89–100% of diethyl phthalate (5.0 mg $L^{-1}$) was degraded in 24 h. Moreover, ROS species generated from EPFRs under UV radiation also exhibited potential to degrade diethyl phthalate. It was observed that 52.3–72.3% of diethyl phthalate was degraded in 2 hrs reaction time at pH 7.0 (Fang et al. 2015b). It was concluded that biochar derived EPFRs produces $OH^{-}$ and singlet oxygen for the diethyl phthalate degradation.

Following the same hypothesis, Yang studied the important role of $OH^{-}$ in the removal of organic contaminant p-nitrophenol (Yang et al. 2016). In another study, He and coworkers investigated the potential of activated persulfate in iron-porphyrin biochar for the degradation of perfluorooctanoic acid (PFOA). It was found that bioactive free radicals transfer electrons from persulfate to iron-porphyrin to speed up the formation of hydroxyl and sulfate radical. The addition of electronic circulation agent ascorbic acid increases the further rate of reaction. The results showed that in iron-porphyrins biochar-ascorbic acid system, 75.90% of PFOA was degraded in 30 min and reaching up to 90.88% when reaction time was increased (He et al. 2020). For the enhanced activation of persistent free radicals of biochar transition metals are added to further increase the removal of organic pollutants. Fang et al. assessed the effect of phenolic compound and transition metals addition for the formation of EPFRs. Results showed that loaded phenolic compounds and metals not only changed the type of biologically stable radicals but also elevated the concentration of EPFRs in biochar. Manipulation of biochar in this way by metals and phenolic compounds may interpret effective management of EPFRs and so can cater the transformation of organic contaminants (Fang et al. 2015a). In yet another study, a potential role of EPFRs in the remediation of soils contaminated with PAHs and coking byproducts is also documented. The potential role of EPFRs for the remediation of soil contaminated with PAHs and coking process byproduct was also investigated. The results suggested that EPFRs act as an electron shuttle for persulfate and induced the formation of ROS. The generated ROS back reacts with anthracene resulting in its oxidation and complete mineralization (Jia et al. 2018). The semiquinone type persistent radicals also play an important role in the removal of inorganic contaminants from environment. For instance, carbon centered radicals have potency to reduce heavy metal chromium. Similarly, Zhao et al. reported that modified biochar generates EPFRs, which then acts as electron donor for transformation of chromium (Zhao et al. 2018). The observed studies suggested the development of EPFRs-based remediation technologies for environmental pollutants.

## 9 Conclusions

EPFRs are ubiquitous pollutants of emerging concerns, formed of coupled particle pollutants system exhibiting toxicological implications. EPFRs' formation is primarily mediated by transition metals and organic compounds formed during

incomplete combustion or thermal processes. They are capable of inducing oxidative stress through ROS formation. In the past few decades, research investigation for the environmental occurrence and associated health risks of EPFRs has attracted increased research attention. Still the information and research regarding the persistent free radicals are at infant stage. This work provides detailed insight into sources, lifetime, types, decay, as well as toxicity of EPFRs. Based on available literature, we tried to fill the knowledge gaps about the environmental occurrence of EPFRs in various sources. The original data of published work on EPFRs is used to discuss and compare the formation mechanism of EPFRs mediated by different agents. The detailed outlook on the environmental factors affecting the EPFRs' formation such as precursors, process time, temperature, and light radiation provides a way to fully understand generation mechanism. The redox recycling of EPFRs imparts toxicity to surface-bound EPFRs, and considerable focus has been given to discuss the toxic effects of EPFRs on living forms including humans and plants. Recent research studies have provided insights into role of EPFRs for environment remediation. EPFRs possess property for the catalysis and activation of persulfate for producing ROS for the degradation of organic contaminants. Although EPFRs are long-lived environmental pollutants, the tendency to activate free radical generation can make them wide range environmental remediation tool.

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