Persistent organic pollutants (POPs), which are synthetic organic chemical compounds, either intentionally or unintentionally produced, have widely aroused public concern in recent years. These chemicals are toxic and major environmental concern due to their persistence, long range transportability, bioaccumulation and potentially adverse effects on living organisms. Uncontrolled inputs combined with poor environmental management often result in elevated levels of persistent organic pollutants in affected estuaries. Since the Stockholm Convention on POPs was adopted, different techniques have been extensively developed. A major focus revealed the need for low cost methods that can be implemented easily in developing countries such as electrochemical techniques. Persistent organic pollutants are known to be resistant to conventional treatment methods such as flocculation, coagulation, filtration and oxidant chemical treatment. However, various advanced wastewater treatment technologies such as, activated carbon adsorption, biodegradation using membrane bioreactor and advanced oxidation processes (AOPs) have been applied in the treatment of POPs.

**Keywords:** persistent organic pollutants, environmental contaminants, dioxins, biodegradation, wastewater treatment

**1. Introduction**

In the past decades, the health effects of environmental pollution on the population have been a growing source of worry around the world. According to the WHO (World Health Organization), one-third of the diseases afflicting humanity are caused by extended exposure to pollution. Since World War II, scientists have identified a number of chemical contaminants that are toxic, persistent in the environment, bioaccumulative, and prone to long-range atmospheric transboundary migration and deposition, and are expected to have serious health consequences for humans, wildlife, and marine biota both near and far from their source of emission. These toxins are chemical contaminants, also called the dirty dozen [1]. Being volatile substances, POPs evaporate into the air in warm regions of the globe, are transported by air currents up to cold regions and in mountainous regions where they condense [2, 3].
Most POP chemicals are non-polar organic compounds, consequently hydrophobic, with extremely low water solubility. In marine and terrestrial systems, they bind strongly to solids, particularly organic matter, evading the aqueous segment [4]. They are also lipophilic, which means that they accumulate in the fatty tissue of living animals and human beings. The stockpiling in fatty tissue allows the compound to persevere in biota, where the metabolism rate is low [5–8]. Due to the bioaccumulation and biomagnification phenomena, the POP concentration may be much higher in the tissues of the organisms (up to 70,000 higher concentrations). POP concentrations tend to rise as you travel up the food chain, therefore species at the top of the food chain, such as fish, predatory birds, mammals, and humans, have the largest concentrations of these chemicals and are thus at the greatest danger of acute and chronic harmful effects. POPs are mostly man-made chemical products intended to be used in various areas, for an example, in agriculture and industry, or unintentional by-products resulting from industrial processes, or from waste incineration. Different classes of POPs substances such as organochlorinated pesticides (OCP), polychlorinated biphenyl (PCBs), perfluorinated compounds (PFCs), brominated compounds (BFR), dioxins and furans are known. Most of these substances are anthropogenic origin. However, substances such as dioxins and furans may have natural origin (Figure 1), such as volcanic activities and vegetation fires [10–17].

Figure 1.
Classification of persistent organic compounds according to their origin. Picture adapted from [9].

2. Types of POPs

Many POPs were widely used during industrial revolution after World War II. However, many of these chemicals proved to be beneficial in pest and disease control, but they had unforeseen effects on human health and environment. In Stockholm 2001, representatives from 92 countries have agreed to sign the Stockholm Convention on POPs to reduce and/or eliminate the release of 12 original POP substances. More contaminants have been discovered; the main concern is over the original 12. These contaminants are the 10 intentionally produced chemicals: aldrin, endrin, chlordane, DDT, dieldrin, heptachlor, mirex, toxaphene, hexachlorobenzene (HCB) and PCBs and the two unintentionally produced substances polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans
Another type of interest also classified as persistent organic compounds is polycyclic aromatic hydrocarbons (PAHs). Combustion and burning of organic compounds produces these substances unintentionally. Their occurrences are related to anthropogenic processes, and contamination of PAHs in river sediment is especially serious in high-density industrial areas [18]. Persistent organic pollutants (POPs) are a group of chemicals that have been intentionally or unintentionally produced, and introduced into the environment as shown in Figure 2.

2.1 Intentional persistent organic pollutants

Intentionally produced chemicals currently or were once used in agriculture, manufacturing, disease control or industrial processes. These intentional POPs, shown in Figure 3, will be produced as wanted products by different chemical reactions that include chlorine. These types are organic molecules with linked chlorine atoms, high lipophilicity and, usually, high neurotoxicity, and they are called organochlorine compounds. Some of the well-known examples of organochlorine compounds are the chlorinated insecticides, such as dichlorodiphenyltrichloroethane, and polychlorinated biphenyls. They have several compounds which can be divided into two types that are industrial chemicals and organochlorine pesticides [22, 23].

2.1.1 Industrial chemicals

Polychlorinated biphenyls, very stable mixtures that are resistant to extreme temperature and pressure, are a group of manmade chemicals, oily liquids or solids, clear to yellow in color, with no smell or taste. They have been discovered in water, sediments, avian tissue, and fish tissue all throughout the planet. These chemicals make up a significant subset of special wastes. PCBs are a group of chemical compounds in which the biphenyl molecule has 2–10 chlorine atoms linked to it. When explaining PCBs, monochlorinated biphenyls (i.e., one chlorine atom bonded to the biphenyl molecule) are frequently mentioned. The chemical structure of chlorinated biphenyls is depicted in Figure 4. There are 209 distinct PCB congeners in theory. Many of them are resistant to degradation, allowing them to survive for lengthy periods of time in the environment and spread via air and water transport mechanisms [25–27].

Many industrial applications, such as fire-resistant transformers and insulating condensers, relied heavily on PCBs. Prior to 1977, they were utilized as heat exchanger fluids and in the fabrication of aluminum, copper, iron, and steel [27]. Apart from
their usage in the above applications, they were also applied as plasticizers in natural and synthetic rubber products, as well as adhesives, insulating materials, flame retardants, lubricants in the treatment of wood, clothing, paper, and asbestos, chemical stabilizers in paints and pigments, and as dispersing agents in aluminum oxide formulations. PCBs are frequently discovered in the effluent and sludge of municipal wastewater treatment plants. Although prohibited in the 1980s, PCBs are presently employed in transformers in some parts of the world, especially Brazilian [28, 29].

Figure 3. Intentionally persistent organic pollutants chemical structures. Adapted from [21].

Figure 4. Industrial POPs chemical structure. Adapted from [24].
2.1.2 Organochlorine pesticides

Organochlorine (OC) pesticides are typically man-made synthetic pesticides widely used all over the world. They belong to the group of chlorinated hydrocarbon derivatives, which have vast application in the chemical industry and in agriculture. Pesticides are a class of chemicals used to kill insects, weeds, fungi, bacteria, and other organisms. Insecticides, fungicides, bactericides, herbicides, and rodenticides are some of the terms used to describe them. The majority of pesticides may kill a wide range of pests and weeds, but some are targeted at specific pests or pathogens. Although these substances are typically man-made, plant derivatives and naturally occurring inorganic minerals are examples of exceptions that occur naturally. Since the first naturally occurring pesticide, nicotine derived from tobacco leaf extracts, was employed to control the plum curculio and the lace bug in the seventeenth century. Many chlorinated hydrocarbon insecticides were created in the 1940s, although they were not widely used until the 1950s. Aldrin, dieldrin, heptochlor, and endrin form part of the reported chlorinated hydrocarbon insecticides. However, in spite of their early promise, these organochlorine insecticides are now much less used because of their environmental pollution impact [30, 31].

Pesticides are employed for many different purposes. Pesticide use has increased due to increased agricultural production, resulting in increased pollution of environmental compartments such as soil, water, and air. Pesticide properties like high lipophilicity, bioaccumulation, long half-life, and potential for long-range transport have enhanced the risk of contamination in air, water, and soil, even after many years of use. This occurrence has the potential to become a long-term hazard to the ecosystem’s plant and animal groups’ coexistence. Pest problems result in the loss of nearly a third of the world’s agricultural productivity each year, despite the fact that pesticide consumption exceeds two millio liters each year. A study by Pimentel showed that only a small percentage (0.3%) of applied pesticides goes into the target pest while 99.7% go somewhere else into the environment [32].

Although the application of organochlorine pesticides has been forbidden for a considerable period in many countries, the residues continue to induce a significant impact on the environment and its ecosystems [33]. Overuse or misuse of pesticides has a negative impact on environmental health as well as ecosystem services. Many aquatic and terrestrial animals, have been documented to be toxicated by pesticides. Pesticides have a negative impact on aquatic ecosystems, including microbes, animals, plants, and fish [34–38].

During the last three or four decades, insecticide manufacturing has been rather constant. Insecticides and fungicides, on the other hand, are the most important pesticides for human exposure in food since they are sprayed just before or after harvesting. Herbicide output has risen as chemicals have increasingly supplanted land cultivation in weed management, accounting for the majority of agricultural pesticides. Large amounts of pesticides have the ability to enter water either directly, as in mosquito control applications, or indirectly, as in drainage of agricultural lands [39–41].

DDT was widely employed during World War II to protect soldiers and civilians from malaria, typhoid, and other diseases caused by insects before its insidious effects on humans and wildlife were discovered. DDT was employed to manage disease after the war, and it was sprayed on a number of agricultural crops, particularly cotton. It did the job, reducing the threat of malaria and the loss of income to the agriculture industry [42]. DDT continues to be applied against mosquitoes in several countries to control malaria. Its stability, its persistence, and its widespread use have meant that DDT residues can be found everywhere; residual DDT has even been detected in the Arctic.
2.2 Unintentionally POPs

Unintentionally produced chemicals (see Figure 5) are a result of combustion of medical waste, incarnation and some industrial processes. They are divided into three types, viz., polycyclic aromatic hydrocarbons (PAHs), dioxin and furan compounds.

2.2.1 Polycyclic aromatic hydrocarbons (PAHs)

PAHs are ubiquitous group of several hundreds of chemicals that comprise two or more fused benzene rings in linear, angular or cluster arrangements, containing only carbon and hydrogen. The central molecular structure is held together by stable carbon-carbon bonds. They are mostly caused by incomplete combustion of natural or man-made fuels such as coal and wood, as well as vehicular pollutants and cigarette smoke [44]. Dietary exposure accounts for more than 70% of human exposure in non-smokers [45]. According to a dietary survey conducted in the United Kingdom, cereals and oils/fats account for a significant portion of PAH intake [46]. Typical PAH contamination occurs when food is subjected to combustion products in technical procedures such as direct fire drying [47]. High PAH concentrations in charcoal grilled/barbecued foods may also result from certain traditional home cooking methods such as grilling, roasting, frying, and smoking [48]. However, the greatest amounts of PAHs released into the environment are via anthropogenic processes like fossil fuel combustion and by-products of industrial processing. The Environmental Protection Agency (EPA) of the United States included 16 PAHs on a priority pollutants list because they are considered potential or probable human carcinogens. As a result, their dispersal and the likelihood of human exposure have received a lot of interest. PAHs have been found in soil, air, and sediments, as well as on a variety of food and beverage products [49–51].

2.2.2 Dioxins and dibenzofurans

Polychlorinated dibenzo-\(\text{p}\)-dioxins (PCDDs), dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) constitute three groups of relevant persistent organic pollutants with enhanced chronic toxicity. PCDD/Fs (Figure 6) are emitted by a

Figure 5.
Unintentional produced POPs chemical structures. Adapted from [43].
variety of human activities and industrial processes, and can be referred as undesirable by-products. PCBs are ubiquitous environmental pollutants as a result of their large-scale manufacture till the end of the 1980s and their continued use. PCDD/Fs and PCBs can also be released from stationary sources such as waste incineration and biomass and fossil fuel combustion. PCDD/Fs and PCBs can be considered environmental markers of anthropogenic activities in light of this information, as their occurrence is invariably linked to human activities. PCDDs and PCDFs, commonly called “dioxins”, are two classes of “quasi-planar” tricycles aromatic ethers with 210 different compounds (congeners) in total [53].

PCDDs and PCDFs are solids at room temperature and have a rather low volatility. Dispersion in the atmosphere is thus likely to occur mainly in particulate aerosols. The PCDD/F have been of concern for decades because of their toxic properties. A structurally similar series of compounds, the chlorinated dibenzo-furans (furans), have similar chemical properties and toxic effects. The most toxic and most extensively studied representative of the chlorinated dioxins (PCDDs) is 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). In recent years there has been a growing trend to include a specific subgroup of PCBs, the so-called dioxin-like PCBs (Figure 5) which has finally been added to methods along with the dioxins and furans. It is widely acknowledged that man-made sources and activities contribute far more to the environmental burden of PCDDs and PCDFs than natural processes, particularly since the 1930s, when environmental levels have steadily increased in tandem with the large-scale production and use of chlorinated chemicals [54, 55]. Chemical processes, combustion processes, and secondary sources are the three primary categories of man-made sources of PCDDs and PCDFs [56].

3. Sources of POPs

In the past decades, many reports on the dependents of POPs by industry and agricultural sectors were seen. POPs proved to be beneficial in pest and disease control, crop production, and industrial applications. Many were widely used commercially during the boom in industrial production after World War II, resulting in wide geographical distribution. Figure 7 shows some of the sources related to POPs [57].

POPs are extremely stable in all environmental elements. They are discharged into the atmosphere through a variety of industrial sources, including power plants, heating plants, and incinerating facilities, as well as from domestic furnaces, transportation, agricultural sprays, and evaporation from water surfaces, soil, and landfills. Other sources of POPs compounds, such as inadvertent generation, can be present in incinerations, chemical plants, other combustions, forest fires, putrefaction, and PCB-containing wastes. This type of trash can be found in a variety of
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Figure 7.
Schematic depicting POPs in the environment and main environmental processes during long-distance atmosphere transport, bioaccumulation, and biomagnification. Adapted from [57].

Wastewaters from plants generating or using POPs, as well as runoff from fields and roads, and atmospheric deposition, are the origins of pollutants, oil, fates, liquid fuels, dirt, ash, and silt entering the water system. Oceans and seas are their greatest reservoirs, where they collect from river sediments, air deposition, trash disposal, and accidents. They are retained in sediments on the bottoms of seas,

Figure 8.
Conceptual model for the behavior of persistent organic pollutants in the air-plant soil system. Adapted from [60].
oceans, and huge lakes, where they can be released and re-enter the atmosphere after a period of time, as indicated in Figure 8 [42, 60].

4. Methods for treatment of persistent organic pollutants

POPs have adversely posed a health concern worldwide for ages. Due to their concerning health issues, some countries have resorted to reduce the use of chemicals or processes that produce POPs, while others have prohibited them entirely. However, most processes that result in the production of POPs are beneficial to both human and environmental health. This is because some POPs are produced during production of synthetic chemicals for crop production, medication, clothing etc. In addition, some POPs are unavoidable since they may be produced unintentional from simple combustions. Since most of these POPs end up in water streams, various methods for wastewater treatment have been implement and reported in literature. These methods ensure the conversion of wastewater into portable water by removing harmful and hazardous chemicals [61]. Conventional treatment refers to some of the most effective water treatment procedures used in the service and distribution of industrial or municipal potable water. At different stages of a typical treatment method, any of the physical, chemical, or biological channels provide good combination.

Preliminary, primary, secondary, and tertiary wastewater treatment stages are in sequence of increasing treatment level, with final pH adjustments as needed. The chosen conventional approach must be able to meet the regulatory authority’s recommended microbiological and chemical criteria while operating and maintaining at a low cost [62].

Conventional treatment methods such as flocculation, coagulation, filtration, and oxidant chemical treatment are ineffective against POPs. The chemical properties of POPs, such as, low water and high fat solubility, stability to all degradation processes and low vapor pressure, are the main components for their efficiency as pesticides and for their persistence in the environment [63]. The inability in some instances to remove POPs from wastewater using conventional methods have prompted scientists to develop other methods. Various advanced wastewater treatment technologies such as, activated carbon adsorption, biodegradation using membrane bioreactor [64] and advanced oxidation processes [65] have been applied in the treatment of POPs. This is because of growing number of emerging POPs that are being identified in water and the concerns that are accompanied by human and environmental health hazard [66]. Various setbacks such as cost, sophisticated instrumentation, low degradation efficiency, generation of toxic secondary chemicals and massive sludge production have recently been addressed using advanced methods and technologies. Below is the short discussion of biodegradation and advanced oxidation processes wastewater treatment technologies.

4.1 Biodegradation

Biodegradation is an evolving technology that comprises the application of selected living microorganisms to degrade, metabolize/immobilize any unwanted substances such as pesticides, organic pollutants and hydrocarbons from soil and water, to improve its quality [67]. Although every microorganism has the ability to eradicate pollutants, only few particular or engineered microorganisms are used broadly to eradicate pollutants efficiently. Bioremediation technology, applied in perspective to POPs removal, takes into consideration the following methods: (1) bioventing: aerating water to stimulate in situ biodegradation of organic
contaminants and promote bioremediation, (2) biostimulation: modification of contaminated media to provide the nutrition to soil microbiota by adjusting pH, addition of limiting nutrient to improve C: N: P ratio, and (3) bioaugmentation: addition of microbial community (bacteria and fungi) and any biocatalyst (gene and enzyme) to degrade organic/inorganic pollutants [68]. One of the most important variables in the efficient breakdown of petrochemical wastes in a given ecosystem is microorganism selection. It is because only those microbial species are adapted to work in that specific habitat. Likewise, intermediates created during photocatalytic degradation processes are harmful to a variety of creatures in the environment [69].

Currently, the membrane bioreactor does not always achieve the desired results in the treatment of POPs, and it performs poorly in the removal of non-biodegradable aliphatic and aromatic hydrocarbon compounds, halogenated organic compounds, organic dyes, pesticides, and phenols and their derivatives. The process technicalities and economic feasibilities are the two most significant assessment elements for achieving the goal in wastewater treatment technology [70].

4.2 Advanced oxidation processes

The use of conventional methods is not wholly accepted nowadays because of the high costs and operational problems. Consequently, it is necessary to adopt modern systems like advanced oxidative processes (AOPs) [71]. Some of the AOPs’ characteristics include: (1) potential capacity for mineralization of organic pollutants to carbon dioxide and water, as well as oxidation of inorganic compounds and ions such as chlorides, nitrates, and others; (2) non-selective reactivity with the vast majority of organic compounds, which is particularly appealing to avoid the presence of potentially toxic by-products from the primary pollutants that can be produced by other methods that do not achieve complete oxidation [65]. Some of the AOPs discussed below.

4.2.1 Catalysts in advanced oxidation processes

AOPs have successfully used both homogeneous and heterogeneous catalysts. Heterogeneous systems have obvious advantages over homogeneous systems, such as the ability to separate the catalyst easily for reuse from the treated water, the lack of a secondary treatment to remove dissolved metals from the treated water, and the ability to withstand extreme operating conditions. The system is also effective over a broader pH range including the common pH for natural water and wastewater (pH 2–9) [72].

The AOPs, as water treatment processes, are performed at pressure and temperature close to environmental conditions. They involve the generation of hydroxyl radicals in sufficient quantity to interact with the organic compounds of the medium. Hydroxyl radicals are the best of the powerful oxidants because they meet a number of criteria, including: (1) they do not generate additional waste; (2) they are not toxic and have a short lifetime; (3) they are not corrosive to equipment; and (4) usually produced by easy-to-manipulate assemblies [73]. The following are some of the most common approaches used for this purpose: UV alone, UV/H\textsubscript{2}O\textsubscript{2}, UV/Fe\textsuperscript{3+}, UV/H\textsubscript{2}O\textsubscript{2}/Fe\textsuperscript{3+}, UV/O\textsubscript{3}, UV/S\textsubscript{2}O\textsubscript{8}\textsuperscript{2−}, UV/TiO\textsubscript{2}, UV/chlorine and UV in combination with other photocatalysts. The major issue is the removal efficiency of specific target contaminants by the UV AOPs. UV AOP removal rates vary depending on the molecular structure of the pollutants, both in terms of direct photolysis and radical processes. Furthermore, water matrix effects have a significant influence on removal rates. As a result, each UV AOP system must be individually controlled.
in line with its water matrix and targeted contaminant removal for optimal POPs control [74]. In most situations, the UV/chlorine oxidation process outperformed UV alone or chlorination, according to Xiang et al. [75]. During the UV/chlorine reaction, hydroxyl and Cl radicals were produced, with the hydroxyl radical taking the lead in the oxidation process. Its contribution to the rate of diuron degradation was calculated to be 28.95%.

4.2.2 Photo-Fenton oxidation

Most AOPs use a combination of oxidants and irradiation (O$_3$/H$_2$O$_2$/UV) or a catalyst and irradiation (Fe$^{2+}$/H$_2$O$_2$/UV/TiO$_2$) to achieve their goals. The disadvantages that make them economically undesirable vary depending on the AOP are: (1) high electricity demand (for example, ozone and UV-based AOPs), (2) relatively large volumes of oxidants and/or catalysts (for example, ozone, hydrogen peroxide, and iron-based AOPs), and (3) pH operating conditions (e.g. Fenton and photo-Fenton) [76]. Photo-Fenton oxidation system has been identified as a feasible oxidation system for treating these wastewaters. In Fenton and Fenton-like reactions, hydroxyl radicals are usually generated from H$_2$O$_2$ catalyzed by iron (Fe$^{2+}$, α-Fe$_2$O$_3$, Fe$_3$O$_4$, H$_2$Fe$_2$O$_4$, α-FeOOH, etc.) [77]. Nonetheless, the cost effectiveness is one of the major concerns. However, the cost reduction can be obtained through application of heterogeneous catalysts, chelating agent, solar energy and integration with biological treatment technologies [78].

4.2.3 Electrochemical oxidation processes

Electrochemical oxidation procedures, among the numerous AOPs, are gaining popularity for water and wastewater decontamination due to their low cost and high efficiency. Dissolved organic contaminants are primarily oxidized in electrochemical oxidation processes by (i) direct anodic oxidation on the anode surface via charge transfer, and (ii) interaction with physio- and/or chemisorbed hydroxyl radical produced during water oxidation [79]. Electrochemical AOPs have been widely explored for the total degradation of POPs. The electrochemical oxidation is an effective and environmentally friendly technology because it does not require chemicals, only electric current is consumed. The first one is direct oxidation which occurs when the compound reacts directly at the anode’s surface or by physisorbed or chemisorbed •OH. The second mechanism is indirect oxidation, which is achieved through the electrochemical generation of a mediator in the bulk solution such as ozone (O$_3$), hydrogen peroxide (H$_2$O$_2$), active chlorine, active bromine or S$_2$O$_8^{2-}$, among others [80].

Recently, coupling approaches including an electrochemical pre-treatment followed by a biological process have been proposed as cost-effective and reliable remediation methods for persistent chemicals mineralization. This opens the door to more selective electrochemical methods than those involving hydroxyl radicals do, because the goal of the pre-treatment is no longer to achieve total mineralization of non-biodegradable species, but rather to improve their biodegradability by focusing on functional groups that have been shown to reduce biodegradability [81].

4.2.4 Nanofibers

In the one-time elimination of POPs, nanofibers have demonstrated to be the most effective. These adsorbents, on the other hand, demonstrate adaptability in the collection of pollutants. The use of fiber layers with varied pore channels and surface chemistry to produce selectivity for a target chemical could be researched
Because adsorption is a common water treatment method, the production and operational costs of adsorbent materials are crucial to the introduction of any new classes of materials [82]. Physically and chemically stable carbon-based materials alone (without metals) have also been successfully used as the electro-catalysts [83]. Inexpensive, non-noble transition metals or their oxides supported in carbon nanotube has been reported for treatment of POPs. Bismuth-based nanocomposites [84], copper-reduced graphene oxide electrode [85], boron-doped diamond [86], with different boron and substrate silicon or niobium content [87] have indicated to be an efficient technology for treating POPs wastewater.

5. Conclusions

The POPs are organic compounds of anthropogenic origin, and are resistant to environmental degradation through chemical, biological, or photolytic processes and as a result, accumulate in the food chain. Contamination by POPs is widespread, and circulate globally via the atmosphere, oceans, and other pathways. The Stockholm Convention defines criteria for new POP candidates in terms of their persistence, long-range transport, bioaccumulation and toxicity. Recognizing the dangers of POPs, countries began limiting their production, use, and release. This global, legally binding agreement is to reduce and eliminate the release of 12 POPs, including pesticides and industrial chemicals, as well as unintentionally produced POPs. Conventional water treatment facilities have failed to effectively degrade persistent contaminants from wastewater. However, advanced water treatment options such as activated carbons, membrane bioreactors and advanced oxidation processes are well documented for their capital intensive treatment of these recalcitrant pollutants.

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Conflict of interest

Authors report no conflict of interest.
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