



Identification and Toxicity Evaluation of Water-Soluble Chemicals Generated by the Photooxidative Degradation of Expanded Polystyrene

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In this study, expanded polystyrene (EPS) was photodegraded *in vitro*, and its water-soluble degradation products were extracted using solid-phase extraction. An *in vivo* test using the MTT assay showed that EPS exhibited increased toxicity upon photodegradation. This clearly demonstrates the necessity of investigating the degradation products at a molecular level, and thus, we conducted analyses using high-resolution mass spectrometry coupled with liquid chromatography. Overall, 68 compounds were detected, of which 13 were identified after comparing the retention times and tandem mass spectra of the extracted compounds with those of standards. The toxicity of the degraded EPS was studied by examination of the detected compounds combined with published reports. In addition, the quantification of the most abundant compounds showed that discarded EPS can generate a significant amount of chemicals by UV degradation. The data in this study show that degraded EPS can pose a significant environmental threat as a source of potentially hazardous chemicals. This study provides a fundamental basis for the evaluation of the fate and toxicity of photodegraded EPS.

Keywords: microplastics, photodegradation, expanded polystyrene, high-resolution mass spectrometry, toxicity

INTRODUCTION

Plastics are essential in modern society and reports suggest that the annual production is >300 million tons worldwide (Scarr and Hernandez, 2019), of which only 10% are recycled, whereas ~8 million tons are thrown into the ocean (Picó and Barceló, 2019). The potential plastic pollution problem has recently attracted public attention (Alliance to End Plastic Waste, 2020) since discarded plastic is decomposed and degraded by ultraviolet (UV) rays from the Sun, with the photooxidation mechanisms being complex (ter Halle et al., 2016; Song et al., 2017). In addition, the plastic waste being further degraded into microplastics (Naik et al., 2020) with physical breaks, weakening, and weathering are caused by environmental factors, such as wind and waves (Eo et al., 2018; van Sebille et al., 2020).

Microplastics are present in coastal areas, seas, rivers, soil, and air (Bakir et al., 2014; Davis and Murphy, 2015; Jang et al., 2017; Prata, 2018). It has been reported that microplastics were detected in

the stomachs of the carcasses of marine animals washed up ashore (Nelms et al., 2019) and in the intestines of deep-sea shrimps that live in Peru–Chile and Mariana Trench, which are the deepest locations in the world (Jamieson et al., 2019). Microplastics are also present in the human environment and have been detected in drinking water and seafood (Kosuth et al., 2018; Garrido Gamarro et al., 2020). Global efforts on reducing plastic usage have led to the enforcement of policies and campaigns (Xanthos and Walker, 2017), however, the amount of plastic waste has increased since the coronavirus outbreak. The increased demand for sanitation, healthcare, and hygiene products has increased the use of disposable plastic (Prata et al., 2020; Patrício Silva et al., 2021). Globally, the rise of the delivery industry due to the outbreak of the pandemic has led to increasing the use of single-use products (Chu et al., 2020).

Expanded polystyrene (EPS) is one of the most widely used plastics (e.g., construction, packaging, and food containers) and according to Statista, 26.56 million metric tons of EPS were used in 2020 (Statista, 2021). Even though EPS is relatively light in weight compared to other household wastes, it occupies a large volume and is the most ubiquitous waste along the coast (Davis and Murphy, 2015). It is one of the most frequently found microplastics on South Korean beaches, with a size of 1–5 mm per unit area (Eo et al., 2018). EPS is used in packaging and shipping of frozen food as well as in buoys in aquaculture (Jang et al., 2016; Grandviewresearch, 2021), which are often lost or discarded into the sea. EPS can be easily blown away by wind because of its lightweight, thus, it often serves as a carrier of pollutants (Bakir et al., 2014; Hüffer and Hofmann, 2016).

The styrene bond in EPS can be degraded by sunlight *via* photocatalytic oxidation (Yousif and Haddad, 2013; Gewert et al., 2015) and fragmented into smaller particles (Song et al., 2020). Fragmentation increases the surface area of the EPS, thereby accelerating its photodegradation. Plastic surfaces can be a source of radical formation and inherent phototransformation (Naik et al., 2020) since the benzyl carbon in styrene can form free radicals after UV exposure and react with oxygen, water, or other molecules (Gewert et al., 2015). The photodegradation of EPS generates dissolved organic carbon *via* complex degradation pathways (Ward et al., 2019) making EPS a significant source of chemical pollution (Rochman et al., 2013; Jang et al., 2016).

Several studies have reported the generation of micro/nanoplastics from the degradation of EPS (Song et al., 2020), and the effects of EPS leachate (Thaysen et al., 2018). However, only a few have conducted extensive analyses for the comprehensive identification of the EPS photodegradation chemicals (Gewert et al., 2018).

High-resolution mass spectrometry (HRMS) has been widely used to study environmental pollutants (Cho et al., 2019; Solihat et al., 2019) since it can identify unknown compounds (Schymanski et al., 2014). Electrospray ionization (ESI)-mass spectrometry is the most widely used method in environmental analyses since it is suitable for the analysis of polar molecules (Kim et al., 2019; Vanini et al., 2020).

In this study, a toxicity test was performed for the water-soluble compounds generated from the UV degradation of EPS, and the products were thoroughly investigated at a molecular

level using ESI coupled with HRMS. The data of the identified compounds were then combined to explain the observed toxicity.

MATERIALS AND METHODS

Sample Preparation

Water and methanol were purchased from J.T. Baker (Phillipsburg, NJ, United States) and were used without further purification. The standard compounds listed in **Supplementary Table S1** were purchased from TCI (Tokyo, Japan) and Sigma-Aldrich (St. Louis, MO, United States). An EPS box was cut into a size weighing 0.5 g as described in a previous study (ter Halle et al., 2016). The samples were placed in a transparent quartz crucible containing 100 ml of purified water. The output of the UV lamp (6,258 Xenon arc lamp, Newport Corporation, Irvine, CA, United States of America) was at 300 W, and the exposure time of the lamp corresponds to the sum of the annual cumulative amount of UV A and B in Korea.

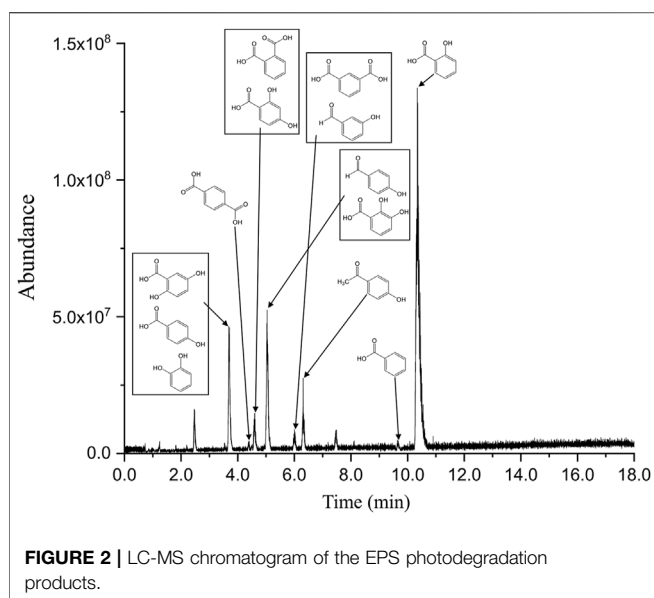
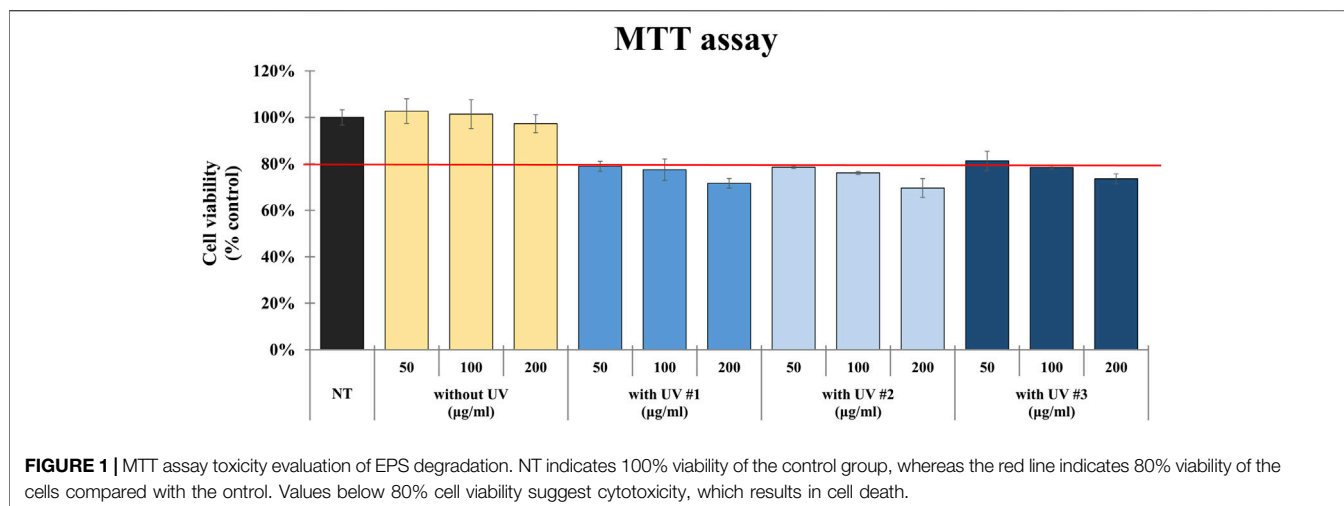
Based on data published by the Korea Meteorological Administration (National Institute of Meteorological Sciences, 2018), the annual cumulative amount of UV A and B in Korea is 267.27 MJ/m² (National Institute of Meteorological Sciences, 2018). During the UV exposure, the sample was stirred using a magnetic stirring bar. After UV exposure, the isolation of the compounds dissolved in water was performed with solid-phase extraction (SPE) using an Oasis PRiME HLB extraction cartridge (Waters, Milford, MA, United States). The cartridge was washed with 20 ml water and activated with 20 ml methanol. Blank samples were prepared by irradiating the solvent with UV radiation without EPS. The obtained solutions were treated using the aforementioned method.

In Vitro Toxicity Test

Human keratinocytes (HaCaT; AddexBio Technologies, San Diego, CA, United States) were used to evaluate the toxicity of the prepared samples. Cells were maintained in a Dulbecco's modified essential medium supplemented with 100 units/ml penicillin–streptomycin and 10% heat-inactivated fetal bovine serum (Grand Island, NY, United States) in a humidified atmosphere of 5% CO₂ at 37°C. The MTT assay was performed to evaluate the cellular toxicity of the prepared samples (Alam et al., 2021). Briefly, cells (1×10^5 cells/ml) were seeded in a 96-well black clear bottomed plate (Corning Inc., Corning, NY, United States) and cultured at 37°C with 5% CO₂ for 24 h. The prepared samples (6 μ l) were then treated with the cells and incubated for 24 h. Subsequently, the medium was suctioned, 10% of MTT solution was added, and the preparation was incubated for 1 h. Colored formazan crystals dissolved in 100% dimethyl sulfoxide were added to the previously incubated preparation, and the optical density of the mixture was measured at 590 nm using a microplate reader (Victor3, PerkinElmer, Waltham, MA, United States).

Mass Spectrometry and Instrumentation

The SPE extract was analyzed using an ESI-Q-Exactive Orbitrap mass spectrometer (Thermo Fisher Scientific, Waltham, MA,



United States) in the negative mode. The extracted sample was introduced into the mass spectrometer using a syringe pump (Hamilton Co., NV, United States) at a flow rate of 5 $\mu\text{l}/\text{min}$ for direct injection analysis and into an ACQUITY ultrahigh-performance liquid chromatography (UPLC) system (Waters, Milford, MA, United States) at 300 $\mu\text{l}/\text{min}$. The capillary temperature, spray voltage, and S-lens were maintained at 300°C, 3.2 V, and 50, respectively. The automatic gain control target was set at 5×10^5 for direct injection and 2×10^5 for liquid chromatography–mass spectrometry (LC–MS) and tandem mass spectrometry (MS/MS). Sheath, aux, and sweep gas flow rates were set at 5, 2, and 0 (arbitrary units) for direct injection analysis and 50, 15, and 2 for LC–MS and MS/MS analysis, respectively. MS/MS was set to one loop count and 0.4 mass-to-charge ratio (m/z) isolation window. Chromatographic separations were performed with an ACQUITY 1.7- μm BEH C18 column (2.1×100 mm) attached to an ACQUITY 1.7- μm BEH C18 guard cartridge

(Waters, Milford, MA, United States). The column was maintained at 40°C and eluted with an A/B gradient, where A = water/0.1% formic acid (v/v) and B = acetonitrile/0.1% formic acid (v/v). The gradient of LC for the compound separation is shown in **Supplementary Table S2**.


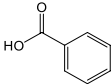
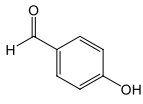
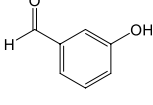
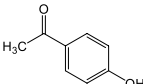
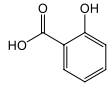
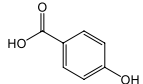
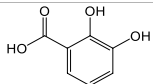
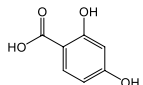
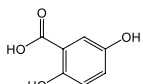
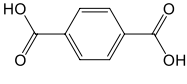
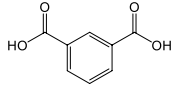
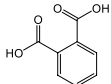
A Xevo TQ-S micro triple-quadrupole (TQ) mass spectrometer coupled with an ACQUITY UPLC system was used for quantitative analysis. The TQ parameters were set to 3.50 kV capillary and a 5 V cone for source voltage at an operating multiple reaction monitoring mode, with the desolvation and source temperatures set at 300 and 120°C, respectively. The desolvation and source gas flow rates were 650 and 10 L nitrogen/h, respectively. Argon was used as the collision gas for the MS/MS analysis.

Data Processing

Xcalibur software (version 4.0; Thermo Fisher Scientific, Waltham, MA, United States) was used to collect and process the data obtained using the Orbitrap mass spectrometer. Peaks with S/N ratios greater than 30 and an abundance greater than 1×10^5 were selected and processed. Molecular compositions were assigned using the Composer64 version 1.5.6 software (Sierra Analytics Inc., Modesto, CA, United States). The chemical formula $\text{C}_x\text{H}_y\text{O}_z$ was assigned with constraints of C (6–50), H (6–200), and O (0–10), and the calibration was performed according to a previously described method (Cho et al., 2021). The chemical structures were assigned to the chemical formulas based on the interpretation of the MS/MS spectra and database search using METLIN (Smith et al., 2005) and mzCloud (<https://www.mzcloud.org>, HighChem LLC, Bratislava, Slovakia). The MassLynx V4.2 software (Waters, Milford, MA, United States) was used for data processing in quantitative analysis.

The toxicity database was retrieved from Tox-Info provided by the National Institute of Food and Drug Safety Evaluation under the Ministry of Food and Drug Safety (www.nifds.go.kr/toxinfo), and the hazardous substances databank was retrieved from PubChem under the National Center for Biotechnology Information (pubchem.ncbi.nlm.nih.gov).

TABLE 1 | List of the EPS photodegradation products identified by LC-MS. Compounds are listed in order to m/z values of ions in the negative mode.

Molecular formula	Theoretical m/z of ion	Observed m/z of ion	Homologous series (Y/N)	MS/MS	Structures
C ₆ H ₆ O ₂	109.0295	109.0284	N	109, 108	
C ₇ H ₆ O ₂	121.0295	121.0284	Y	121	
		121.0284	Y	121, 92	
		121.0285	Y	121, 93, 92, 65	
C ₈ H ₈ O ₂	135.0451	135.0441	Y	135, 120, 92,	
C ₇ H ₆ O ₃	137.0244	137.0232	Y	137, 93, 65	
		137.0235	Y	137, 93, 65	
C ₇ H ₆ O ₄	153.0193	153.0186	Y	153, 109, 91	
		153.0186	Y	153, 109, 67, 65	
		153.0184	Y	153, 109, 108	
C ₈ H ₆ O ₄	165.0193	165.0185	Y	165, 121, 77	
		165.0185	Y	165, 121, 92	
		165.0185	Y	165, 121	

RESULTS AND DISCUSSION

EPS floating on water was exposed to UV light, as described in the experimental section. The irradiated EPS samples

produced physically fragmented fine particles rendering the water turbid and yellowish. The turbid water was filtered, and the dissolved organic compounds were extracted using SPE.

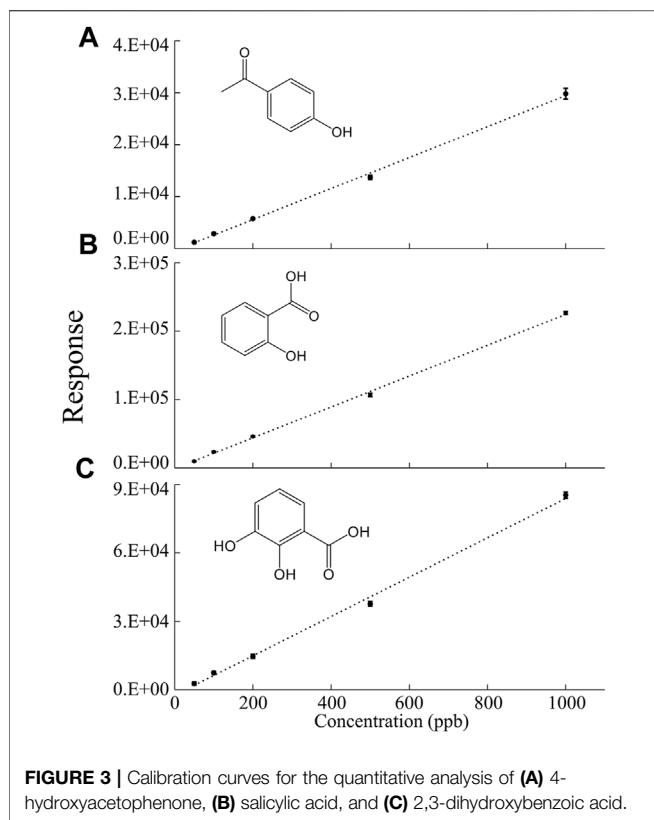


FIGURE 3 | Calibration curves for the quantitative analysis of (A) 4-hydroxyacetophenone, (B) salicylic acid, and (C) 2,3-dihydroxybenzoic acid.

The potential cellular toxicity of the prepared samples was evaluated using an MTT assay after SPE. The UV-exposed EPS samples were prepared in triplicate whereas the control sample was prepared without UV exposure. The cell viability results obtained from the MTT assay are shown in **Figure 1**. The EPS solutions without UV irradiation did not show any potential toxicity towards the HaCaT cells; however, those with UV irradiation showed significant cellular toxicity in a concentration-dependent manner compared to the non-UV irradiated EPS solutions. Approximately 80% of the cells survived in 50 ppm of the EPS samples. The cell viability dropped to approximately 70% in the 200 ppm EPS samples. Overall, the cell viability in the EPS solutions with UV irradiation was lower than that without UV irradiation. It has been reported that the leachate of polystyrene can be toxic (Gunaalan et al., 2020), with hexabromocyclododecanes and styrene oligomers playing an important role in its toxicity (De-la-Torre et al., 2020). It was thus concluded that the photodegradation products of EPS by UV irradiation can exhibit cellular toxicity toward HaCaT cells.

To identify the chemicals generated by the UV irradiation of EPS, the SPE eluted solution was analyzed using LC coupled with HRMS and the obtained chromatogram is shown in **Figure 2**. Positive-mode ESI-MS was also performed. However, the peaks in the spectra showed low abundance and no significant peaks were observed. Overall, 68 compounds were detected (**Supplementary Table S3**) and the elemental formulas were assigned to the peaks based on mass accuracy. Schymanski

TABLE 2 | Limit of detection (LOD) and limit of quantitation (LOQ) of the calibration curve for the quantitative analysis of the obtained compounds.

Compound name	LOD (ppb)	LOQ (ppb)
4-Hydroxyacetophenone	22.93	76.42
Salicylic Acid	21.13	70.43
2,3-Dihydroxybenzoic Acid	57.80	192.66

et al. (2014) proposed a confidence level for identifying small molecules with HRMS which was used in this study. The observed compounds corresponding to level 1 are listed in **Table 1**. The confirmed structures, based on the reference standard compounds, were assigned in level 1. Tentative candidates were obtained based on the exact mass, and the tandem mass spectra were designated as level 3. The compounds that were not found in the database or in the MS/MS spectra were marked as level 4. The chemical structures of the compounds with confidence levels of 3 and 4 were tentative.

To confirm the chemical structures of the observed compounds, standard reference compounds were purchased and analyzed by LC-MS. The obtained tandem mass spectra and LC retention times of the standard compounds were compared with those of the SPE eluents. Overall, 13 compounds were identified using this combined approach. The confirmed structures are listed in **Table 1**. In a previous study, $C_{11}H_{12}O_4$ was assigned to the structure listed in **Supplementary Table S3** with a confidence level of 1 (Gewert et al., 2018). $C_9H_{10}O_3$, $C_{17}H_{18}O_3$, and $C_{25}H_{26}O_3$ have been proposed as homologous series in a previous study. In this study, 13 additional homologous series were identified.

Based on the MS data and previous studies on styrene degradation (Sheldrick and Vogl, 1976; Geuskens et al., 1978; Weir, 1978; Mailhot and Gardette, 1992), the reaction pathways to generate the compounds listed in **Table 1** and **Supplementary Table S3** are very complex, including a series of oxidation, β -scission, H abstraction, rearrangement, and isomerization reactions. Furthermore, various reaction products, including isomers, can be generated depending on the part of the polystyrene molecule that is cut by UV photolysis.

The toxicity of the identified compounds was examined using data from literature. Catechol, also known as pyrocatechol or 1,2-dihydroxybenzene, is used as a corrosion inhibitor and colorant in various industrial applications and it can cause eczematous dermatitis and irritation of the skin and eyes (Powell et al., 2001; Williams, 2013). In addition, catechol is classified as a human carcinogen corresponding to group 2 B by the IARC carcinogen classification (International Agency for Research on Cancer, 2021). Benzoic acid is a commonly used antimicrobial preservative in food and beverages. Although contact allergy symptoms may take several days to appear, exposure to benzoic acid causes allergic symptoms such as mild conjunctival congestion and in rare cases, it can lead to severe anaphylactic shock (Pevny and Danhauser, 1981; Johnson et al., 2017). Salicylic acid is used as an anti-inflammatory and topical antibacterial agent. It causes hypoglycemia by remarkably decreasing glucose neogenesis and increasing glucose utilization (Raschke et al., 1991), irritation of the nose and throat, nausea, vomiting, tinnitus,

dizziness, headache, stuffiness, confusion, sweating, rapid pulse and breathing, and skin rash (Inchem, 1998). Severe exposure causes delirium, hallucinations, convulsions, coma, respiratory failure, and cardiovascular collapse (Chiaretti et al., 1997; Fiume, 2003). 4-hydroxybenzoic acid is used as a preservative and antioxidant. At low concentrations, it has no significant effects, whereas exposure to high concentrations causes irritation of the respiratory tract and has potential toxic effects on the liver and blood [European Chemicals Agency (ECHA), 2021]. Phthalic acid, terephthalic acid, and isophthalic acid exhibit reproductive and developmental toxicity (Bang et al., 2011). Therefore, the list of the observed compounds and their reported toxicity strongly supports the finding that photodegradation can increase the toxicity of EPS.

Quantitative analysis was conducted for the three most abundant compounds found in the LC-MS spectra of the degradation products and the results are presented in **Figure 3**. The limit of detection (LOD) and limit of quantitation (LOQ) obtained from the m/z peaks are listed in **Table 2**. The raw data used to obtain the information in **Table 2** are provided in Supporting Information (**Supplementary Table S4**).

Based on the calibration curve presented in **Figure 3**, the amounts of 4-hydroxyacetophenone, salicylic acid, and 2, 3-dihydroxybenzoic acid generated from EPS (0.5 g) after 1 year of UV exposure were calculated. $8.1 \pm 0.77 \mu\text{g}$ of 4-hydroxyacetophenone, $110 \pm 7.6 \mu\text{g}$ of salicylic acid, and $12. \pm 1.9 \mu\text{g}$ of 2,3-dihydroxybenzoic acid were estimated to be generated and the detailed calculations are shown in the Supporting Information (**Supplementary Table S4**). As stated in the previous section, only a small percentage of EPS is recycled [U.S. Environmental Protection Agency (EPA), 2018] and this study revealed that EPS quantities as low as 0.5 g were able to produce micrograms of chemicals. Therefore, considering the enormous amount of EPS produced and the low recycling rate, the data clearly shows that the total amount of chemicals generated by EPS can pose a significant environmental threat.

CONCLUSION

Compounds generated by the degradation of EPS were thoroughly investigated by LC coupled with HRMS. The MS data revealed the presence of various water-soluble chemicals, including hydrocarbon molecules of styrene monomers and oxidized degradation products. The results revealed 68 compounds of which 13 were identified using reference standards. The toxicity of EPS increased after photodegradation, indicating the necessity to examine the water-soluble compounds generated from photodegradation at a molecular level. Our study showed that the photodegradation products of EPS should be considered equally threatening as the micro- or nanosized EPS particles and additives. Considering the

enormous amount of EPS produced and the low recycling rate, it is expected that a large amount of potentially hazardous chemicals will be generated by the degradation of EPS. Therefore, this study indicates the urgency of monitoring chemicals in degraded EPS, with the results offering a fundamental basis for the evaluation of the fate and toxicity of photodegraded EPS.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

SL: Conceptualization, Methodology, Data curation, Writing—Original draft preparation, Visualization, Investigation, Validation, and Formal analysis. MA: Visualization, Investigation, Validation, and Resources. M-JJ: Conceptualization, Methodology, Writing—Review and Editing. SL: Conceptualization, Methodology, and Writing—Review and Editing. K-HL: Conceptualization, Methodology, and Writing—Review and Editing. S-HL: Formal analysis, Validation, Resources, and Writing—Review and Editing. SK: Writing—Reviewing and Editing, Supervision, Project administration, and Funding acquisition.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fenvs.2022.938120/full#supplementary-material>

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