APPENDIX A
A Review of Environmental Pollution from the Use and Disposal of Cigarettes and Electronic Cigarettes: Contaminants, Sources, and Impacts

Marc W. Beutel,1* Thomas C. Harmon,1 Thomas E. Novotny,2 Jeremiah Mock,3 Michelle E. Gilmore,1 Stephen C. Hart,4 Samuel Traina,1 Srimanti Duttagupta,5 Andrew Brooks,6 Christopher L. Jerde,6 Eunha Hoh,2 Laurie C. Van De Werfhorst,7 Van Butsic,8 Ariani C. Wartenberg,8 Patricia A. Holden7

1 Environmental Systems Graduate Group, University of California, Merced, CA
2 School of Public Health, San Diego State University, San Diego, CA
3 Institute for Health and Aging, University of California, San Francisco, CA
4 Department of Life & Environmental Sciences and Sierra Nevada Research Institute, University of California, Merced, CA
5 San Diego State University Research Foundation, San Diego State University, San Diego, CA
6 Marine Science Institute, University of California, Santa Barbara, CA
7 Bren School of Environmental Science & Management, University of California, Santa Barbara, CA
8 Environmental Science, Policy and Management Department, University of California, Berkeley, CA
Review

A Review of Environmental Pollution from the Use and Disposal of Cigarettes and Electronic Cigarettes: Contaminants, Sources, and Impacts

Marc W. Beutel 1,*, Thomas C. Harmon 1, Thomas E. Novotny 2, Jeremiah Mock 3, Michelle E. Gilmore 1, Stephen C. Hart 4,5, Samuel Traina 1, Srimanti Duttagupta 2,6, Andrew Brooks 7, Christopher L. Jerde 7, Eunha Hoh 2, Laurie C. Van De Werfhorst 8, Van Butsic 9, Ariani C. Wartenberg 9 and Patricia A. Holden 9

1 Environmental Systems Graduate Group, University of California, Merced, CA 95343, USA; tharmom@ucmerced.edu (T.C.H.); mgilmore61@gmail.com (M.E.G.); straina@ucmerced.edu (S.T.)
2 School of Public Health, San Diego State University, San Diego, CA 92182, USA; tnovotny@sdsu.edu (T.E.N.);
3 Institute for Health and Aging, University of California, San Francisco, CA 94110, USA;
4 Department of Life & Environmental Sciences, University of California, Merced, CA 95343, USA; shart4@ucmerced.edu
5 Sierra Nevada Research Institute, University of California, Merced, CA 95343, USA
6 San Diego State University Research Foundation, San Diego State University, San Diego, CA 92182, USA
7 Marine Science Institute, University of California, Santa Barbara, CA 93106, USA;
8 Bren School of Environmental Science & Management, University of California, Santa Barbara, CA 93106, USA; lvandewerfhorst@bren.ucsb.edu (L.C.V.D.W.);
9 Environmental Science, Policy and Management Department, University of California, Berkeley, CA 94720, USA; vanbutsic@berkeley.edu (V.B.); awartenberg@berkeley.edu (A.C.W.)

* Correspondence: mbeutel@ucmerced.edu

Abstract: While the impacts of cigarette smoking on human health are widely known, a less recognized impact of tobacco product use and disposal is environmental pollution. This review discusses the current literature related to cigarette and e-cigarette contamination in the context of environmental sources and impacts, with a focus on the documented influences on biota, ranging from bacteria to mammals. Cigarette butts and electronic cigarette components can leach contaminants into soil, water, and air. Cellulose acetate cigarette filters comprising the butts are minimally degradable and are a source of bulk plastic and microplastic pollution, especially in aquatic ecosystems where they tend to accumulate. Cigarette combustion and aerosol production during e-cigarette use result in air contamination from sidestream, exhaled, and third-hand pathways. The chemical byproducts of tobacco product use contaminate wastewater effluents, landfill leachates, and urban storm drains. The widespread detection of nicotine and cotinine in the environment illustrates the potential for large-scale environmental impacts of tobacco product waste. Studies show that cigarette butt leachate and nicotine are toxic to microbes, plants, benthic organisms, bivalves, zooplankton, fish, and mammals; however, there remain critical knowledge gaps related to the environmental impacts of tobacco product waste on environmental health and ecosystem functioning.

Keywords: cigarette butts; cotinine; environmental contamination; microplastics; nicotine; tobacco product waste

1. Introduction

Tobacco product use is extensive and continues to grow worldwide (Figure 1). Over six trillion conventional combustible cigarettes are produced and consumed globally each year [1,2]. In addition, the use of electronic cigarettes (e-cigarettes) has increased dramatically, and sales of e-cigarettes are growing rapidly [3]. In the United States (USA),
approximately 60 million e-cigarettes and refills are sold annually, and one-third of these are designated single use [4]. E-cigarettes are especially popular among youth and young adults [5-7]. Other practices that are growing in popularity include waterpipe smoking [8] and the use of heated tobacco products, which are new forms of nicotine delivery systems recently approved by the US Food and Drug Administration [9].

Figure 1. The planet as cigarette waste. Reproduced with permission from Bridget Parlato, Full Circuit Studio, 2021.

The impacts of cigarette smoking on human health are widely known, with tobacco-attributable deaths of around eight million per year globally, or one in ten deaths annually [10]. A less recognized effect of tobacco product use and disposal is the indirect impact on human welfare from environmental pollution, which may impair the provision of critical ecosystem services such as clean water, clean air, and food production [11]. Smoke, tar (the particulate fraction of tobacco smoke), and waste from cigarettes and e-cigarettes contain numerous toxic compounds, including nicotine, polycyclic aromatic hydrocarbons (PAHs), and metals. Trillions of pollutant-containing cigarette butts (CBs) are discarded to the environment annually, making CBs ubiquitous waste items worldwide, especially in coastal regions [1]. CBs can leach pollutants into the soil, surface water, and groundwater as they age and break apart, exposing biota to a range of contaminants, some of which may bioaccumulate in food webs [12,13]. CBs themselves largely consist of filters made of cellulose acetate, a synthetic polymer that is resistant to biodegradation, making CBs significant sources of fibrous plastic pollution to the environment [14]. Waste associated with e-cigarettes includes replaceable capsules with concentrated nicotine residuals, batteries, and electronic circuitry that can also leach pollutants into water and soil [15]. Areas frequented by adolescents and young adults, including schools, are hot spots for e-cigarette debris, much of which originates from the use of flavored tobacco products [16].
The objective of this review is to expand beyond the recent focus on CBs and discuss the current literature related to cigarette and e-cigarette contamination regarding environmental sources and impacts, with a focus on the documented influences on biota, ranging from bacteria to mammals. The paper complements recent papers and reviews focused on the significance of CB disposal to the environment \cite{1,11,13,17,18} and the environmental footprint of the tobacco supply chain \cite{11}. While waste from the consumption of tobacco products includes a wide range of items such as packaging, combustion initiators (e.g., matches and lighters), water pipes, and smokeless tobacco products, this paper focuses on the environmental contamination from conventional combustible cigarette and e-cigarette use and disposal. Cited sources herein are predominantly peer-reviewed studies but include some governmental reports and books; most sources were published after 2010.

The review first presents an overview of the chemical makeup of environmental contamination associated with cigarette- and e-cigarette-related waste, focusing on nicotine and cotinine, tobacco-specific nitrosamines (TSNAs), polycyclic aromatic hydrocarbons (PAHs), and metals. Next, we discuss key sources of cigarette- and e-cigarette-related contaminants and waste to the environment, including air contamination from combustible cigarettes, smoked CBs, e-cigarette waste, and from waste management systems such as wastewater treatment plants and landfills. We then discuss the impacts of these contaminants and waste on biota, including microorganisms, plants, animals, and humans, acknowledging that these indirect effects on ecosystem health differ in scope from the direct health effects of tobacco use. We also discuss the potential economic impacts associated with cigarette- and e-cigarette-related waste in the environment. We conclude by highlighting key findings and knowledge gaps associated with cigarette- and e-cigarette-related waste in the environment.

2. Contaminants

2.1. Nicotine

The alkaloid nicotine (3-(1-methyl-2-pyrrolidinyl)pyridine) is one of the most abundant chemicals in tobacco products. Cigarettes contain ~7–15 mg each, depending on the brand \cite{19}. At most, an estimated 20% of that nicotine is absorbed systemically by smokers \cite{20}, with the balance of the nicotine and its transformation products being re-leased with combustion products or retained on the cigarette filter. Nicotine contamination pathways to environments exist throughout the tobacco life cycle, from tobacco cultivation and cigarette production \cite{2} to cigarette combustion \cite{21}, CB disposal \cite{1,2,13}, and the passage of nicotine and its metabolites, primarily as cotinine and trans-3’-hydroxycotinine, into human wastewater streams \cite{22}.

Due to its historical use as a fumigant and pesticide, the vapor pressure of nicotine has been well-characterized. At ambient temperatures, its volatility is relatively low (~5.6 Pa at 25 °C). This is about 35 times less than the vapor pressure of 1,4-dichlorobenzene (1,4-DCB), a common ecotoxicity benchmark chemical; however, like most compounds, the vapor pressure of nicotine increases appreciably with the increasing temperatures associated with tobacco combustion \cite{23}. Whether nicotine is dispersed in significant quantities as a vapor depends on environmental conditions. The nicotine molecule has two basic nitrogen groups (pK\textsubscript{a1} = 3.12, pK\textsubscript{a2} = 8.02 at 25 °C) and can exist as a neutral free base, or as monoprotonated and diprotonated salts. The free-base form of nicotine has a greater tendency to partition from the water or solid phase to the air phase. For example, an ammonia addition to cigarette tobacco can elevate the pH during tobacco combustion, resulting in a decrease in nicotine partitioning onto smoke particles as speciation shifts to the more volatile, free-base form \cite{24}.

In aquatic systems, nicotine fate and transport have not been well studied. In most natural waters, the monoprotonated form is dominant and water miscible; however, the fraction of free-base increases under more alkaline conditions. The free-base form is relatively soluble in water, but also retains some hydrophobicity as indicated by its significant octanol–water partitioning coefficient value (log K\textsubscript{ow}~1.2) \cite{25,26}, that for comparison, is
lower than that for the benchmark nonpolar toxicant 1,4-DCB (log $K_{ow}$ ~3.4). The partitioning of the nicotine from water to environmental solids, or its bioconcentration potential, is strongly affected by pH. Under acidic to neutral conditions, nicotine is ionized and less prone to partition into organic matter or lipids (log $K_{ow}$ < 0.2) [27]. Nicotine tends to adsorb to charged surfaces such as bentonite clays [28] and engineered ion exchange resins [29]. Under basic conditions, significant nonionized, free-base nicotine is present and more prone to partition into organisms [20]. There is limited information regarding the abiotic and biotic transformations of nicotine in the environment. Relatively rapid photocatalytic oxidation has been demonstrated under laboratory conditions [30]. Half-life values estimated in a laboratory study of monoprotonated nicotine (pH 6.5–7.0) ranged from months to a year [31]. A study by the R.J. Reynolds Tobacco Company reported nicotine hemisulfate biodegradation half-lives of ~3 d in aerobic soil slurries and 0.5 d in unacclimated activated sludge incubations [26], which likely promote higher degradation rates relative to actual, more static environmental conditions.

2.2. Tobacco-Specific Nitrosamines

Nicotine and other tobacco alkaloids produce additional toxic and potentially carcinogenic transformation products, TSNAs, that are formed in the post-harvest curing process and during combustion [32]. During the tobacco curing process, TSNAs are products of reactions between nicotine and nitric acid. The main TSNAs of concern in tobacco are nitrosoanabasine (NAB), nitrosoanatabine (NAT), N’-nitrosonornicotine (NNN), and 4-(methylnitrosamo)-1-(3-pyridyl)-1-butano (NNK). All four have been found in substantial levels in tobacco smoke and in lesser amounts in e-cigarette aerosol [33]. NNN and NNK are the most carcinogenic [32]. Tobacco includes other TSNAs, including nitrosamines 4-(methylnitrosamo)-1-(3-pyridyl)-1-butanol (NNAL), 4-(methylnitrosamo)-4-(3-pyridyl)-1-butanol (iso-NNAL), and 4-(methylnitrosamo)-4-3-pyridyl) butyric acid (iso-NNA). Tobacco smoke tar is known to include non-volatile nitrosamines [34]. TSNAs are also formed in surface-catalyzed reactions on fine particulate matter on indoor surfaces [21, 35] producing third-hand smoke (THS) hazards [36]. Third-hand smoke (THS) encompasses the pollutants on surfaces and in dust after tobacco has been smoked in a closed environment [37]. Ramírez et al. found TSNAs in nonsmokers’ homes in addition to smokers’ homes, indicating that ambient air can act as the common source [21]. Little is known about the transport and fate of TSNAs in outdoor air and surfaces, and in aquatic ecosystems.

2.3. Polycyclic Aromatic Hydrocarbons

PAHs are organic compounds comprised of multiple aromatic rings and are produced by the incomplete combustion of organic matter. Mainstream and second-hand smoke (SHS) contain numerous PAHs that mainly reside in the particulate tar fraction [34, 38, 39]. Tobacco smoke tar contains around 0.02% PAHs by mass [38]. While many PAHs in tar are carcinogenic, they alone do not account for the toxicity of tobacco smoke tar, pointing to the complex nature of this substance [38]. The three most abundant PAHs in tobacco smoke tar are the low molecular weight two-ring naphthalene, and the three-ring PAHs fluorene and phenanthrene. The high molecular weight prototypic PAH benzo[a]pyrene, a five-ring PAH, is classified as a Group 1 carcinogen to humans. PAHs are nonpolar and hydrophobic, and many PAHs, especially those of lower molecular weight, are reasonably water soluble, volatile and biodegradable by soil and aquatic microorganisms [40, 41]. PAHs tend to accumulate on particles in environments, such as smoke, dust, soil and sediment that facilitate PAH transport in the atmosphere [42] and in soils and groundwater [43]. Once in environments, the fate of the PAHs depends on the physical properties of the specific PAH, temperature and moisture conditions. PAHs can persist for decades in environments when they are strongly sorbed to soil and less bioavailable, or present at higher concentrations or agglomerated states in contaminated industrial sites [44, 45].
Laboratory and field studies demonstrate that PAHs are primary tobacco-related contaminants and that CBs release PAHs into environments, presumably from captured tar [1,46–48]. Dobaradaran et al. measured 16 PAHs in freshly smoked CBs, week-old CBs from city streets, and aged CBs in urban river areas, and found that concentrations decreased with CB age [46]. The results also showed that the concentrations of PAHs with fewer rings decreased with time, a finding attributed to the relatively greater water solubility and volatility of these compounds. For example, mean levels of naphthalene (two-ring PAH) dropped from 5.8 to 2.9 to 0.8 mg/kg in each of the three CB samples. In contrast, levels of the potent carcinogen benzo[a]pyrene (five-ring PAH) remained constant at ~1.3 µg/g. Being a byproduct of tobacco combustion in cigarettes, the range of PAH molecules associated with CBs has substantial overlap with that from other sources, such as fuel combustion in urban settings; however, a study of roadside environments, high-density disposal sites for CBs, has identified significant levels of CB-derived PAHs in these areas, particularly the smaller 3- and 4-ring PAHs along with benzo[a]pyrene [49]. While these studies clarify the general behavior of PAHs in CBs, the release rates of PAHs from CBs and their persistence with aging in environments are not well understood.

2.4. Metals and Metalloids

The tobacco plant, Nicotiana tabacum, can readily accumulate metals from soil [50–52]. As a result, manufactured tobacco products such as cigarettes can be enriched in metals, and their subsequent consumption and disposal can be an additional source of metal pollution to the environment [53–55]. While essentially all elements present in soil can be found in tobacco plant tissue and many of these are of concern regarding human exposure via cigarette smoke, a subset are also of potential concern to the natural environment. These include the metals cadmium, chromium, lead, mercury, nickel, and zinc, and the metalloid arsenic. All these elements occur naturally in soil, but elevated concentrations are attributed to the presence of underlying marine sediments, agronomical applications of municipal or industrial wastes, the presence of mine tailings or smelter residues, excessive use of naturally contaminated phosphorus fertilizers, and atmospheric deposition [55–57].

The bioavailability of metals is commonly linked to their dissolved concentrations in soil solutions or aqueous environments [38]. Metals are surface reactive and sorb to organic and inorganic surfaces in soils and sediments. Cadmium, lead, nickel, and zinc are most commonly present in solution as divalent cations, both as free aqueous ions and complexed with organic or inorganic ligands. The aqueous solubility of these solutes increases with a decreasing solution pH. Arsenic and chromium can exist in multiple oxidation states under typical environmental conditions. Lower oxidation state species tend to follow the general pH-dependent trend seen for the divalent cations. Higher oxidation state species typically complex with oxygen to form oxyanions. These negatively charged species routinely exhibit increasing solubility, mobility, and bioavailability with an increasing solution pH in soil, sediment, and aquatic environments [59].

Upon tobacco combustion, metals can be released in smoke and tar [34,60–62], captured by the CB filter material, or remain in the resulting ash [63]. The fraction of these elements remaining in the filter is subject to leaching into terrestrial and aquatic environments [49,62–67]. Several metallic materials are also used in the construction of e-cigarettes, resulting in the presence of toxic metal ions in e-liquids and in vapors produced by these devices [68–73]. The inappropriate disposal of e-cigarettes can pose a significant source of toxic metals to both terrestrial and aquatic environments, as do many electronic consumer devices [74]. The association of metals with nanoparticles is notable, as such particles may be more readily transported through soil and sediment than relatively reactive metals that are fully dissolved [75,76]. The amount of toxic metals released globally to the environment from the leaching of CBs may be significant [65,76]. Chevalier et al. report that CBs could release millions of tons of chromium and nickel into the environment annually [76].
3. Contaminant Sources

3.1. Cigarette Butts

CBs, which in addition to the filter can include tobacco remnants, ash, and chemicals and tar from tobacco smoke, are the most prevalent forms of solid tobacco product waste worldwide. An estimated 4.5 trillion CBs are littered each year into the environment [13], commonly in urban districts near hospitality venues, public transportation hubs, and entrances to educational facilities and playgrounds [77]. Many littered CBs find their way into urban waterways [46,78] and coastal environments [1]. The Ocean Conservancy reported collecting 4.2 million CBs during their 2019 annual International Coastal Cleanup, the second most collected item of the event [79]. Given their ubiquitous presence and persistence in the environment, there is growing interest in assessing the environmental impacts of discarded CBs [80–84].

The cellulose acetate of CBs is a synthetic plastic, derived by reacting cellulose from cotton and wood pulp with acetic anhydride and acetic acid [85]. Cellulose acetate CBs are persistent in the environment. While susceptible to photodegradation, they are relatively resistant to biodegradation, and may take months to years to degrade depending on environmental conditions [86–88]. CB waste comprises a significant source of plastic pollution to the environment [14,89]. Recent degradation experiments suggest that CBs are also a chronic source of toxic plastic micro-fibers to the environment [90].

A wide range of pollutants can leach from disposed CBs [91]. These leachates include: nicotine, aromatic amines, and nitrosamines [92–94]; PAHs [47,49]; metals [66,95]; BTEX compounds, including benzene, toluene, ethylbenzene, o-xylene, and p-xylene [96]; and phenols [94]. Roder Green et al. found that nicotine rapidly leached from test CBs, and estimated that one CB can contaminate 1000 L of water with nicotine to levels that are chronically toxic to biota [92]. CBs leach low-molecular weight PAHs while retaining larger PAHs [46]. They also rapidly (24 h) leach a range of toxic metals [66]. The pH of smoked CB leachate is also reported to be slightly acidic (4.5), which could have significant implications for contaminant fate and toxicity [97]. An emerging concern related to CB pollution is the release of nanoparticles found in cigarette smoke, and how these particles can facilitate the transport of surface-bound metals and organic contaminants in the environment [98]. CBs can be sources of several pollutants to the atmosphere, including alcohols, carbonyls, hydrocarbons, and pyrazines [18,40,41]. Given they are a source of toxic chemicals and plastic pollution to the environment, CBs could be categorized as hazardous waste [82,99,100].

3.2. Air Contamination from Combustible Cigarettes

When smoked, combustible cigarettes generate volatile air contaminants, chemical-rich tar, the particulate mass of tobacco smoke, and residual solid waste comprised of ash and CBs. Cigarette smoke, the airborne emission from combustible cigarettes, contains thousands of chemicals, many toxic, including carbon monoxide, nicotine, formaldehyde, PAHs, nitrosamines, metals, and dioxins [34]. SHS is the main source of air pollution from cigarette consumption and includes exhaled mainstream smoke and sidestream smoke from a burning cigarette or other combusted tobacco product [37]. Most research on SHS focuses on the indoor environment [101]; however, a handful of studies suggest that tobacco smoke can be a source of outdoor pollution, including nicotine, fine particulates, and tobacco-specific nitrosamines [35,102–105]. In some cases, tobacco smoke pollutants have been found in indoor settings with no indoor smoking source [21,106,107]. This “outdoor to indoor drift” suggests that these pollutants move around the outdoors where they could impact the environment. In support of this contention, tobacco smoke pollutants have been discovered in the environment of outdoor smoking venues [108–110]. An unfortunate aspect of efforts to curtail human exposure to indoor tobacco smoke is a greater discharge of smoke to the outdoor environment as smokers are encouraged to smoke outdoors [13,111,112].

THS results from the tobacco smoke carrying and distributing particulates, compounds, and gas-phase chemicals produced by combustion and exhalation that drift in
ambient air and become affixed to and interact with surrounding materials [101]. Exposure pathways for THS include inhalation, ingestion, and dermal contact [113]. Pollutants associated with THS can reemit into the gas-phase or can react with other compounds in the environment to yield secondary pollutants [114]. Of particular concern with THS is the formation of secondary organic pollutants, including carcinogenic TSNAs, which form on indoor surfaces when nicotine reacts with common indoor pollutants [101].

An additional potential pollution source related to THS smoke is the disposal of items with contaminated surfaces. Particulates and gas-phase chemicals from tobacco smoke are small and mobile and can contaminate micro-surfaces throughout the indoor environment, including carpet, upholstery, mattresses, pillows, blankets, clothes, curtains, cabinets, doors, wallpaper, painted walls, and ceiling tiles [115,116]. Many of these contaminants remain on surfaces for months after initial exposure to THS [115]. Disposal of contaminated household items and deconstruction debris may partly account for the presence of cigarette pollution in landfill leachate [84,117]. Matt et al. notes that the “toxic legacy” related to THS on household surfaces goes largely unnoticed; they argue that cigarettes manufacturers, suppliers, and retailers bear some responsibility for preventing and mitigating associated environmental impacts [118].

3.3. Electronic Cigarettes

Electronic nicotine delivery systems, commonly known as e-cigarettes, are battery-operated devices that heat a liquid containing nicotine, propylene glycol or glycerol, and flavoring agents into an inhaled aerosol [119-122]. E-cigarettes have rapidly increased in popularity, particularly among youth and young adults [5-7,123,124]. E-cigarettes range in appearance from small plastic pens or universal serial bus (USB) keys to larger customizable hand-size “tank” devices. Most e-cigarettes share similar components, including: a battery, a heating element and aerosolization chamber called an atomizer, an e-liquid reservoir, and a mouthpiece. Devices range in reusability and may have rechargeable or replaceable batteries, replaceable atomizers, and refillable or single-use disposable reservoirs commonly called “pods.” Non-reusable one-piece disposable e-cigarettes are becoming popular because of their low cost and exemption from flavor restrictions [72,125,126].

While there are few studies of the prevalence of e-cigarette waste in the environment, it is probable that the recent increase in e-cigarette usage has been accompanied by an increase in littering of e-cigarette waste, with an associated chemical contaminant release. A recent study at San Francisco Bay Area high schools in the US showed that e-cigarette products comprised 19% of smoking litter found around exterior perimeters, second only to CBs [16]. Littering of e-liquid containers from e-cigarettes poses a particularly serious threat of environmental pollution because they can contain high concentrations of residual nicotine [127]. Besides nicotine, e-liquids contain numerous additives for flavoring [122,128], many of which are known to be toxic or have suspected or unknown toxicities [129-133]. These include various aldehydes, TSNAs, benzyl alcohol, glycerol-1,2-diacetate, and dioxyolane compounds. While the level of toxicants in e-cigarette vapors may be lower than in combustible tobacco smoke as they do not include tobacco combustion products [134], vapors from e-cigarettes are potent sources of environmental air pollution, particularly aldehydes and carbon monoxide [135-138].

Disposed e-cigarettes are also sources of metal contamination to the environment, both directly as the result of the breakdown of electronic components and indirectly via contaminated e-liquids. Common metals in the components of e-cigarette products include aluminum, barium, cadmium, chromium, copper, iron, lead, nickel, silver, tin, and zinc [69,72]. In leaching tests of e-cigarette components, lead in the resultant leachate exceeded US regulatory thresholds for hazardous-waste designation by up to ten-fold [127]. Toxic metals have also been detected in e-liquids with levels increasing after use, indicating that metals can seep into e-liquids [69]. Metals and metalloids have been detected in e-cigarette atomizers and components that heat and vaporize e-liquids [72]. The potentially cytotoxic metal, copper, was detected in e-cigarette aerosols at concentrations ~6 times
higher than combustible cigarette smoke [139]. Additional toxic or potentially toxic compounds have also been detected in e-cigarette filters, mouthpieces, rubber stoppers, and pod plastic [140].

3.4. Waste Management Systems

Several studies have measured nicotine metabolites in the influent and effluent at wastewater treatment plants [112,141–146]. The primary source of these chemicals is excretion from smokers. Nicotine absorbed into the body from tobacco products is metabolized into a range of compounds in the human liver, mainly cotinine and trans-3′-hydroxycotinine, and released mostly in urine [147]. As a percentage of the absorbed nicotine, urine typically contains ~5–10% cotinine, ~10–30% cotinine, ~35–45% trans-3′-hydroxycotinine, and a range of less common cotinine metabolites [141,148,149]. A typical nicotine equivalent excretion rate for a smoker, assuming 1.25 mg nicotine absorption per cigarette and a 12-cigarettes-per-day smoking rate, is around 15 mg/d [141].

A comprehensive assessment of wastewater treatment plants in Zurich, Switzerland, measured cotinine at 1.5–2.9 µg/L and 3′-hydroxycotinine at 3.0–9.5 µg/L in wastewater influent [150]. Nicotine was measured in a wastewater treatment plant near Barcelona, Spain, at concentrations ranging from 100–3250 µg/L. In many studies, researchers observed substantial removal of nicotine, cotinine, and 3′-hydroxycotinine during the treatment process. Because nicotine in wastewater can originate from other sources (e.g., discarded cigarettes, nicotine patches, and nicotine gum) and is potentially more degradable in the environment, cotinine is considered a better biomarker of cigarette consumption [22]. Some trace metabolites, such as N-formylornicotine, appear resistant to degradation during wastewater treatment, and therefore could also be used as biomarkers of cigarette pollution [150]. Studies have also tracked nearby receiving waters and discovered nicotine and its metabolites in surface waters [22,150–152]. In a comprehensive assessment of surface waters in the US, cotinine was one of the five most commonly detected chemicals, underscoring the ubiquitous nature of tobacco use pollution in the environment [153].

Several other waste management-related sources have been linked to contamination of groundwater with pollutants such as nicotine and cotinine, which could be related to the use and disposal of cigarettes. Compared to surface waters, groundwater pollution appears less extensive [153,154]; however, nicotine and cotinine have been observed in groundwater near septic tank discharges [155–158]. The discharge of reclaimed tertiary-treated wastewater used for irrigation and groundwater recharge can also be a source of cotinine in the environment [159,160]. Another source of anthropogenic pollutants to groundwater is landfills, especially systems that lack modern leachate containment systems [117,161]. Two studies of legacy pollution from unlined landfills in the US detected cotinine in the groundwater, but the sources could not be conclusively linked to the disposal of tobacco product waste [162,163]. Other studies have detected nicotine and cotinine in leachate collected from lined domestic and industrial landfills [117,164,165].

There is a growing acknowledgment that sewers and stormwater collection systems are potential sources of water-based pollutants to shallow groundwater, which in turn can contaminate deeper groundwater resources used for potable supply and hydrologically connected surface waters [166,167]. In urban settings, discarded CBs appear to be a significant source of nicotine to stormwater collection systems [92]. Recent assessments of urban stormwater quality in the United States consistently measured nicotine and cotinine [167,168]. A related source, in terms of a high density of CB litter in urban environments, is roadsides [82,169]. A handful of studies have shown that roadway CB litter contributes nicotine, metal, and PAH pollution [49,170].

4. Environmental Impacts

4.1. Microorganisms

Microorganisms include prokaryotes (Bacteria including bacteria and cyanobacteria, and Archaea), eukaryotes (Eukarya, such as fungi and protozoans), symbioses (e.g., plant
root nodules, or lichens), and viruses. Such organisms respond to ambient chemicals in marine and freshwaters, soils and sediments, and waste treatment systems (i.e., all environmental compartments where cigarette waste can accumulate [171]). As is the case for other agricultural plants, there is a diverse and dynamic [172,173] microbiome associated with tobacco [173–176]. This includes a wide range of microbial organisms associated with cigarettes that are known human disease pathogens [177]. Tobacco-associated microbes introduced into the human oral cavity may change microbiomes as occurs with the use of smokeless tobacco [178], tobacco smoking [179,180], and vaping [181]. Recent studies also point to differences in the gut microbiomes in adult smokers compared to non-smokers, as well as infants and children exposed to THS [182,183].

Microbial biodegradation of tobacco waste chemicals may influence the fate and environmental risk of such chemicals; however, biodegradation depends on many factors, including if the chemicals undergoing degradation are toxic to microorganisms. Nicotine is known to be toxic to higher organisms and can also be antimicrobial [184]. Oropesa et al. found that nicotine concentrations up to 1000 µg/L were not acutely toxic to the marine bacterium *Vibrio fischeri*, with a no observed effect concentration (NOEC) of <200 µg/L nicotine [185]; however, many microorganisms, including bacteria [186] and fungi [187], can metabolize nicotine. For example, in soil contaminated with tobacco waste, inoculation with a nicotine-degrading bacterial strain of *Pseudomonas* led to these populations proliferating during biodegradation [188]. Such introduced bacteria exploiting the nicotine in soil suggests that, where microbial nicotine metabolic pathways exist either with natural populations or those arriving with tobacco waste, associated genes could be expressed in the environment.

The complex mixture of contaminants found in CB leachate can be toxic to bacteria. Micevsk et al. reported that 30 min EC50 (50% effects concentration measured via bioluminescence) values for the marine bacterium *Vibrio fischeri* ranged from ~100–200 CB/L for a range of cigarette brands [189]. This may explain why CBs, the most prevalent form of littered plastic, do not readily biodegrade despite evidence of the microbial metabolism of the pure cellulose acetate that comprises CBs [190–192]. The leachate from smoked CBs has been shown to exert toxicity [193] inhibiting biodegrading microorganisms in various aquatic microbial populations [194]. Such toxicity may constrain nicotine and cellulose acetate biodegradation under field conditions. This was implied in a composting study of cellulose-only versus plastic (cellulose acetate) CBs. Both types of smoked butts inhibited cigarette filter biodegradation [88], stemming from the toxic chemical milieu of leached smoke pollutants [100]; however, in a five-year experiment of CB decomposition in various soils, after an initial phase in which chemical toxicity inhibited biodegradation, a more rapid biodegradation phase was observed [75]. Available nitrogen was a major factor identified as potentially limiting biodegradation rates [75]. This suggests that factors influencing the persistence of cigarette chemical pollution on various landscapes, if better understood, could be managed to accelerate biodegradation.

There is limited literature on how cigarette waste in the environment affects key ecosystem services delivered by microorganisms, such as nutrient cycling [195]. As noted below, environmentally relevant concentrations of nicotine can impair aquatic primary producers and eukaryotic predators [185]. Thus, population dynamics and food web interactions are at risk where environmental nicotine enters aquatic systems. Additionally, the impacts of CBs on the diversity of microbial communities in the environment have recently been reported [196]. Over a 96 h exposure, marine sediments treated with smoked CBs had altered microbial communities, including decreases in two taxonomic families, Cyanobacteria and Bacteroidetes, involved in photosynthetic (primary production) and organic matter biodegradation activities, respectively [196]. Koroleva et al. assessed the effects of leachate from smoked biodegradable cellulose versus cellulose acetate CBs to soil bacterial communities [197]. Bacterial community diversity did not appear to vary significantly when comparing the butt leachate treatments to each other and to the no-treatment control [197]. Longer-term incubations in soil could be useful to determine if
differences in communities arise. The implications of microbial community taxa shifts, when they occur and if attributable to toxins released from CBs, are important to understand for a broad environmental risk assessment related to tobacco product waste.

4.2. Plants

Research interest in the plant uptake of nicotine from the environment originates, in part, from numerous detections of nicotine in plant tissues in phylogenetically diverse food crops and other plant-derived products, such as spices and teas. These plants are not known for endogenous nicotine synthesis, and elevated nicotine concentrations in their tissues can be found under conditions where nicotine-containing insecticides had not been applied [198–200]. Elevated nicotine levels in commodity plants are a concern due to the human health risks, which may result in the commodity being pulled from the market, causing economic losses for farmers and distributors. In response to unexpectedly high levels of nicotine contamination, the European Union temporarily increased its maximum nicotine residue level in commodity crops so as to not overly burden the commerce of these products [201].

Xenobiotics, including herbicides and fungicides, veterinary medicines, and other phytotoxic compounds, are taken up by plant roots from the soil and translocated to the shoots [202,203]. This suggests that nicotine might also be acquired from the soil by agriculturally important plants. In support of this hypothesis, [198] demonstrated nicotine uptake from soil using peppermint plants (Mentha piperita), suggesting an uptake from nicotine-contaminated soils due to discarded CBs. Subsequently, this pathway has been supported in additional studies with basil (Ocimum basilicum), parsley (Petroselinum crispum), and coriander (Coriandrum sativum), which all showed a significant accumulation of nicotine applied to soil either as tobacco leaf tissue or CBs [204]. Significant accumulation of nicotine was observed in acceptor plants even when the CB concentrations were as low as one per square meter [201].

Nicotine may also cycle through the plant and soil system via horizontal transfer of nicotine from donor plants to acceptor plants. This could occur directly between two living plants, or indirectly via the decomposition of acceptor plant tissues deposited in soil during plant tissue senescence or from discarded nicotine-containing products such as CBs [204]. Transfers of nicotine between living plants is presumed to be primarily from root exudation by the donor plant [205] and subsequent uptake of nicotine by the acceptor plant growing nearby; however, the potential importance of nicotine transfer between plants via shared mycorrhizal networks [206] has not been studied. In addition to the direct effects of nicotine on reducing plant herbivory and pathogenicity on plants, release of nicotine into the soil from root exudation or during plant litter decomposition can improve plant survival and growth of the donor plant. This benefit to donor plants appears to result from nicotine increasing the availability of several plant nutrients in the soil [207–209]. With regards to aquatic ecosystems, Oropesa et al. reported that nicotine was not acutely toxic to the freshwater unicellular green algae Pseudokirchneriella subcapitata, but it did inhibit growth at concentrations of 100–200 µg/L [185].

Several studies have documented the effects of CBs in soil and cigarette smoke on plant processes. Montalvão et al. found that the smoked CB leachate had cytotoxic, genotoxic, and mutagenic effects on onion (Allium cepa) roots at environmental concentrations (1.9 µg/L of nicotine) [210]. Discarded CBs reduced the germination success and shoot length after 21 days of both perennial ryegrass (Lolium perenne) and white clover (Trifolium repens) [211]. These researchers suggested that their study demonstrates the potential for littered CBs to reduce the net productivity of terrestrial plants while da Silveira Fleck et al. reported elevated levels of metals in plants (Eugenia uniflora and Tradescantia pallida) near a designated outdoor smoking area, suggesting that SHS can result in the contamination of nearby flora [109]. Noble found a universal decrease in the germination rate of radish (Raphanus raphanistrum subsp. Sativus), kale (Brassica oleracea), lettuce (Lactuca sativa L.), amaranth (Amaranthus spp.), wheat (Triticum spp.), rice (Oryza spp.),
barley (*Hordeum vulgare* L.), and rye (*Secale cereale* L.) seeds when exposed to tobacco smoke [212]. This negative response was not due to the presence of nicotine in the smoke, but rather to other non-volatile components. In contrast, Tileklioglu et al. reported that tobacco smoke increased the biomass of wheat and duckweed (*Lemna minor* L.) plants [213], and Mondal et al. found relatively little effect of tobacco smoke on the germination rate of Bengal gram (*Cicer arietinum* L.) [214]. Metal accumulation in plants is a common phenomenon and can affect humans indirectly by lowering plant nutritional value and directly through consumption of contaminated crops, even at low levels via chronic exposure [215].

We found no studies that conclusively linked tobacco-related pollution with the elevated levels of metals in plants.

### 4.3. Non-Mammalian Animals

Much of the limited research on the impacts of tobacco-product waste on animals is related to CBs in the environment. A recent study by Venugopal et al. measured a range of compounds, including nicotine, PAHs, metals, phthalates, and volatile organic compounds known to be very toxic to aquatic organisms, in leachate from field-collected CBs [91]. Another recent study showed that leachate from field-collected CBs in the marine environment impaired copepod reproduction (*Notokru sp*) at low butt concentrations [216]. Dobaradaran et al. recently reviewed the toxicity of CBs to aquatic organisms and showed that CB leachate is toxic to a wide range of aquatic animals, including freshwater zooplankton, sea snails, frogs, frog embryos, and marine and freshwater fish [217]. In one study, Slaughter et al. assessed the toxicity of CB leachate to fish [218]. They reported leachate from smoked CBs, which include the smoked filter plus remnants of tobacco, to be acutely toxic to both the saltwater topsmelt (*Atherinopsis affinis*) and the freshwater fathead minnow (*Pimephales promelas*). The lethal concentration at which 50% of the test individuals died (i.e., LC50) of approximately one CB per liter of water was observed for both species. We note that non-lethal but observable negative effects, mainly immobilization, were found at lower leachate CB concentrations. There is further evidence in the literature of sub-lethal impacts to animals from tobacco-related pollutants, such as developmental, physiological, or chronic changes in behavior, that may result in fitness loss with subsequent impacts to populations [217]. Belzagui et al. recently showed that microfibers from degraded CBs enhanced the toxicity of CB leachate to freshwater zooplankton (*Daphnia magna*) in experimental 48 h toxicity tests, suggesting that the microfibers pose an intrinsic risk to small aquatic animals [90]. In another recent study, Green et al. compared the toxicity of leachate from conventional plastic cellulose acetate CBs and cellulose CBs, which are being promoted as a biodegradable and environmentally safe alternatives [219]. Both smoked butt types exhibited toxicity to, and decreased activity in, freshwater snails (*Bithynia tentaculata*). A subsequent study showed that smoked cellulose acetate CBs increased clearance rates in marine blue mussels (*Mytilus edulis*), while cellulose CBs did not [220].

Several theses have reported the bioaccumulation of CB pollutants in aquatic animals and potential chronic impacts on growth and behavior. Yabes found rainbow trout (*Oncorhyncus mykiss*) exposed to non-lethal CB leachate at a concentration of 0.5 CB/L for 28 days bioaccumulated a range of contaminants including nicotine, nicotyrine, myosmine, and 2,2′-bipyridine [221]. In addition, Yabes documented a reduced weight of fish exposed to the CB leachate compared to controls. Metals did not accumulate under similar conditions with the same organism [222]. Filter feeding organisms that process high volumes of water like bivalves are susceptible to the bioaccumulation of pollutants. Wei found 22 compounds in CB leachate also present in an exposed marine mussel (*Mytilus galloprovincialis*), some of which are potentially toxic if consumed by humans or wildlife [223]. No research has been reported on the trophic transfer of CB pollutants, a phenomenon in which the effects of toxins to wildlife are mostly noticeable in top predators as the toxin accumulates through the aquatic food web as the predators consume prey [224].

In one of the few studies to assess the impacts of CBs in situ, Suárez-Rodríguez et al. found that ectoparasite counts decreased with increasing cellulose fiber weight in the nests...
of urban house sparrows (Passer domesticus) and house finches (Carpodacus mexicanus) [225]. The authors hypothesized that the observation was the result of CB-associated nicotine, a long-known pesticide. Decreased parasite load is a known fitness advantage to numerous wildlife, and further study revealed that hatching and fledging success increased with nest composition incorporating CB litter; however, blood samples from nesting birds also showed an increasing risk of genetic mutation and cancer (i.e., genotoxicity), leading to speculation that any fitness advantage from a reduced parasite load may be nullified.

4.4. Mammalian Animals

Little is known about the environmental toxicity of tobacco in mammalian wildlife; however, tobacco has long been known to be lethal to various mammals, and nicotine has been used in rodenticides. In vivo laboratory studies of nicotine toxicity have been conducted in a variety of mammalian species, particularly rats and mice, and demonstrated a wide range of effects, including acute toxicity, cell mutation, reproductive effects, and behavior changes [226]. Because rodents are an important part of the food chain in many environments, findings from animal models give some indication of the potential effects of exposure in the wild. In rats, the lethal dose of nicotine at which 50% of the test animals die (i.e., LD50) is 50 mg/kg weight, and in mice 3.3 mg/kg [227]. One recent study showed that nicotine hydrogen tartrate administered ad libitum in drinking water to rats (52 ppm nicotine) and mice (514 ppm nicotine) for four weeks induced increased urinary tract cell proliferation (urothelial hyperplasia) [228]. Prenatal exposure of mice to nicotine in vivo induces underdeveloped or involuted thymus (thymic hypoplasia), impairing the immune systems of offspring through adulthood [229]. Cotinine, the major metabolite of nicotine, administered ad libitum in drinking water to rats can induce cell proliferation and hyperplasia in rat urinary bladder and renal tissues, albeit to a lesser degree than nicotine. Mice exposed to e-cigarette aerosol have been shown to develop lung adenocarcinoma and bladder urothelial hyperplasia, lesions that are extremely rare in control mice [230]. Exposure to e-cigarette aerosol also damages mouse DNA and impairs DNA repair activity in mouse lung tissues [231]. Plastic CBs made of minimally degradable cellulose acetate also pose a threat to animals via inadvertent CB consumption, which may lead to vomiting and neurological toxicity [1,232].

4.5. Humans

Some studies suggest that environmental contamination from cigarette and e-cigarette use and disposal may affect human health. One recent study measured nicotine and TSNAs in urban outdoor air at concentrations exceeding public health standards [35]. Other studies have discovered nicotine and particulate matter derived from tobacco smoke in urban outdoor air as potential human toxins [102,104,108–110,112]. Passive exposure from e-cigarettes has been detected via TSNAs in the urine of non-users [233], but human health effects of e-cigarette aerosols remain under-evaluated [3,136,233]. Accidental ingestion of CBs is most acutely hazardous due to the nicotine poisoning risk, especially among children [232,234,235]. E-liquids from e-cigarette devices can also be mistaken for other ingestible items and misused [236–240].

Several studies have found tobacco contaminants in key environmental compartments, including water [153], soil [49], dust [170], and plants [199,201]. There is evidence that drinking water could be a significant exposure route. In a comprehensive study of untreated drinking water sources in the United States, Focazio detected cotinine in half of the potable water samples studied [153]. A broad survey of potable tap water samples from cities in Europe, Japan, and Latin American reported mean (maximum) nicotine and cotinine concentrations of 18 ng/L (305 ng/L) and 2 ng/L (14 ng/L), respectively [241]. González Alonso discovered nicotine in bottled spring waters in Spain [242]. As noted earlier, nicotine has also been detected in a variety of food crops and plant-derived commodities, and presents an additional possible source for human exposure [201]. Other contaminants and particles that are leached into the environment from cigarettes and
e-cigarette components (e.g., metals, PAHs, TSNAs and plastic nanoparticles) may bioaccumulate in plants and animals and pose additional exposure risks to humans consuming them [13], but there is no definitive health research on this topic.

A limited number of recent studies using mice and human cell-based assays suggest that tobacco waste pollution is toxic to humans, though the potential pathways of exposure to tested pollutants is not obvious. Bekele and Ashall reported negative developmental effects in mice that ingested CB leachate, including reduced weight gain and lower organ mass [243]. Begum et al. reported a range of neurotoxicological effects in human embryonic stem cells exposed to aqueous cigarette tar extract derived from CBs [244]. Xu et al. used a battery of in vitro human cell-based assays to assess the toxicity and biological activities of CB leachate [193]. They noted significant impacts on key biological pathways, such as aryl hydrocarbon receptor (AhR), estrogen receptor (ER), and p53 response pathways, and identified specific compounds, including 2-methylindole, most responsible for the AhR response.

### 4.6. Economic Impacts of Contamination

While health care costs associated with tobacco use have been estimated [245], there is a significant gap in the literature regarding the costs related to the environmental impacts of combustible cigarette and e-cigarette use and disposal. Of particular concern is the cellulose acetate cigarette filter in CBs, a form of plastic which, as noted earlier, exhibits limited biodegradability [86] and sheds microplastic into the environment [90]. This economic burden may be significant given the scope of the CB waste problem, especially given that people generally do not know that CBs are plastic and that casual disposal of CBs is a normative component of smoking [246,247]. Many CBs smoked in public are littered to the urban environment rather than disposed of in proper receptacles [92]. Adding to the burden of CBs is the waste associated with the growing use of e-cigarettes [16]. In the United States, schools must now manage confiscated e-cigarettes and e-cigarette litter as hazardous waste, likely incurring significant costs associated with their collection, storage, and disposal [126].

The cleanup and disposal of tobacco product waste, much of it related to cigarette use, is a negative economic externality, which can be defined as a harmful effect to a third party not directly involved in the transaction and for which they are not compensated. This externality is borne by non-smokers, taxpayers, communities, and voluntary groups that conduct cleanups. The tobacco industry has supported a “blame-the-victim approach” by calling mainly for smoker responsibility and enforcement of litter regulation, as opposed to preventive policies such as the elimination of plastic filters from cigarettes [13,248]. Cities incur significant cleanup and disposal annual costs for public areas, ranging on the order of USD 4 million for Portland and Las Vegas, USD 22 million for San Francisco, and USD 80 million for New York City [249,250].

In addition to the direct impacts associated with litter cleanup, there is a range of indirect impacts that need evaluation in more detail. Cigarette waste degrades environmental quality by fouling beach environments, despoiling public lands such as parks, and degrading neighborhoods and public spaces [251]. Such indirect environmental impacts may translate to significant economic consequences due to a reduced delivery of ecosystem services such as food supply, regulating services such as water and waste purification, and cultural and aesthetic services including tourism and recreation [252]. Single-use plastic pollution related to the littering of cellulose acetate CBs, e-cigarettes, or plastic lighters also likely has a significant environmental footprint. Plastic pollution substantially impacts the delivery of ecosystem services, especially those in marine environments [253]. Increased building fire and wildfire risk due to improper CB disposal causes an estimated 130,000 fires in the United States annually, resulting in over USD 2 billion in costs associated with firefighting and USD 6 billion in property damage [254,255].
5. Conclusions

Contaminants associated with CB pollution are numerous. They include: nicotine; its key metabolites cotinine and trans-3'-hydroxycotinine; tobacco-specific nitrosamines; metals; and PAHs. Some of these compounds may be relatively short lived in the environment (e.g., nicotine), while others can persist (e.g., metals and larger PAHs) or bioaccumulate in biota (nicotine, cotinine, and metals). Some pollutants (e.g., metals and organic pollutants) may undergo facilitated transport in the environment due to their association with the nanoparticles produced during combustion. While the chemical pollutants associated with cigarette pollution are well characterized, their fate in the environment, including in aquatic systems that are commonly the endpoint for tobacco product-related pollutants, are not. Nicotine, cotinine and trans-3'-hydroxycotinine are important tracers of cigarette pollution in the environment. In contrast to PAHs and metals, these compounds have fewer natural sources that may confound source attribution. Cotinine appears to be monitored more frequently than nicotine in environmental studies, likely because it can be measured simultaneously with a suite of pollutants via solid phase extraction and liquid chromatography/mass spectrometry. In contrast, nicotine requires different analytical treatment and methods because of its high pK value. Environmental studies should strive to measure nicotine in addition to cotinine, particularly because nicotine is a potent environmental toxin. In addition, since nicotine and cotinine can come from non-tobacco sources, studies should focus on measuring the “metabolites of metabolites” such as trans-3'-hydroxycotinine, or tobacco-specific alkaloid biomarkers such as anabasine [256], which are more conclusive indicators of environmental contamination from human tobacco use. Additionally, because of their relative stability in aquatic environments, some less common nicotine metabolites (e.g., N-formylNornicotine) may be good tracers of environmental contamination from human tobacco use.

The trillions of CBs littered into the environment every year are sources of pollution via leaching and emission of gas-phase pollutants. CB chemical release rates are not well-characterized for either water or air and require more research focus. Cellulose acetate CBs are a form of bulk plastic non-point source pollution, as well as micro-plastics as the CBs age and break apart in the environment; the effects of this pollution merit further exploration. Environmental contamination from e-cigarette use and disposal is less well documented and requires more attention, especially given the growing popularity of these products. Pollution sources include discarded e-liquid pods and their contents, other e-cigarette components that include batteries and other metallic components, and entire single-use, e-cigarette systems. Additional attention should be given to the environmental impacts of newly developed heated tobacco products. The market for these products may grow dramatically given recent actions of the US Food and Drug Administration to approve them as reduced exposure tobacco products and widespread global marketing by tobacco companies.

A less recognized source of combustible cigarette contamination to the environment is SHS, a complex amalgam of mainstream and sidestream smoke, and THS, which accumulates on surfaces exposed to smoking. Most of the research to date has focused on indoor settings and the associated human health impacts. Elevated nicotine, particulates, and metals from cigarette smoke have been detected in urban air and near public smoking areas. Pollutants from smoke, including toxic TSNAs, are detected on a wide variety of indoor surfaces. Expanding the focus of SHS and THS to outdoor settings is a ripe area for new research.

Because of the ubiquitous disposal of used cigarettes and e-cigarettes, several waste management systems may be sources of tobacco pollutants to the environment. These include the effluents of treated domestic wastewater, leachate seeping out of landfills, and discharges from urban storm drains and because there may be non-tobacco sources of nicotine, it is sometimes difficult to link nicotine pollution to tobacco use, especially for landfills. Nicotine and the cotinine metabolite have been extensively detected in a variety of surface waters, and to a lesser extent in ground waters. Of particular concern, and
a needed focus of future research, is the assessment of the continuous releases of low-concentration tobacco pollutants from wastewater and stormwater discharges, which have the potential for chronic toxicological effects on aquatic biota and possibly human health. Source tracking of cigarette-specific pollutants is also needed to conclusively link tobacco products as the sources of contaminants in multi-input, waste management systems.

While the chemical makeup and sources of environmental cigarette pollution have been identified, the extent to which this pollution impacts the provisioning of ecosystem services is understudied. For instance, to date, there have been only a few laboratory studies that show CB leachate is toxic to or bioaccumulated in microbes, plants, benthic organisms, bivalves, zooplankton, and fish. A limited number of studies also showed that, as a toxic waste product, CB leachate can negatively impact microbes, plants, and animals. Given that environmental microorganisms catalyze key biogeochemical cycles (e.g., carbon, nitrogen, phosphorus, sulfur, and iron) and ecosystem services (e.g., waste attenuation and agricultural food production), there is a need to understand how this pollution impacts microorganisms and associated ecological processes, including microbial-plant interactions, under field conditions. More studies are also needed to assess how the many toxins associated with cigarette and e-cigarette use and disposal affect plant establishment, survival, and yield of food crops under field conditions. There is also a need to more conclusively document the impacts of cigarette pollutants on plants and animals, especially the bioaccumulation of contaminants such as metals and CB-specific microplastics, in the outdoor environment to complement experimental laboratory studies. Finally, more studies documenting the impacts on wildlife and human health are needed that go beyond suggesting an exposure pathway (e.g., tobacco smoke in urban air, cotinine-contaminated water, and TSNA inputs on the surfaces of deconstruction debris) or testing a single contaminant in a laboratory setting. These studies are needed to conclusively show the health impacts due to field-relevant concentrations and chemical mixtures of cigarette and e-cigarette contaminants in the environment.

A final under-recognized impact of cigarette contaminants in the environment is the economic burden of cleanup, mitigation, and prevention. To support effective policies to reduce the negative economic externalities of cigarette and e-cigarette pollution, a more comprehensive picture of direct and indirect environmental costs of cigarette and e-cigarette use and disposal is needed. The estimation of scientifically defensible environmental costs, coupled with more extensive studies of the sources and impacts of these environmental pollutants, could encourage policy changes that limit environmental damages, while also shifting responsibility for these damages away from the public and upstream to tobacco product producers, suppliers, and retailers.

**Author Contributions:** Writing—original draft preparation, M.W.B., T.C.H., T.E.N., J.M., M.E.G., S.C.H., S.T., S.D., A.B., C.L.J. and P.A.H.; writing—review and editing, E.H., L.C.V.D.W., V.B. and A.C.W. All authors have read and agreed to the published version of the manuscript.

**Funding:** Funds for this project were provided by the California Tobacco-Related Disease Research Grants Program Office of the University of California, Grant Number 29NP-0001, with support from the University of California Natural Reserve System (UC NRS), Office of the President.

**Conflicts of Interest:** The authors declare no conflict of interest.

**References**

1. Aratijo, M.C.B.; Costa, M.F. A critical review of the issue of cigarette butt pollution in coastal environments. *Environ. Res.* 2019, 172, 137–149. [CrossRef]
2. Novotny, T.E.; Bialous, S.A.; Burt, L.; Curtis, C.; Costa, V.L.D.; Iqtidar, S.U.; Liu, Y.; Pujari, S.; Tursan d’Espaignet, E. The environmental and health impacts of tobacco agriculture, cigarette manufacture and consumption. *Bull. World Health Organ.* 2015, 93, 877–880. [CrossRef]
3. Pisenger, C.; Dessing, M. A systematic review of health effects of electronic cigarettes. *Prev. Med.* 2014, 69, 248–260. [CrossRef]
4. Marynak, K.L.; Gammon, D.; Rogers, T.; Coats, E.M.; Singh, T.; King, B.A. Sales of Nicotine-Containing Electronic Cigarette Products: United States, 2015. *Am. J. Public Health* 2017, 107, 702–705. [CrossRef]
5. Cullen, K.A.; Gentzke, A.S.; Sawdye, M.D.; Chang, J.T.; Anic, G.M.; Wang, T.W.; Creamer, M.R.; Jamal, A.; Ambrose, B.K.; King, B.A. e-Cigarette Use Among Youth in the United States, 2019. JAMA 2019, 322, 2095. [CrossRef]

6. European Commission. Special Eurobarometer 438 Attitudes of Europeans towards Tobacco and Electronic Cigarettes; Report; European Union: Brussels, Belgium, 2017; ISBN 978-92-79-69104-1.

7. Gentzke, A.S.; Creamer, M.; Cullen, K.A.; Ambrose, B.K.; Willis, G.; Jamal, A.; King, B.A. Vital Signs: Tobacco Product Use Among Middle and High School Students—United States, 2011–2018. MMWR Morb. Mortal. Wkly. Rep. 2019, 68, 157–164. [CrossRef]

8. Maziak, W.; Ben Taleb, Z.; Bahelah, R.; Islam, F.; Jaber, R.; Auf, R.; Salloum, R.G. The global epidemiology of waterpipe smoking. Tob. Control 2015, 24, i3–i12. [CrossRef]

9. Simonavicius, E.; McNeill, A.; Shahab, L.; Brose, L.S. Heat-not-burn tobacco products: A systematic literature review. Tob. Control 2019, 28, 582–594. [CrossRef]

10. World Health Organization. Tobacco Fact Sheet. Available online: https://www.who.int/news-room/fact-sheets/detail/tobacco (accessed on 1 June 2021).

11. Zafeiridou, M.; Hopkinson, N.S.; Voulvoulis, N. Cigarette Smoking: An Assessment of Tobacco’s Global Environmental Footprint Across Its Entire Supply Chain. Environ. Sci. Technol. 2018, 52, 8087–8094. [CrossRef]

12. Hoh, E.; Wei, H.-H.; Richardson, W.; Dodder, N.; Watanabe, K.; Cibor, A.; Novotny, T.E.; Gersberg, R. Determination of Leachable Organic Compounds in Smoked Cigarettes and Their Bioaccumulation Potentials in the Marine Mussel, Mytilus galloprovincialis. In Proceedings of the 2019 Annual Meeting Society for Research on Nicotine and Tobacco, San Francisco, CA, USA, 20–23 February 2019.

13. Novotny, T.E.; Slaughter, E. Tobacco Product Waste: An Environmental Approach to Reduce Tobacco Consumption. Curr. Environ. Health Rep. 2014, 1, 208–216. [CrossRef]

14. Van Schalkwyk, M.C.I.; Novotny, T.E.; McKee, M. No more butts. BMJ 2019, 367, l5890. [CrossRef]

15. Hendlin, Y.H. Alert: Public Health Implications of Electronic Cigarette Use. Am. J. Public Health 2018, 108, 1489–1490. [CrossRef]

16. Mock, J.; Hendlin, Y.H. Notes from the Field: Environmental Contamination from E-cigarette, Cigarette, Cigar, and Cannabis Products at 12 High-Schools—San Francisco Bay Area, 2018–2019. MMWR Morb. Mortal. Wkly. Rep. 2019, 68, 897–899. [CrossRef]

17. Araújo, M.C.B.; Costa, M.F. From Plant to Waste: The Long and Diverse Impact Chain Caused by Tobacco Smoking. Int. J. Environ. Res. Public Health 2019, 16, 2690. [CrossRef]

18. Poppeldeiek, D.G.; Khurshid, S.S.; Emmerich, S.J. Measuring Airborne Emissions from Cigarette Butts: Literature Review and Experimental Plan; National Institute of Standards and Technology US Department of Commerce: Gaithersburg, MA, USA, 2016. [CrossRef]

19. Kozłowski, L.T.; Mehta, N.Y.; Sweeney, C.T.; Schwartz, S.S.; Vogler, G.P.; Jarvis, M.J.; West, R.J. Filter ventilation and nicotine content of tobacco in cigarettes from Canada, the United Kingdom, and the United States. Tob. Control 1998, 7, 369–375. [CrossRef]

20. Benowitz, N.L.; Hukkanen, J.; Jacob, P. Nicotine Chemistry, Metabolism, Kinetics and Biomarkers. In Handbook of Experimental Pharmacology; Springer: Berlin/Heidelberg, Germany, 2009; Volume 2009, pp. 29–60. [CrossRef]

21. Ramirez, N.; Özel, M.Z.; Lewis, A.; Marcé-Recasens, R.M.; Borrull, F.; Hamilton, J.F. Exposure to nitrosamines in thirdhand tobacco smoke increases cancer risk in non-smokers. Environ. Int. 2014, 71, 139–147. [CrossRef]

22. Benotti, M.J.; Brownawell, B.J. Distributions of Pharmaceuticals in an Urban Estuary during both Dry- and Wet-Weather Conditions. Environ. Sci. Technol. 2007, 41, 5795–5802. [CrossRef]

23. Banyasz, J.L. The Physical Chemistry of Nicotine. In Analytical Determination of Nicotine and Related Compounds and Their Metabolites; Gorrod, J.W., Jacob, P., III, Eds.; Elsevier: Amsterdam, The Netherlands, 1999; pp. 149–190.

24. Pankow, J.F.; Mader, B.T.; Isabelle, L.M.; Luo, W.; Pavlick, A.; Liang, C. Conversion of Nicotine in Tobacco Smoke to Its Volatile and Available Free-Base Form through the Action of Gaseous Ammonia. Environ. Sci. Technol. 1997, 31, 2428–2433. [CrossRef]

25. Li, L.; Lee, Y.; Pappone, P.; Palma, A.; McNamee, M. Site-specific mutations of nicotinic acetylcholine receptor at the lipid-protein interface dramatically alter ion channel gating. Biophys. J. 1992, 62, 61–63. [CrossRef]

26. Seckar, J.A.; Stavanja, M.S.; Harp, P.R.; Yi, Y.; Garner, C.D.; Doi, J. Environmental fate and effects of nicotine released during cigarette production. Environ. Toxicol. Chem. 2008, 27, 1505–1514. [CrossRef]

27. Morie, G.P. Fraction of Protonated and Unprotonated Nicotine in Tobacco Smoke at Various PH Values. Tob. Sci. 1972, 16, 127.

28. Akçay, G.; Yurdakoğlu, K. Removal of Nicotine and Its Pharmaceutical Derivatives from Aquose Solution by Raw Bentonite and Dodecylammonium-Bentonite. J. Ind. Eng. Ind. Res. 2008, 67, 451–454.

29. de Lucas, A.; Cañizares, P.; García, M.A.; Gómez, J.; Rodríguez, J.F. Recovery of Nicotine from Aqueous Extracts of Tobacco Wastes by an H+–Form Strong-Acid Ion Exchanger. Ind. Eng. Chem. Res. 1998, 37, 4783–4791. [CrossRef]

30. Medana, C.; Santoro, V.; Bello, F.D.; Sala, C.; Pazzi, M.; Sarro, M.; Calza, P. Mass spectrometric fragmentation and photocatalytic transformation of nicotine and cotinine. Rapid Commun. Mass Spectrom. 2016, 30, 2617–2627. [CrossRef]

31. Passananti, M.; Temussi, F.; Iesce, M.R.; Previtera, L.; Mailhot, G.; Vione, D.; Brigante, M. Photoenhanced transformation of nicotine in aquatic environments: Involvement of naturally occurring radical sources. Water Res. 2014, 55, 106–114. [CrossRef]

32. Konstantinou, E.; Fotopoulou, F.; Drosos, A.; Dimakopoulou, N.; Zagoriti, Z.; Niarchos, A.; Makrynioti, D.; Kouretas, D.; Farsalinos, K.; Lagoumintzis, G.; et al. Tobacco-specific nitrosamines: A literature review. Food Chem. Toxicol. 2018, 118, 198–203. [CrossRef]

33. Leigh, N.J.; Palumo, M.N.; Marino, A.M.; O’Connor, R.J.; Goniewicz, M.L. Tobacco-specific nitrosamines (TSNA) in heated tobacco product IQOS. Tob. Control 2018, 27, s37–s38. [CrossRef]
Pappas, E.; Campbell, R.C.J.; Sposito, Traina, Springer: Traina, Products. Golia, Moriwaki, Dobaradaran, Lampblack Manzetti, Poppendieck, D.; Lee, – H.; Wang, R.; Kitajima, Soils 

Lodovici, Lee, M.R.; Poppendieck, J. Controls on the Valence Species of Arsenic in Tobacco Smoke: XANES Implications of temperature, relative humidity, and water saturation on airborne emissions from cigarette butts. Sci. Total Environ. 2020, 723, 134–222. [CrossRef]

Hildemann, L.M.; Markowski, G.R.; Cass, G.R. Chemical composition of emissions from urban sources of fine organic aerosol. Environ. Sci. Technol. 1991, 25, 744–759. [CrossRef]

Schwarz, K.; Gocht, T.; Grathwohl, P. Transport of polycyclic aromatic hydrocarbons in highly vulnerable karst systems. Environ. Pollut. 2011, 159, 133–139. [CrossRef]

Manzetti, S. Ecotoxicity of polycyclic aromatic hydrocarbons, aromatic amines, and nitroarenes through molecular properties. Environ. Chem. Lett. 2012, 10, 349–361. [CrossRef]

Harmon, T.C.; Burks, G.A.; Ayucager, A.-C.; Jackson, K. Thermally Enhanced Vapor Extraction for Removing PAHs from Lampblack-Contaminated Soil. J. Environ. Eng. 2001, 127, 986–993. [CrossRef]

Dobaradaran, S.; Schmidt, T.C.; Lorenzo-Parodi, N.; Jochmann, M.A.; Nabipour, I.; Raeisi, A.; Stojanović, N.; Mahmoodi, M. Cigarette butts: An overlooked source of PAHs in the environment? Environ. Pollut. 2019, 249, 932–939. [CrossRef]

Dobaradaran, S.; Schmidt, T.C.; Lorenzo-Parodi, N.; Kaziur-Cegla, W.; Jochmann, M.A.; Nabipour, I.; Lutze, H.V.; Telgheder, U. Polycyclic aromatic hydrocarbons (PAHs) leachates from cigarette butts into water. Environ. Pollut. 2020, 259, 113916. [CrossRef]

Gong, M.; Khurshid, S.; Poppendiek, D. What’s in a butt? Environmental contamination from airborne cigarette butt emissions. Integr. Environ. Assess. Manag. 2017, 13, 549–551. [CrossRef]

Moriwaki, H.; Kitajima, S.; Katalhara, K. Waste on the roadside, ‘poi-sute’ waste: Its distribution and elution potential of pollutants into environment. Waste Manag. 2009, 29, 1192–1197. [CrossRef]

Golia, E.E.; Dimirkou, A.; Mitsios, I.K. Accumulation of Metals on Tobacco Leaves (Primings) Grown in an Agricultural Area in Relation to Soil. Bull. Environ. Contam. Toxicol. 2007, 79, 158–162. [CrossRef]

Golia, E.E.; Dimirkou, A.; Mitsios, I.K. Heavy-Metal Concentration in Tobacco Leaves in Relation to Their Available Soil Fractions. Commun. Soil Sci. Plant Anal. 2009, 40, 106–120. [CrossRef]

Liu, H.; Wang, H.; Ma, Y.; Wang, H.; Shi, Y. Role of transpiration and metabolism in translocation and accumulation of cadmium in tobacco plants (Nicotiana tabacum L.). Chemosphere 2016, 144, 1960–1965. [CrossRef]

Fresquez, M.R.; Pappas, R.S.; Watson, C.H. Establishment of Toxic Metal Reference Range in Tobacco from US Cigarettes. J. Anal. Toxicol. 2013, 37, 298–304. [CrossRef]

Armendáriz, C.R.; García, T.; Soler, A.; Ángel, J.G.F.; Glez-Weller, D.; González, G.L.; de la Torre, A.H.; Girónes, C.R. Heavy metals in cigarettes for sale in Spain. Environ. Res. 2015, 143, 162–169. [CrossRef]

Stephens, W.E.; Calder, A.; Newton, J. Source and Health Implications of High Toxic Metal Concentrations in Illicit Tobacco Products. Environ. Sci. Technol. 2005, 39, 477–484. [CrossRef]

Adriano, D.C.; Chlopecka, A.; Kaplan, D.I. Role of Soil Chemistry in Soil Remediation and Ecosystem Conservation. Soil Chem. Ecosys. Health 1998, 52, 361–386.

Traina, S.J. The Environmental Chemistry of Cadmium. In Cadmium in Soils and Plants; McLaughlin, M.J., Singh, B.R., Eds.; Springer: Dordrecht, The Nethelands, 1999; pp. 11–37. ISBN 978-94-010-5916-9.

Traina, S.J.; Laperche, V. Contaminant bioavailability in soils, sediments, and aquatic environments. Proc. Natl. Acad. Sci. USA 1999, 96, 3365–3371. [CrossRef]

Sposito, G. The Chemistry of Soils; Oxford University Press: Oxfordshire, UK, 2008.

Campbell, R.C.J.; Stephens, W.; Finch, A.A.; Geraki, K. Controls on the Valence Species of Arsenic in Tobacco Smoke: XANES Investigation with Implications for Health and Regulation. Environ. Sci. Technol. 2014, 48, 3449–3456. [CrossRef]

Pappas, R.; Polzin, G.; Zhang, L.; Watson, C.; Paschal, D.; Ashley, D. Cadmium, lead, and thallium in mainstream tobacco smoke particulate. Food Chem. Toxicol. 2006, 44, 714–723. [CrossRef] [PubMed]

Dobaradaran, S.; Schmidt, T.C.; Nabipour, I.; Ostovar, A.; Raeisi, A.; Saeedi, R.; Khorsand, M.; Khajehmadi, N.; Keshhtkar, M. Cigarette butts abundance and association of mercury and lead along the Persian Gulf beach: An initial investigation. Environ. Sci. Pollut. Res. 2018, 25, 5465–5473. [CrossRef]
63. Pelit, F.O.; Demirdoğen, R.E.; Henden, E. Investigation of heavy metal content of Turkish tobacco leaves, cigarette butt, ash, and smoke. *Environ. Monit. Assess.* 2013, 185, 9471–9479. [CrossRef]

64. Koutela, N.; Fernández, E.; Saru, M.-L.; Psilakis, E. A comprehensive study on the leaching of metals from heated tobacco sticks and cigarettes in water and natural waters. *Sci. Total Environ.* 2020, 714, 136700. [CrossRef]

65. Mansouri, N.; Elehari, M.; Ebrahimi, A.; Ebrahimpour, K.; Rahimi, B.; Hassanazadeh, A.Arsenic Content of Cigarette Butt Leachate of Five Cigarette Brands into Water. *Int. J. Environ. Health Res.* 2020, 9, 13.

66. Moerman, J.W.; Potts, G.E. Analysis of metals leached from smoked cigarette litter. *Tob. Control* 2011, 20, i30–i35. [CrossRef]

67. Qamar, W.; Abdelgali, A.A.; Aljarboa, S.; Alhuzani, M.; Altamimi, M. Cigarette waste: Assessment of hazard to the environment and health in Riyadh city. *Saudi J. Biol. Sci.* 2020, 27, 1380–1383. [CrossRef]

68. Mikheev, V.B.; Brinkman, M.C.; Granville, C.A.; Gordon, S.M.; Clark, P.I. Real-Time Measurement of Electronic Cigarette Aerosol Size Distribution and Metals Content Analysis. *Nicotine Tob. Res.* 2016, 18, 1895–1902. [CrossRef]

69. Olmedo, P.; Goessler, W.; Tanda, S.; Grau-Perez, M.; Jarmul, S.; Aherrera, A.; Chen, R.; Hilpert, M.; Cohen, J.E.; Navas-Acien, A.; et al. Metal Concentrations in e-Cigarette Liquid and Aerosol Samples: The Contribution of Metallic Coils. *Environ. Health Perspect.* 2018, 126, 027010. [CrossRef]

70. Saffari, A.; Daher, N.; Ruprecht, A.; De Marco, C.; Pozzi, P.; Boffi, R.; Hamad, S.H.; Shafer, M.M.; Schauer, J.J.; Westerdahl, D.; et al. Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: Comparison of emission rates and secondhand exposure. *Environ. Sci. Process. Impacts* 2014, 16, 2259–2267. [CrossRef]

71. Williams, M.; Villarreal, A.; Bozhilov, K.; Lin, S.; Talbot, P. Metal and Silicate Particles Including Nanoparticles Are Present in Electronic Cigarette Cartomizer Fluid and Aerosol. *PLoS ONE* 2013, 8, e57987. [CrossRef]

72. Williams, M.; Bozhilov, K.N.; Talbot, P. Analysis of the elements and metals in multiple generations of electronic cigarette atomizers. *Environ. Res.* 2019, 175, 156–166. [CrossRef]

73. Zervas, E.; Matsouki, N.; Kyriakopoulos, G.; Pouloupolou, S.; Ioannides, T.; Katsaounou, P. Transfer of metals in the liquids of electronic cigarettes. *Inhal. Toxicol.* 2020, 32, 240–248. [CrossRef]

74. Song, Q.; Li, J. Environmental effects of heavy metals derived from the e-waste recycling activities in China: A systematic review. *Waste Manag.* 2014, 34, 2587–2594. [CrossRef]

75. Bonanomi, G.; Maisto, G.; De Marco, A.; Cesarano, G.; Zotti, M.; Mazzei, P.; Libralato, G.; Staropoli, A.; Siciliano, A.; De Filippis, F.; et al. The fate of cigarette butts in different environments: Decay rate, chemical changes and ecotoxicity revealed by a 5-years decomposition experiment. *Environ. Pollut.* 2020, 261, 114108. [CrossRef]

76. Chevalier, Q.; El Hadri, H.; Petitjean, P.; Coz, M.B.-L.; Reynaud, S.; Grassl, B.; Gigault, J. Nano-litter from cigarette butts: Environmental implications and urgent consideration. *Chemosphere* 2018, 194, 125–130. [CrossRef]

77. Valiente, R.; Escobar, F.; Pearce, J.; Bilal, U.; Franco, M.; Sureda, X. Estimating and mapping cigarette butt littering in urban environments: A GIS approach. *Environ. Res.* 2020, 183, 109142. [CrossRef]

78. Hoellein, T.; Rojas, M.; Pink, A.; Gasior, J.; Kelly, J. Anthropogenic Litter in Urban Freshwater Ecosystems: Distribution and Microbial Interactions. *PLoS ONE* 2014, 9, e98485. [CrossRef]

79. Ocean Conservancy. *International Coastal Cleanup: 2020 Report*; Ocean Conservancy: Washington, DC, USA, 2020; p. 32.

80. Healton, C.G.; Cummings, K.M.; O’Connor, R.J.; Novotny, T.E. Butt really? The environmental impact of cigarettes. *Tob. Control* 2011, 20, i1. [CrossRef]

81. Kungskulniti, N.; Charoena, N.; Hamann, S.L.; Pitayarangsarit, S.; Mock, J. Cigarette Waste in Popular Beaches in Thailand: High Densities that Demand Environmental Action. *Int. J. Environ. Res. Public Health* 2018, 15, 630. [CrossRef]

82. Novotny, T.E.; Lum, K.; Smith, E.; Wang, V.; Barnes, R. Cigarette Butts and the Case for an Environmental Policy on Hazardous Cigarette Waste. *Int. J. Environ. Res. Public Health* 2009, 6, 1691–1705. [CrossRef]

83. Wallbank, L.A.; MacKenzie, R.; Beggs, P.J. Environmental impacts of tobacco product waste: International and Australian policy responses. *Ambio* 2016, 46, 361–370. [CrossRef]

84. World Health Organization. *Tobacco and Its Environmental Impact: An Overview*; World Health Organization: Geneva, Switzerland, 2017; ISBN 978-92-4-151249-7.

85. Fischer, S.; Thümmler, K.; Volkert, B.; Hettrich, K.; Schmidt, I.; Fischer, K. Properties and Applications of Cellulose Acetate. *Macromol. Symp.* 2008, 262, 89–96. [CrossRef]

86. Bonanomi, G.; Incerti, G.; Cesarano, G.; Gaglione, S.A.; Lanzotti, V. Cigarette But Decomposition and Associated Chemical Changes Assessed by 13C CPMAS NMR. *PLoS ONE* 2015, 10, e0117393. [CrossRef]

87. Kadir, A.A.; Sarani, N.A. Cigarette Butts Pollution and Environmental Impact—A Review. *Appl. Mech. Mater.* 2015, 773–774, 1106–1110. [CrossRef]

88. Joly, F.-X.; Coulis, M. Comparison of cellulose vs. plastic cigarette filter decomposition under distinct disposal environments. *Waste Manag.* 2018, 72, 349–353. [CrossRef]

89. Harris, B. The intractable cigarette ‘filter problem’. *Tob. Control* 2011, 20, i10–i16. [CrossRef]

90. Belzagui, F.; Buscio, V.; Gutiérrez-Bouzán, C.; Vilaseca, M. Cigarette butts as a microfiber source with a microplastic level of concern. *Sci. Total Environ.* 2021, 762, 144165. [CrossRef]

91. Venugopal, P.D.; Hanna, S.K.; Gagliano, G.G.; Chang, H.W. No Butts on the Beach: Aquatic Toxicity of Cigarette Butch Leachate Chemicals. *Tob. Regul. Sci.* 2021, 7, 17–30. [CrossRef]
92. Green, A.L.R.; Putschew, A.; Nehls, T. Littered cigarette butts as a source of nicotine in urban waters. *J. Hydrol.* **2014**, *519*, 3466–3474. [CrossRef]

93. Zhao, J.; Zhang, N.; Qu, C.; Wu, X.; Zhang, J.; Zhang, X. Cigarette Butts and Their Application in Corrosion Inhibition for N80 Steel at 90 °C in a Hydrochloric Acid Solution. *Ind. Eng. Chem. Res.* **2010**, *49*, 3986–3991. [CrossRef]

94. Zhao, J.; Zhang, N.; Qu, C.; Zhang, J.; Zhang, X. Comparison of the Corrosion Inhibitive Effect of Anaerobic and Aerobic Cigarette Butts Water Extracts on N80 Steel at 90 °C in Hydrochloric Acid Solution. *Ind. Eng. Chem. Res.* **2010**, *49*, 12452–12460. [CrossRef]

95. Dobraradaran, S.; Nabipour, J.; Saedii, R.; Ostovar, A.; Khorsand, M.; Khajehnadi, N.; Hayati, R.; Keshhtkar, M. Association of metals (Cd, Fe, As, Ni, Cu, Zn and Mn) with cigarette butts in northern part of the Persian Gulf. *Tob. Control* **2017**, *26*, 461–463. [CrossRef]

96. Dobraradaran, S.; Schmidt, T.C.; Kazizur-Cegla, W.; Joehmann, M.A. BTEx compounds leachates from cigarette butts into water environment: A primary study. *Environ. Pollut.* **2021**, *269*, 116185. [CrossRef]

97. Lawal, M.S.; Ologundudu, S.O. Toxicity of Cigarette Filter Leachates on Hymenochirus Curtipes and Clarias Gariepinus in Nigeria. *J. Environ. Ext.* **2013**, *11*, 7–14.

98. Van Dijk, W.D.; Gopal, S.; Speeckers, P.T.J. Nanoparticles in cigarette smoke: real-time undiluted measurements by a scanning mobility particle sizer. *Anal. Bioanal. Chem.* **2011**, *399*, 3573–3578. [CrossRef]

99. Rebischung, F.; Chabot, L.; Blaudet, H.; Pandard, P. Cigarette butts: A small but hazardous waste, according to European regulation. *Waste Manag.* **2018**, *82*, 9–14. [CrossRef]

100. Torkashvand, J.; Farzadkia, M.; Sobhi, H.R.; Esfarafi, A. Littered cigarette butt as a well-known hazardous waste: A comprehensive systematic review. *J. Hazard. Mater.* **2020**, *383*, 121242. [CrossRef]

101. Jacob, I.P.; Benowitz, N.L.; Destaillats, H.; Gundel, L.; Hang, B.; Martins-Green, M.; Matt, G.E.; Quintana, P.J.E.; Samet, J.M.; Schick, S.F.; et al. Thirdhand Smoke: New Evidence, Challenges, and Future Directions. *Chem. Res. Toxicol.* **2017**, *30*, 270–294. [CrossRef]

102. Cecinato, A.; Balducci, C.; Romagnoli, P.; Perilli, M. Airborne psychotropic substances in eight Italian big cities: Burdens and behaviours. *Environ. Pollut.* **2012**, *167*, 140–147. [CrossRef]

103. Klepeis, N.E.; Ott, W.R.; Switzer, P. Real-Time Measurement of Outdoor Tobacco Smoke Particles. *J. Air Waste Manag. Assoc.* **2007**, *57*, 522–534. [CrossRef]

104. Rogge, W.F.; Hildemann, L.M.; Mazurek, M.A.; Cass, G.R.; Simoneit, B.R.T. Sources of Fine Organic Aerosol. 6. Cigarette Smoke in the Urban Atmosphere. *Environ. Sci. Technol.* **1994**, *28*, 1375–1388. [CrossRef]

105. Schauer, J.J.; Rogge, W.F.; Hildemann, L.M.; Mazurek, M.A.; Cass, G.R.; Simoneit, B.R. Source apportionment of airborne particulate matter using organic compounds as tracers. *Atmos. Environ.* **1996**, *30*, 3837–3855. [CrossRef]

106. Brennan, E.; Cameron, M.; Warne, C.; Durkin, S.; Borland, R.; Travers, M.J.; Hyland, A.; Wakefield, M.A. Secondhand smoke drift: Examining the influence of indoor smoking bans on indoor and outdoor air quality at pubs and bars. *Nicotine Tob. Res.* **2010**, *12*, 271–277. [CrossRef]

107. Sureda, X.; Martínez-Sánchez, J.M.; Lopez, M.J.; Fu, M.; Agüero, F.; Saltó, E.; Nebot, M.; Fernández, E. Secondhand smoke levels in public building main entrances: Outdoor and indoor PM2.5 assessment. *Tob. Control* **2012**, *21*, 543–548. [CrossRef]

108. Cho, H.; Lee, K.; Hwang, Y.; Richardson, P.; Bratset, H.; Teeters, E.; Record, R.; Riker, C.; Hahn, E.J. Outdoor tobacco smoke exposure at the perimeter of a tobacco-free university. *J. Air Waste Manag. Assoc.* **2014**, *64*, 863–866. [CrossRef]

109. Fleck, A.D.S.; Carneiro, M.F.H.; Barbosa, F.; Thiesen, F.V.; Amantéa, S.L.; Rhoden, C.R. Monitoring an outdoor smoking area by means of PM2.5 measurement and vegetal biomonitoring. *Environ. Sci. Pollut. Res.* **2015**, *23*, 21187–21194. [CrossRef]

110. Ott, W.R.; Acevedo-Bolton, V.; Cheng, K.; Jiang, R.T.; Klepeis, N.E.; Hildemann, L.M. Outdoor fine and ultrafine particle measurements at six bus stops with smoking on two California arterial highways – Results of a pilot study. *J. Air Waste Manag. Assoc.* **2013**, *64*, 47–60. [CrossRef]

111. Kaufman, P.; Zhang, B.; Bendy, S.J.; Klepeis, N.; Ferrence, R. Not just ‘a few wisps’: Real-time measurement of tobacco smoke at entrances to office buildings. *Tob. Control* **2011**, *20*, 212–218. [CrossRef]

112. López, M.J.; Fernández, E.; Gorini, G.; Moshammer, H.; Polanska, K.; Clancy, L.; Dautzenberg, B.; Delrieu, A.; Invernizzi, G.; Muñoz, G.; et al. Exposure to Secondhand Smoke in Terraces and Other Outdoor Areas of Hospitality Venues in Eight European Countries. *PloS ONE* **2012**, *7*, e42130. [CrossRef]

113. Matt, G.; Quintana, P.J.E.; Destaillats, H.; Gundel, L.A.; Sleiman, M.; Singer, B.C.; Jacob, P.; Benowitz, N.; Winickoff, J.P.; Rehan, V.; et al. Thirdhand Tobacco Smoke: Emerging Evidence and Arguments for a Multidisciplinary Research Agenda. *Environ. Health Perspect.* **2011**, *119*, 1218–1226. [CrossRef]

114. Diez-Izquierdo, A.; Cassanello-Peñarroya, P.; Lidón-Moyano, C.; Matilla-Santander, N.; Balaguer, A.; Martinez-Sánchez, J.M. Update on thirdhand smoke: A comprehensive systematic review. *Environ. Res.* **2018**, *167*, 341–371. [CrossRef]

115. Matt, G.E.; Quintana, P.J.E.; Zakarian, J.M.; Hoh, E.; Hovell, M.F.; Mahabee-Gittens, M.; Watanabe, K.; Datuwin, K.; Vue, C.; Chatfield, D.A. When smokers quit: Exposure to nicotine and carcinogens persists from thirdhand smoke pollution. *Tob. Control* **2017**, *26*, 548–556. [CrossRef]

116. Singer, B.C.; Hodgson, A.T.; Guevarra, K.S.; Hawley, E.L.; Nazaroff, W.W. Gas-Phase Organics in Environmental Tobacco Smoke. 1. Effects of Smoking Rate, Ventilation, and Furnishing Level on Emission Factors. *Environ. Sci. Technol.* **2002**, *36*, 846–853. [CrossRef]
117. Masoner, J.R.; Kolpin, D.W.; Furlong, E.T.; Cozzarelli, I.M.; Gray, J.L.; Schwab, E.A. Contaminants of emerging concern in fresh leachate from landfills in the conterminous United States. *Environ. Sci. Process. Impacts* **2014**, *16*, 2335–2354. [CrossRef]

118. Matt, G.E.; Quintana, P.J.; Hoh, E.; Zakarian, J.M.; Dodder, N.; Record, R.A.; Hovell, M.E.; Mahabee-Gittens, E.M.; Padilla, S.; Markman, L.; et al. Persistent tobacco smoke residue in multiunit housing: Legacy of permissive indoor smoking policies and challenges in the implementation of smoking bans. *Prev. Med. Rep.* **2020**, *18*, 101088. [CrossRef]

119. Berthonol, J.; Becquemin, M.; Annesi-Maesano, I.; Dautzenberg, B. Electronic Cigarettes: A Short Review. *Respiration* **2013**, *86*, 433–438. [CrossRef]

120. Caponnetto, P.; Campagna, D.; Papale, G.; Russo, C.; Polosa, R. The emerging phenomenon of electronic cigarettes. *Expert Rev. Respir. Med.* **2012**, *6*, 63–74. [CrossRef]

121. Grana, R.; Benowitz, N.; Glantz, S.A. E-Cigarettes. *Circulation* **2014**, *129*, 1972–1986. [CrossRef]

122. U.S. Department of Health and Human Services. *E-Cigarette Use among Youth and Young Adults: A Report of the Surgeon General*; U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health: Atlanta, GA, USA, 2016; p. 295.

123. Breland, A.; Soule, E.; Lopez, A.; Ramia, C.; El-Hellani, A.; Eissenberg, T. Electronic cigarettes: What are they and what do they do? *Ann. N. Y. Acad. Sci.* **2017**, *1394*, 5–30. [CrossRef]

124. Dai, H.; Leventhal, A.M. Prevalence of e-Cigarette Use Among Adults in the United States, 2014–2018. *JAMA* **2019**, *322*, 1824–1827. [CrossRef]

125. Delnevo, C.; Giovenco, D.P.; Hrywna, M. Rapid proliferation of illegal pod-mod disposable e-cigarettes. *Tob. Control* **2020**, *29*, 150–151. [CrossRef]

126. U.S. Department of Health and Human Services. *Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market without Premarket Authorization: Guidance for Industry*. Office of Compliance and Enforcement, Office of Health Communication and Education, Office of Regulations, and Office of Science in the Center for Tobacco Products, Food and Drug Administration, U.S. Department of Health and Human Services: Silver Spring, MD, USA, 2020.

127. Krause, M.; Townsend, T.G. Hazardous waste status of discarded electronic cigarettes. *Waste Manag.* **2015**, *39*, 57–62. [CrossRef]

128. Herrington, J.S.; Myers, C. Electronic cigarette solutions and resultant aerosol profiles. *J. Chromatogr. A* **2015**, *1418*, 192–199. [CrossRef]

129. Czoli, C.D.; Goniewicz, M.; Palumbo, M.; Leigh, N.; White, C.M.; Hammond, D. Identification of flavouring chemicals and potential toxicants in e-cigarette products in Ontario, Canada. *Can. J. Public Health* **2019**, *110*, 542–550. [CrossRef]

130. Fagan, P.; Pokhrel, P.; Herzog, T.; Moolchan, E.T.; Cassel, K.D.; A Franke, A.; Li, X.; Pagano, I.; Trudeau, D.R.; Sakum, K.-L.; et al. Sugar and Aldehyde Content in Flavored Electronic Cigarette Liquids. *Nicotine Tob. Res.* **2017**, *20*, 985–992. [CrossRef]

131. Khlystov, A.; Samburova, V. Flavoring Compounds Dominate Toxic Aldehyde Production during E-Cigarette Vaping. *Environ. Sci. Technol.* **2016**, *50*, 13080–13085. [CrossRef]

132. Sassano, M.F.; Davis, E.; Keating, J.E.; Zorn, B.T.; Kochar, T.K.; Wolfgang, M.C.; Glish, G.L.; Tarran, R. Evaluation of e-liquid toxicity using an open-source high-throughput screening assay. *PLoS Biol.* **2018**, *16*, e2003904. [CrossRef]

133. A Tierney, P.; Karpinski, C.D.; E Brown, J.; Luo, W.; Pankow, J.F. Flavour chemicals in electronic cigarette fluids. *Tob. Control* **2016**, *25*, e10–e15. [CrossRef]

134. Czogala, J.; Goniewicz, M.L.; Fidelus, B.; Zielinska-Danch, W.; Travers, M.J.; Sobczak, A. Secondhand Exposure to Vapors From Electronic Cigarettes. *Nicotine Tob. Res.* **2014**, *16*, 655–662. [CrossRef]

135. Farsalinos, K.E.; Kistler, K.A.; Pennington, A.; Spyrou, A.; Kouretas, D.; Gillman, G. Aldehyde levels in e-cigarette aerosol: Findings from a replication study and from use of a new-generation device. *Food Chem. Toxicol.* **2018**, *111*, 64–70. [CrossRef]

136. Logue, J.M.; Sielem, M.; Montesinos, V.N.; Russell, M.L.; Litter, M.I.; Benowitz, N.L.; Gundel, L.A.; Destaillats, H. Emissions from Electronic Cigarettes: Assessing Vapers’ Intake of Toxic Compounds, Secondhand Exposures, and the Associated Health Impacts. *Environ. Sci. Technol.* **2017**, *51*, 9271–9279. [CrossRef]

137. Sielem, M.; Logue, J.M.; Montesinos, N.; Russell, M.L.; Litter, M.I.; Gundel, L.A.; Destaillats, H. Emissions from Electronic Cigarettes: Key Parameters Affecting the Release of Harmful Chemicals. *Environ. Sci. Technol.* **2016**, *50*, 9646–9651. [CrossRef]

138. Casebolt, R.; Cook, S.J.; Islas, A.; Brown, A.; Castle, K.; Dutcher, D.D. Carbon monoxide concentration in mainstream e-cigarette emissions measured with diode laser spectroscopy. *Tob. Control* **2019**, *29*, 652–655. [CrossRef]

139. Lerner, C.A.; Sundar, I.K.; Watson, R.; Elder, A.; Jones, R.; Done, D.; Kurtzman, R.; Ossip, D.J.; Robinson, R.; McIntosh, S.; et al. Environmental health hazards of e-cigarettes and their components: Oxidants and copper in e-cigarette aerosols. *Environ. Pollut.* **2015**, *198*, 100–107. [CrossRef]

140. Cromwell, B.; Mota, L.C.; Levine, M. Detection of Potentially Toxic Additives in Electronic Cigarettes and Cigarette Flavourings. *Anal. Lett.* **2019**, *53*, 1407–1415. [CrossRef]

141. Castiglioni, S.; Senta, I.; Borsotti, A.; Davoli, E.; Zuccato, E. A novel approach for monitoring tobacco use in local communities by wastewater analysis. *Tob. Control* **2015**, *24*, 38–42. [CrossRef]

142. Hedgepeth, M.L.; Sapozhnikova, Y.; Pennington, P.; Clum, A.; Fairey, A.; Wirth, E. Pharmaceuticals and personal care products (PPCPs) in treated wastewater discharges into Charleston Harbor, South Carolina. *Sci. Total Environ.* **2012**, *437*, 1–9. [CrossRef]
143. Huerta-Fontela, M.; Ventura, F. Traceability of Emerging Contaminants from Wastewater to Drinking Water. In Emerging Contaminants from Industrial and Municipal Waste; Barceló, D., Petrovic, M., Eds.; Springer: Berlin/Heidelberg, Germany, 2008; Volume SS/1, pp. 143–168, ISBN 978-3-540-74793-2.

144. Maessen, G.C.; Wijnhoven, A.M.; Neijzen, R.L.; Paulus, M.C.; Van Heel, D.A.M.; Bomers, B.H.A.; Boersma, L.E.; Konya, B.; Van Der Heyden, M.A.G. Nicotine intoxication by e-cigarette liquids: A study of case reports and pathophysiology. Clin. Toxicol. 2019, 58, 1–8. [CrossRef]

145. Santos, J.L.; Aparicio, I.; Callejón, M.; Alonso, E. Occurrence of pharmaceutically active compounds during 1-year period in wastewaters from four wastewater treatment plants in Seville (Spain). J. Hazard. Mater. 2009, 164, 1509–1516. [CrossRef] [PubMed]

146. Senta, L.; Lor, E.G.; Borsotti, A.; Zuccato, E.; Castiglioni, S. Wastewater analysis to monitor use of caffeine and nicotine and evaluation of their metabolites as biomarkers for population size assessment. Water Res. 2015, 74, 23–33. [CrossRef] [PubMed]

147. Hukkanen, J.; Jacob, P., III; Benowitz, N.L. Metabolism and Disposition Kinetics of Nicotine. Pharmacol. Rev. 2005, 57, 79–115. [CrossRef]

148. Heinrich, J.; Hölscher, B.; Seiwert, M.; Carty, C.L.; Merkel, G.; Schulz, C. Nicotine and cotinine in adults’ urine: The German Environmental Survey 1998. J. Expo. Sci. Environ. Epidemiol. 2004, 15, 74–80. [CrossRef]

149. Zarrelli, A.; DellaGreca, M.; Parolisi, A.; Jesce, M.R.; Cermola, F.; Temussi, F.; Isidori, M.; Lavorgna, M.; Passananti, M.; Previtera, L. Chemical fate and genotoxic risk associated with hypochlorite treatment of nicotine. Sci. Total Environ. 2012, 426, 132–138. [CrossRef]

150. Buerge, I.J.; Kahle, M.; Buser, H.-R.; Müller, M.D.; Poiger, T. Nicotine Derivatives in Wastewater and Surface Waters: Application as Chemical Markers for Domestic Wastewater. Environ. Sci. Technol. 2008, 42, 6354–6360. [CrossRef]

151. Ekpeghere, K.I.; Sim, W.-J.; Lee, H.-J.; Oh, J.-E. Occurrence and distribution of carbamazepine, nicotine, estrogenic compounds, and their transformation products in wastewater from various treatment plants and the aquatic environment. Sci. Total Environ. 2018, 640–641, 1015–1023. [CrossRef] [PubMed]

152. Bueno, M.M.; Ucles, S.; Hernando, M.; Davoli, E.; Fernández-Alba, A. Evaluation of selected ubiquitous contaminants in the aquatic environment and their transformation products. A pilot study of their removal from a sewage treatment plant. Water Res. 2011, 45, 2331–2341. [CrossRef]

153. Focazio, M.J.; Kolpin, D.W.; Barnes, K.K.; Furlong, E.; Meyer, S.D.; Zaugg, S.D.; Barber, L.B.; Thurman, E.M. A national reconnaissance for pharmaceuticals and other organic wastewater contaminants in the United States—II. Untreated drinking water sources. Sci. Total Environ. 2008, 402, 201–216. [CrossRef]

154. Barnes, K.K.; Kolpin, D.W.; Furlong, E.; Zaugg, S.D.; Meyer, S.D.; Barber, L.B. A national reconnaissance of pharmaceuticals and other organic wastewater contaminants in the United States—I. Groundwater. Sci. Total Environ. 2008, 402, 192–200. [CrossRef]

155. Godfrey, E.; Voessner, W.W.; Benotti, M.J. Pharmaceuticals in On-Set Sewage Effluent and Ground Water, Western Montana. Ground Water 2007, 45, 263–271. [CrossRef] [PubMed]

156. Schaider, L.A.; Ackerman, J.M.; Rudel, R.A. Septic systems as sources of organic wastewater compounds in domestic drinking water wells in a shallow sand and gravel aquifer. Sci. Total Environ. 2016, 547, 470–481. [CrossRef] [PubMed]

157. Stuart, M.; Lapworth, D.; Crane, E.; Hart, A. Review of risk from potential emerging contaminants in UK groundwater. Sci. Total Environ. 2012, 416, 1–21. [CrossRef]

158. Verstraeten, I.; Fetterman, G.; Meyer, M.; Bullen, T.; Sebree, S. Use of tracers and isotopes to evaluate vulnerability of water in domestic wells to septic waste. Ground Water Monit. Remediat. 2005, 25, 107–117. [CrossRef]

159. Kinney, C.A.; Furlong, E.T.; Werner, S.L.; Cahill, J.D. Presence and distribution of wastewater-derived pharmaceuticals in soil irrigated with reclaimed water. Environ. Toxicol. Chem. 2006, 25, 317–326. [CrossRef] [PubMed]

160. Teijon, G.; Candela, L.; Tamoh, K.; Molina-Díaz, A.; Fernández-Alba, A. Occurrence of emerging contaminants, priority substances (2008/105/CE) and heavy metals in treated wastewater and groundwater at Depurbaix facility (Barcelona, Spain). Sci. Total Environ. 2010, 408, 3584–3595. [CrossRef]

161. Lapworth, D.J.; Baran, N.; Stuart, M.E.; Ward, R.S. Emerging organic contaminants in groundwater: A review of sources, fate and occurrence. Environ. Pollut. 2012, 163, 287–303. [CrossRef]

162. Barnes, K.K.; Christenson, S.C.; Kolpin, D.W.; Focazio, M.J.; Furlong, E.T.; Zaugg, S.D.; Meyer, M.T.; Barber, L.B. Pharmaceuticals and Other Organic Waste Contaminants Within a Leachate Plume Downgradient of a Municipal Landfill. GroundWaterMonit. Remediat. 2004, 24, 119–126. [CrossRef]

163. Buszka, P.M.; Yeskis, D.J.; Kolpin, D.W.; Furlong, E.; Zaugg, S.D.; Meyer, M. Waste-Indicator and Pharmaceutical Compounds in Landfill-Leachate-Affected Ground Water near Elkhart, Indiana, 2000–2002. Bull. Environ. Contam. Toxicol. 2009, 82, 653–659. [CrossRef]

164. Baderna, D.; Maggioni, S.; Boriani, E.; Gemma, S.; Molteni, M.; Lombardo, A.; Colombo, A.; Bordonali, S.; Rotella, G.; Lodi, M.; et al. A combined approach to investigate the toxicity of an industrial landfill’s leachate: Chemical analyses, risk assessment and in vitro assays. Environ. Res. 2011, 111, 603–613. [CrossRef]

165. Schwarzbauer, J.; Heim, S.; Brinker, S.; Littke, R. Occurrence and alteration of organic contaminants in seepage and leakage water from a waste deposit landfill. Water Res. 2002, 36, 2275–2287. [CrossRef]

166. Lee, D.G.; Reoerdanz, P.R.; Feraud, M.; Ervin, J.; Anumol, T.; Jia, A.; Park, M.; Tamez, C.; Morelius, E.W.; Gardea-Torresdey, J.L.; et al. Wastewater compounds in urban shallow groundwater wells correspond to exfiltration probabilities of nearby sewers. Water Res. 2015, 85, 467–475. [CrossRef] [PubMed]
193. Xu, E.G.; Richardot, W.H.; Li, S.; Buruaem, L.; Wei, H.-H.; Dodder, N.G.; Schick, S.F.; Novotny, T.; Schlenk, D.; Gersberg, R.M.; et al. Assessing Toxicity and in Vitro Bioactivity of Smoked Cigarette Leachate Using Cell-Based Assays and Chemical Analysis. *Chem. Res. Toxicol.* **2019**, *32*, 1670–1679. [CrossRef]

194. Baran, W.; Majeed-Knyasuk, D.; Sobczak, A.; Adamek, E. The influence of waste from electronic cigarettes, conventional cigarettes and heat-not-burn tobacco products on microorganisms. *J. Hazard. Mater.* **2020**, *385*, 121591. [CrossRef]

195. Costanza, R.; D’Arge, R.; De Groot, R.; Farber, S.; Grasso, M.; Hannon, B.; Limburg, K.; Naeem, S.; O’Neill, R.V.; Paruelo, J.; et al. The value of the world’s ecosystem services and natural capital. *Nature* **1997**, *387*, 253–260. [CrossRef]

196. Quéméneur, M.; Chifflet, S.; Akrout, F.; Belaya-Zouari, A.; Belhassen, M. Impact of cigarette butts on microbial diversity and dissolved trace metals in coastal marine sediment. *Estuar. Coast. Shelf Sci.* **2020**, *240*, 106785. [CrossRef]

197. Koroleva, E.; Mqulwa, A.Z.; Norris-Jones, S.; Reed, S.; Tambe, Z.; Visagie, A.; Jacobs, K. Impact of cigarette butts on bacterial community structure in soil. *Environ. Sci. Pollut. Res.* **2021**, *28*, 33030–33040. [CrossRef] [PubMed]

198. Selmar, D.; Engellhardt, U.H.; Hänsel, S.; Thräne, C.; Nowak, M.; Kleinwächter, M. Nicotine uptake by peppermint plants as a possible source of nicotine in plant-derived products. *Agron. Sustain. Dev.* **2015**, *35*, 1185–1190. [CrossRef]

199. Radwan, D.S.A. Horizontal Natural Product Transfer: A so far Unconsidered Source of Contamination of Plant-Derived Commodities. *J. Environ. Anal. Toxicol.* **2015**, *5*, [CrossRef]

200. Weidner, M.; Martins, R.; Müller, A.; Simon, J.; Schnitz, H. Uptake, transport and accumulation of nicotine by the Golden Potho (*Epipremnum aureum*): The central role of root pressure. *J. Plant Physiol.* **2005**, *162*, 139–150. [CrossRef]

201. Selmar, D.; Radwan, A.; Abdalla, N.; Taha, H.; Wittke, C.; El-Henawy, A.; Alshaia, T.; Amer, M.; Kleinwächter, M.; Nowak, M.; et al. Uptake of nicotine from discarded cigarette butts – A so far unconsidered path of contamination of plant-derived commodities. *Environ. Pollut.* **2018**, *238*, 972–976. [CrossRef]

202. Boxall, A.B.A.; Johnson, P.; Smith, E.J.; Sinclair, C.J.; Stutt, A.E.; Levy, L.S. Uptake of Veterinary Medicines from Soils into Plants. *J. Agric. Food Chem.* **2006**, *54*, 2288–2297. [CrossRef]

203. Trapp, S.; Legind, C.N. Uptake of Organic Contaminants from Soil into Vegetables and Fruits. In *Dealing with Contaminated Sites*; Springer: Singapore, 2010; pp. 369–408.

204. Selmar, D.; Wittke, C.; Wolfersdorf, I.B.-V.; Klier, B.; Lewerenz, L.; Kleinwächter, M.; Nowak, M. Transfer of pyrrolizidine alkaloids between living plants: A disregarded source of contaminations. *Environ. Pollut.* **2019**, *248*, 456–461. [CrossRef]

205. Zhao, B.; Agblevor, F.A.; Ritesh, C.; Jelesto, J.G. Enhanced production of the alkaloid nicotine in hairy root cultures of *Nicotiana tabacum L.* *Plant Cell Tissue Organ Cult.* (PCTOC) **2012**, *113*, 121–129. [CrossRef]

206. Simard, S.W.; Beiler, K.J.; Bingham, M.A.; Deslippe, J.R.; Philip, L.J.; Teste, F.P. Mycorrhizal networks: Mechanisms, ecology and modelling. *Fungal Biol. Rev.* **2012**, *26*, 39–60. [CrossRef]

207. Batish, D.R.; Singh, H.P.; Kaur, S.; Kohli, R.K.; Yadav, S.S. Caffeic acid affects early growth, and morphogenetic response of hypocotyl cuttings of mung bean (*Phaseolus aureus*). *J. Plant Physiol.* **2008**, *165*, 297–305. [CrossRef]

208. Darwent, M.J.; Paterson, E.; McDonald, A.J.S.; Tomos, A.D. Biosensor reporting of root exudation from *Hordeum vulgare* in relation to shoot nitrate concentration. *J. Exp. Bot.* **2003**, *54*, 325–334. [CrossRef]

209. Walker, T.S.; Bais, H.P.; Grotewold, E.; Vivanco, J.M. Root Exudation and Rhizosphere Biology. *Plant Physiol.* **2003**, *132*, 44–51. [CrossRef]

210. Montalvão, M.F.; Sampaio, L.G.G.; Gomes, H.H.F.; Malafaia, G. An insight into the cytotoxicity, genotoxicity, and mutagenicity of smoked cigarette butt leachate by using *Allium cepa* as test system. *Environ. Sci. Pollut. Res.* **2018**, *26*, 20133–2021. [CrossRef]

211. Green, D.S.; Boots, B.; Carvalho, J.D.S.; Starkey, T. Cigarette butts have adverse effects on initial growth of perennial ryegrass (gramininae: *Lolium perenne* L.) and white clover (leguminosae: *Trifolium repens* L.). *Ecotoxicol. Environ. Saf.* **2019**, *182*, 109418. [CrossRef]

212. Noble, R.E. Effect of cigarette smoke on seed germination. *Sci. Total Environ.* **2001**, *267*, 177–179. [CrossRef]

213. Tileklioglu, B.; Battal, P.; Isler, S. The effect of cigarette smoke on the growth and development of wheat (*Triticum vulgare* Vill.) and duckweed (*Lemna minor* L.). *J. Environ. Sci. Health Part A: Environ. Sci. Eng. Toxicol.* **1996**, *31*, 2577–2581. [CrossRef]

214. Mondal, N.K.; Dey, U.; Khatun, S.; Das, K.; Das, C.R. Toxic Effect of Cigarette Origin Tobacco Leaf (*Nicotiana tabacum* L.) and Cigarette Smoke Extract on Germination and Bio-Chemical Changes of Bengal Gram (*Cicer arietinum* L.). *J. Stress Physiol. Biochem.* **2014**, *10*, 135–144.

215. Khan, A.; Khan, S.; Khan, M.A.; Qamar, Z.; Waqas, M. The uptake and bioaccumulation of heavy metals by food plants, their effects on plants nutrients, and associated health risk: A review. *Environ. Sci. Pollut. Res.*** **2015**, *22*, 13772–13799. [CrossRef]

216. Lima, C.F.; dos Pinto, M.A.S.; Choueri, R.B.; Moreira, L.B.; Italo, B.C. Occurrence, characterization, partition, and toxicity of cigarette butts in a highly urbanized coastal area. *Water Manag.* **2021**, *131*, 10–19. [CrossRef]

217. Dobaradaran, S.; Soleimani, F.; Akbarizadeh, R.; Schmidt, T.C.; Marzban, M.; BasirianJahromi, R. Environmental fate of cigarette butts and their toxicity in aquatic organisms: A comprehensive systematic review. *Environ. Res.* **2021**, *195*, 110881. [CrossRef]

218. Slaughter, E.; Gersberg, R.M.; Watanabe, K.; Rudolph, J.; Stransky, C.; E Novotny, T. Toxicity of cigarette butts, and their chemical components, to marine and freshwater fish. *Tox. Control* **2011**, *20*, 125–129. [CrossRef]

219. Green, D.S.; Kregting, L.; Boots, B. Smoked cigarette butt leachate impacts survival and behaviour of freshwater invertebrates. *Environ. Pollut.* **2020**, *266*, 115286. [CrossRef]

220. Green, D.S.; Kregting, L.; Boots, B. Effects of cigarette butts on marine keystone species (*Ulua lactuca* L. and *Mytilus edulis* L.) and sediment microphytobenthos. *Mar. Pollut. Bull.* **2021**, *165*, 112152. [CrossRef]
Yabes, L.J. Bioaccumulation of Organic Compounds from Smoked Cigarette Litter in the Freshwater Rainbow Trout, *Oncorhynchus mykiss*. Master’s Thesis, San Diego State University, San Diego, CA, USA, 2018.

Kander, M.C. Bioaccumulation of Metals (As, Cd, Cr, Cu, Ni, Pb, Se, and Zn) from Smoked Cigarette Litter in Fish (Rainbow Trout) and Shellfish (Mediterranean Mussels). Master’s Thesis, San Diego State University, San Diego, CA, USA, 2017.

Wei, H.-H. Determination of Organic Compounds in Smoked Cigarette Leachate and the Bioaccumulation Potentials in the Marine Mussel, *Mytilus galloprovincialis*. Master’s Thesis, San Diego State University, San Diego, CA, USA, 2018.

Fire, S.; Wang, Z.; Berman, M.; Langlois, G.W.; Morton, S.L.; Sekula-Wood, E.; Benítez-Nelson, C. Trophic Transfer of the Harmful Algal Toxin Domoic Acid as a Cause of Death in a Minke Whale (*Balaenoptera acutorostrata*) Stranding in Southern California. *Aquat. Mamm.* 2010, 36, 342–350. [CrossRef]

Suárez-Rodríguez, M.; López-Rull, I.; García, C.M. Incorporation of cigarette butts into nests reduces nest ectoparasite load in urban birds: New ingredients for an old recipe? *Biol. Lett.* 2013, 9, 20120931. [CrossRef]

Cardoso, L.S.; Estrela, F.N.; Chagas, T.Q.; Da Silva, W.A.M.; Costa, D.R.D.O.; Pereira, I.; Vaz, B.G.; Rodrigues, A.S.D.L.; Malafaia, G. The exposure to water with cigarette residue changes the anti-predator response in female Swiss albino mice. *Environ. Sci. Pollut. Res.* 2018, 25, 8592–8607. [CrossRef]

Mayer, B. How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. *Arch. Toxicol.* 2014, 88, 5–7. [CrossRef]

Dodmane, P.; Arnold, L.L.; Pennington, K.L.; Cohen, S.M. Orally administered nicotine induces urothelial hyperplasia in rats and mice. *Toxicology* 2014, 315, 49–54. [CrossRef]

Qu, W.; Zhao, W.-H.; Wen, X.; Yan, H.-Y.; Liu, H.-X.; Hou, L.-F.; Ping, J. Prenatal nicotine exposure induces thymic hypoplasia in mice offspring from neonatal to adulthood. *Toxicol. Lett.* 2018, 304, 30–38. [CrossRef]

Tang, M.-S.; Wu, X.-R.; Lee, H.-W.; Xia, Y.; Deng, F.-M.; Moreira, A.L.; Chen, L.C.; Huang, W.; Lepor, H. Electronic-cigarette smoke induces lung adenocarcinoma and bladder urothelial hyperplasia in mice. *Proc. Natl. Acad. Sci. USA* 2019, 116, 21727–21731. [CrossRef]

Lee, H.-W.; Park, S.-H.; Weng, M.-W.; Wang, H.-T.; Huang, W.; Lepor, H.; Wu, X.-R.; Chen, L.C.; Tang, M.-S. E-cigarette smoke damages DNA and reduces repair activity in mouse lung, heart, and bladder as well as in human lung and bladder cells. *Proc. Natl. Acad. Sci. USA* 2018, 115, E1560–E1569. [CrossRef]

Novotny, T.E.; Hardin, S.N.; Hovda, L.R.; Novotny, D.J.; McLean, M.K.; Khan, S. Tobacco and cigarette butt consumption in humans and animals. *Tob. Control* 2011, 20, i17–i20. [CrossRef]

Martínez-Sánchez, J.M.; Ballbè, M.; Pérez-Ortuño, R.; Fu, M.; Sureda, X.; Pascual, J.A.; Peruga, A.; Fernández, E. Secondhand exposure to aerosol from electronic cigarettes: Pilot study of assessment of tobacco-specific nitrosamine (NNAL) in urine. *Gac. Sanit.* 2018, 33, 575–578. [CrossRef]

Huizebos, C.V.; Walhof, C.; De Vries, T.W. Accidental ingestion of cigarettes by children. *Ned. Tijdschr. Voor Geneeskld.* 1998, 142, 2569–2571.

Smolinske, S.; Spoerke, D.; Spiller, S.; Wruck, K.; Kulig, K.; Rumack, B. Cigarette and Nicotine Chewing Gum Toxicity in Children. *Hum. Toxicol.* 1988, 7, 27–31. [CrossRef]

Gill, H.; Rogers, K.; Rehman, B.; Meynihan, J.; Bergey, E.A. Cigarette butts may have low toxicity to soil-dwelling invertebrates: Evidence from a land snail. *Sci. Total Environ.* 2018, 628–629, 556–561. [CrossRef]

Morley, S.; Slaughter, J.; Smith, P.R. Death from Ingestion of E-Liquid. *J. Emerg. Med.* 2017, 53, 862–864. [CrossRef]

Noble, M.J.; Longstreet, B.; Hendrickson, R.G.; Gerona, R. Unintentional Pediatric Ingestion of Electronic Cigarette Nicotine Refill Liquid Necessitating Intubation. *Ann. Emerg. Med.* 2017, 69, 94–97. [CrossRef]

Normandin, P.A.; Benotti, S.A. Pediatric Emergency Update: Lethality of Liquid Nicotine in E-Cigarettes. *J. Emerg. Nurs.* 2015, 41, 357–359. [CrossRef]

Seo, A.D.; Kim, D.C.; Yu, H.J.; Kang, M.J. Accidental ingestion of E-cigarette liquid nicotine in a 15-month-old child: An infant mortality case of nicotine intoxication. *Korean J. Pediatr.* 2016, 59, 490–493. [CrossRef]

Boleda, M.R.; Galceran, M.T.; Ventura, F. Behavior of pharmaceuticals and drugs of abuse in a drinking water treatment plant (DWTP) using combined conventional and ultrafiltration and reverse osmosis (UF/RO) treatments. *Environ. Pollut.* 2011, 159, 1584–1591. [CrossRef]

Alonso, S.G.; Valkárcel, Y.; Montero, J.; Catalá, M. Nicotine occurrence in bottled mineral water: Analysis of 10 brands of water in Spain. *Sci. Total Environ.* 2012, 416, 527–531. [CrossRef]

Bekele, T.T.; Ashall, F.O. Investigation on Toxicity of Leachate of Cigarette Butts Collected from Addis Ababa on Swiss Albino Mice. *Niger. J. Health Biomed. Sci.* 2019, 3, 21–30.

Begum, A.N.; Aguilar, J.S.; Hong, Y. Aqueous cigarette tar extracts disrupt corticogenesis from human embryonic stem cells in vitro. *Environ. Res.* 2017, 158, 194–202. [CrossRef]

Max, W.; Sung, H.-Y.; Shi, Y.; Stark, B. The Cost of Smoking in California. *Nicotine Tob. Res.* 2015, 18, 1222–1229. [CrossRef]

Kotz, D.; Kastaun, S. Do people know that cigarette filters are mainly composed of synthetic material? A representative survey of the German population (the DEBRA study). *Tob. Control* 2021, 30, 345–347. [CrossRef]

Patel, M.; Cuccia, A.F.; Folger, S.; Benson, A.F.; Vallone, D.; Novotny, T.E. Support for cigarette filter waste policies among US adults. *Tob. Control* 2021. [CrossRef]
248. Smith, E.A.; Novotny, T.E. Whose butt is it? tobacco industry research about smokers and cigarette butt waste. *Tob. Control* **2011**, **20**, i2-i9. [CrossRef]

249. Schneider, J.E.; Peterson, N.A.; Kiss, N.; Ebeid, O.; Doyle, A.S. Tobacco litter costs and public policy: A framework and methodology for considering the use of fees to offset abatement costs. *Tob. Control* **2011**, **20**, i36-i41. [CrossRef]

250. Schneider, J.E.; Scheibling, C.M.; Peterson, N.A.; Granados, P.S.; Fulton, L.; Novotny, T.E. Online Simulation Model to Estimate the Total Costs of Tobacco Product Waste in Large U.S. Cities. *Int. J. Environ. Res. Public Health* **2020**, **17**, 4705. [CrossRef]

251. Witkowski, J. Holding Cigarette Manufacturers and Smokers Liable for Toxic Butts: Potential Litigation-Related Causes of Action for Environmental Injuries/Harm and Waste Cleanup. *Tulane Environ. Law J.* **2014**, **28**, 1-36.

252. Newman, S.; Watkins, E.; Farmer, A.; ten Brink, P.; Schweitzer, J.-P. The Economics of Marine Litter. In *Marine Anthropogenic Litter*; Bergmann, M., Gutow, L., Klages, M., Eds.; Springer International Publishing: Cham, Switzerland, 2015; pp. 367–394. ISBN 978-3-319-16509-7.

253. Beaumont, N.J.; Aanesen, M.; Austen, M.C.; Börger, T.; Clark, J.R.; Cole, M.; Hooper, T.; Lindeque, P.K.; Pascoe, C.; Wyles, K.J. Global ecological, social and economic impacts of marine plastic. *Mar. Pollut. Bull.* **2019**, **142**, 189-195. [CrossRef]

254. Komatz, K. Fire Prevention 52: Cigarette Butts. Available online: https://www.nps.gov/articles/p52-cigarette-butts.htm (accessed on 12 February 2021).

255. Leistikow, B.N.; Martin, D.C.; Milano, C.E. Fire Injuries, Disasters, and Costs from Cigarettes and Cigarette Lights: A Global Overview. *Prev. Med.* **2000**, **31**, 91-99. [CrossRef]

256. Bade, R.; White, J.M.; Tscharke, B.J.; Ghetia, M.; Abdelaziz, A.; Gerber, C. Anabasine-based measurement of cigarette consumption using wastewater analysis. *Drug Test. Anal.* **2020**, **12**, 1393-1398. [CrossRef]