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UV weathering alters toxicity and chemical composition of consumer plastic leachates

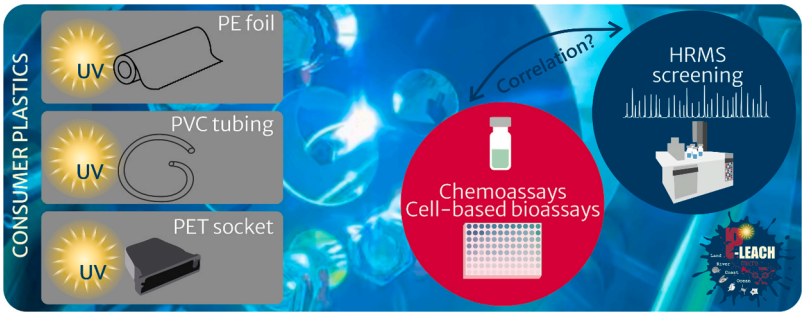
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HIGHLIGHTS

- UV weathering increased the toxicity of specific plastic leachates.
- Cell-based bioassays revealed plastic- and cell-specific toxic effects.
- LC-HRMS identified (un)known plastic-associated chemicals.
- Toxicity was linked to the formation of bioavailable transformation products.
- Microplastics and metals showed weaker links to bioassays effects than organics.

GRAPHICAL ABSTRACT



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ABSTRACT

Plastics release complex mixtures of partially toxic substances into the environment, particularly following UV-induced weathering. Using integrated chemoassays, cell line bioassays, and chemical profiling, we assessed leachates from eight types of consumer plastic products following accelerated UV weathering equivalent to eight months of natural solar weathering in temperate regions to identify key contributors to leachate toxicity. Chemoassays, used as proxies for protein damage, showed UV-induced reactive toxicity, which increased by up to 82 % depending on plastic type. Cell-based bioassays revealed that UV exposure enhanced cytotoxicity up to 13-fold, especially for polyethylene leachates, in liver, skin, lung, and breast cancer cell lines, reflecting cell-specific vulnerabilities. UV exposure substantially altered the chemical composition of leachates shown by liquid chromatography -high resolution mass spectrometry (LC-HRMS) screening which identified 11 target-, 12 suspect-, and 90 non-target chemicals. Furthermore, UV exposure promoted the formation of more bioavailable and hazardous transformation products compared to the dark controls. The increased toxicity was primarily linked to the release and transformation of organic plastic-associated chemicals rather than microplastics or metal(loid)s.

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Overall, these findings highlight UV weathering as a critical driver of enhanced plastic leachate toxicity and emphasize the need for comprehensive chemical and toxicological assessments in environmental risk evaluations of plastics.

1. Introduction

The widespread use of plastics is deeply engrained in many aspects of modern society, providing essential services across numerous sectors. However, it has led to severe environmental pressures [1], with (micro) plastic pollution now impacting air, water, soil, and even human systems [2–7], raising substantial environmental and human health concerns [6]. Beyond the base polymers, plastics contain additives, processing aids, and non-intentionally added substances (NIAS) such as impurities and degradation products. Collectively referred to as plastic-associated chemicals in this study, these substances may leach at various stages of the plastic lifecycle. Of the over 16,000 substances used in plastic manufacturing, at least 4200 meet criteria for concern, yet the toxicity of many additive chemicals remains poorly understood, and their use is unregulated [8,9].

Environmental weathering transforms plastics into microplastics over time, enhancing the leaching of plastic-associated chemicals and sorption of external environmental pollutants with increased surface area-to-volume ratios [10–13]. Among these processes, photoaging by UV light is particularly important due to its impact on surface chemistry and reactivity [14,15]. A key consequence of such weathering is the enhanced leaching of complex chemical mixtures from plastics, which can pose significant environmental risks [16–20]. The release of these substances is determined by their physicochemical properties, plastic composition, environmental factors such as water chemistry and turbulence, and the extent of weathering [16–20].

Plastics leachates in many cases contain complex chemical mixtures capable of interacting with biological systems, posing potential risks that might be exacerbated through environmental factors such as UV exposure, which promotes chemical transformations that can increase toxicity. These effects can be rapidly screened using high-throughput approaches such as chemoassays and *in vitro* cell-based bioassays, providing efficient mechanistic toxicity profiling across multiple endpoints. Chemoassays enable the quantification of specific molecular interactions, serving as proxies for reactive protein toxicities [21–24]. Beyond reactivity, assessing biological impacts through *in vitro* experiments can bridge the gap between toxicological outcomes and chemical composition. Human cancer cell lines are widely used to assess leachate cytotoxicity, with studies showing increased oxidative stress and genotoxicity in response to weathered plastics [25–27]. These cell lines are particularly suited for exploring the diverse cellular responses to leachates, which may vary in severity depending on the polymer type, and environmental conditions [28,29]. Employing a suite of cell lines from different tissues—such as liver, lung, colon, and skin—helps identify organ-specific vulnerabilities [30]. Taken together, this chemo- and bioassay-based screening approach can offer valuable insights into different responses to plastic leachates and the underlying links between chemical reactivity and biological effects.

To explain the observed toxic effects, understanding the shifts in the chemical composition of UV-exposed plastic leachates due to weathering relative to their dark controls (DC) is essential. Liquid chromatography- high-resolution mass spectrometry (LC-HRMS), combined with targeted, suspect, and non-target screening approaches, provides robust identification of a broad spectrum of organic compounds [29,31,32]. Recent HRMS studies have consistently demonstrated extensive chemical migration from plastics, with release patterns influenced by polymer type and particle geometry, UV exposure, and leaching duration [33–35]. A wide range of plastic-associated chemicals have been identified across diverse plastic types, including plasticizers (e.g., phthalates), antioxidants (e.g., Irgafos and hindered phenols), UV stabilizers (e.g., benzotriazoles, benzophenones), and flame retardants (e.g., brominated diphenyl ethers and organophosphates) [36–38].

Our recent study [39] revealed that UV-photodegradation substantially increased the release of microplastics, organic compounds, and metal(loid)s from various consumer plastics into the aqueous phase. According to the U.S. Environmental Protection Agency (EPA) CompTox database [40,41], some organic chemicals detected in the studied plastic leachates were likely to exhibit diverse toxicities, underscoring the need for further investigations.

To the best of our knowledge, this combination—chemoassays of protein-reactive (electrophilic) toxicity, multi-cell-line bioassays, and the U.S. EPA Chemical Transformation Simulator (CTS) pathway predictions [42] —has rarely been applied to UV-weathered plastic leachates (cf. [29,43–46]) to interpret photochemical transformations and related shifts in bioavailability (e.g., changes in log K_{ow}). Integrated with LC–HRMS-based screening, it provides a mechanism-oriented, screening-level framework for prioritization and follow-up risk assessment.

Building on previous findings, this study aimed at investigating the complexity of plastic leachates by integrating insights from chemoassays, human cancer cell lines, and chemical profiling. Specifically, we examined: (1) how UV exposure alters leachate reactivity and cytotoxicity, and the relationship between these effects; (2) how UV weathering influences the chemical composition of leachates; and (3) whether observed toxic effects can be explained by the identified chemical profiles. Together, these questions aim to highlight possible drivers of toxicity in the leachates of plastic consumer products and inform the risk assessment of plastic-derived mixtures.

2. Materials and methods

2.1. Plastic selection and artificial weathering protocol

Detailed descriptions of the methodologies used for selecting consumer plastics and the artificial weathering setup are provided in our recent publication [39]. Briefly, eight plastic consumer products were selected to represent a broad range of applications and polymer types, covering polyethylene (PE), polyethylene terephthalate (PET), and polyvinyl chloride (PVC). The identity of each polymer was initially based on nominal product labeling and then confirmed by Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR) spectroscopy, as described in [39]. Specifically, the selected products were as follows: a greenhouse cover foil (PE1; nominally PE, confirmed as PE); a sun protection cover (PE2; nominally PE, but confirmed as a mixture of PE and PET); a jerrycan (PE3; nominally PE, confirmed as PE); and an agricultural foil (PE4; nominally PE, confirmed as PE). For the PET products, a D-Sub plug housing (PET1; nominally PET, confirmed as a styrene acrylonitrile (SAN) copolymer), and a multipurpose housing (PET2; nominally PET, with an unidentified polymer composition). The PVC products were a cable housing (PVC1; nominally PVC, with an unidentified polymer composition) and a transparent PVC tubing (PVC2; nominally PVC, confirmed as a vinyl chloride–vinyl acetate–hydroxypropyl terpolymer).

Plastic samples were cut into pieces of less than 5 mm in length, and 30 g of these pieces were added to 200 mL of double-distilled water in borosilicate cuvettes. Two parallel samples were prepared for each material: one was exposed to UV light for a period of 10 d, simulating approximately eight months of sunlight exposure under Central European conditions [39], while the other one was wrapped in aluminum foil and subjected to the same agitation and thermal conditions as a dark

control (DC). Both samples were irradiated in a custom-made UV chamber (UVC) equipped with a high-intensity UV light source, and the samples were continuously rotated around the light source to ensure even exposure of all the particles [47].

Weathering was conducted in three independent batches—UVC-1, UVC-2, and UVC-3—each comprising up to three plastic types and one or more blank bottles processed in parallel. These procedural blank samples consisted of double-distilled water subjected to the same protocols as the plastic-containing bottles, including UV irradiation or dark incubation, agitation, thermal cycling, and filtration.

In addition to the primary set of leachates (batch UVC-1), we prepared an independent replicate of PE1 (UVC-3) to assess reproducibility across independently prepared batches. PE1 pieces were weathered under UV and in parallel DC conditions using the same protocol as for UVC-1.

Following treatment, all samples were cooled, filtered to remove plastic particles, and subsamples of the leachates were collected for further analysis. Henceforth, sample names will follow the format *plastic type_treatment*, where the suffix "_UV" or "_DC" indicates UV-irradiated or Dark Control leachates, respectively. For example, PE1_UV refers to the UV-irradiated leachate of PE1. The replicate leachates of PE1 from the third batch are denoted as UVC-3_PE1_UV and UVC-3_PE1_DC.

2.2. Chemo- and cell-based bioassays

The reactivity of the plastic leachates was evaluated using two chemoassays targeting different reactive groups of proteins with the following two model nucleophiles: Glycine-p-nitroanilide (Gly-pNA) for amino groups and tryptophan–cysteine–glycine alcohol (WCG-OH) for sulfhydryl groups. Leachates were tested at a concentration of 66.7 % (v/v) in the assay medium. The percent depletion of each model nucleophilic reagent (Gly-pNA or WCG-OH) upon exposure to leachates was quantified using established methods [21,23,24]. Detailed assay protocols, reagent preparations, incubation conditions, and calculation methods are provided in Supplementary material (SM) Section S1.

Toxicity assessment of plastic leachates was conducted on a suite of human cancer cell lines to evaluate the cytotoxic effects at varying exposure levels. Initial testing (Phase 1) involved treating the cells with plastic leachates and the corresponding background matrix from procedural blanks at concentrations of 1 %, 10 %, and 20 % (v/v) relative to the total cell culture medium. The selected cell lines — HepG2 (liver cancer), A-375 (melanoma), A-549 (lung carcinoma), HCT-116 (colon cancer), and MDA-MB-231 (breast cancer) — were chosen to represent common exposure routes such as ingestion, inhalation, and dermal contact. Subsequent testing (Phase 2) focused exclusively on HepG2 cells, assessing the impact of higher leachate concentrations (50 % and 100 %), by freeze-drying the leachates and reconstituting them in the cell culture media. Culture conditions and other experimental details were as described elsewhere [48] and provided in SM Section S1. Controls included procedural blanks, solvent blanks, untreated cells, and two reference chemical treatments: doxorubicin (100 μg/mL) as a positive control for cytotoxicity, and a mixture of 50 plastic additives (0.02–1.4 μg/mL) as a benchmark for assessing additive-driven toxicity (Tables S1–S2). The assay endpoint was percentage inhibition of cellular metabolic activity measured by CellTiter-Blue (resazurin reduction) relative to untreated controls. We use this endpoint as a proxy for cytotoxicity and refer to it as metabolic inhibition.

All assays were run in technical triplicates, except for PE1, where an independent leachate replicate was prepared. Full replication of leachate generation for all plastic types of this multifactorial design — involving multiple plastic types, treatment conditions (UV vs. DC), and dose levels — was not feasible due to the limited capacity of the UV weathering chamber, which restricted the number of replicates that could be simultaneously processed. Additionally, preparing and analyzing fully replicated leachates is costly and labor-intensive, particularly when combined with multiple chemoassays and cell-based assays across a range of concentrations. Similar single-preparation designs have been widely employed in studies investigating the toxicity of plastic leachates and environmental mixtures [29,44,49,50], and our approach aligns with such precedents.

Inhibition values were calculated by normalizing background-corrected fluorescence signals to the average of untreated control wells, which represent viable cells with no exposure. Negative inhibition values—indicating higher fluorescence than untreated controls—are a known feature of fluorescence-based viability assays such as CellTiter-Blue and typically arise from assay variability, low-level metabolic fluctuations, or chemical interference with the resazurin–resorufin system [51,52]. Consistent with prior studies and guidelines [44,53–56], inhibition values within ±20 % were considered to fall within normal assay variability and were not interpreted as biologically significant unless clearly exceeding this range or corroborated by additional mechanistic endpoints. In the context of complex chemical mixtures like plastic leachates, additional sources of assay perturbation—including redox-active substances and matrix-induced fluorescence shifts—may also contribute to apparent increases in viability signals [51,52]. To avoid overinterpretation, inhibition values were contextualized against procedural blanks but calculated relative to untreated controls (cells + media), ensuring comparability across treatments while avoiding the introduction of variability from unstable baselines.

2.3. Chemical analysis

Plastic leachates were analyzed for organic compounds using three complementary Liquid Chromatography (LC)-HRMS workflows: target, suspect, and non-target screening (see SM Section S2 for details). Target screening for 77 plastic additives was performed using a Thermo Scientific UltiMate 3000 LC coupled to a Q Exactive Orbitrap MS (target compounds in Table S3). Suspect screening employed an Agilent 1290 Infinity II liquid chromatography–quadrupole time-of-flight mass spectrometry (LC-QTOF) system using a merged and curated list of 287 plastic-associated chemicals retrieved from the NORMAN suspect list exchange [57], processed with MassHunter software. Non-target screening was performed using a Thermo Vanquish HPLC and an Orbitrap Exploris 480 MS, with data analyzed in Compound Discoverer. Compound identification relied on exact mass, isotopic pattern, and spectral library matches from mzCloud, and ChemSpider as well as additional reference databases were used to validate tentative identifications. A peak rating score (ranging from 1 to 10) was used in the non-target screening to assess the quality of detected features in Compound Discoverer. This integrated metric considers several parameters such as peak shape, isotopic pattern fidelity, signal-to-noise ratio, and chromatographic reproducibility. Higher scores indicate higher confidence in the peak's validity as a true chemical feature. These scoring principles are outlined in the Compound Discoverer user guide and align with recent literature using similar workflows [58]. Suspect and non-target identifications were reported at Level 2 (probable structure) or Level 3 (tentative candidate) confidence levels according to the Schymanski framework [59].

2.4. Hazard profiling of detected analytes

Bioactivity and hazard profiles of plastic-associated chemicals identified via target, suspect, and non-target screening were evaluated using the US EPA CompTox Chemicals Dashboard [40] and the PlasticMAP database [9]. Toxicity data were retrieved from CompTox using chemical names, CAS Registry Numbers, or InChIKeys. For each compound, the total number of assays, active outcomes, and percentage activity were recorded. Metadata from active assays were further analyzed to classify biological effects. Complementary hazard traits—such as persistence, bioaccumulation, and aquatic toxicity—were extracted from PlasticMAP to support the prioritization of chemicals of concern.

3. Results and discussion

3.1. Effects of leachates

3.1.1. Reactive toxicity of plastic leachates

Chemoassay results (Fig. 1 and Table S4) revealed distinct and UV-dependent reactivity patterns across plastic types. These patterns reflect the chemical specificity of the assays [21–24,60]. WCG detects thiol-reactive electrophiles and reactive oxygen species. In contrast, Gly-pNA responds to amino-reactive compounds such as aldehydes, anhydrides, or isocyanates. Gly-pNA depletion (D_{Gly}) markedly increased following UV exposure in several samples—most notably PE2 (82 %), PE1 (68 %), PE4 (60 %), and PET2 (62 %)—indicating the formation of amino-reactive transformation products.

PE1 and PE2, for instance, are PE-based materials likely containing UV stabilizers [39], which may generate amino-reactive byproducts upon irradiation. In contrast, PVC2—a vinyl chloride–vinyl acetate–hydroxypropyl terpolymer expected to contain non-phthalate plasticizers [39] — showed low Gly-pNA reactivity but a strong UV-induced increase in WCG depletion (D_{WCG}: 35 %), suggesting the formation of thiol-reactive species via oxidation pathways. Meanwhile, PVC1, with an unidentified polymer type but expected to contain flame retardants [39], showed no reactivity under either condition, possibly due to greater UV stability or lack of (pro-)reactive precursor compounds. Interestingly, PE3 exhibited opposing trends across the two assays: WCG reactivity decreased following UV exposure (from 37 % to 18 %) while Gly-pNA reactivity increased (from 2 % to 43 %), suggesting that the UV exposure had degraded thiol-reactive compounds but generated new amino-reactive species. Notably, PE3_DC and PET2_DC showed notable thiol reactivity, indicating that plastics can release reactive substances and pose an environmental risk even without UV exposure.

The additive mix of 50 plastic additives (Table S1), tested as a benchmark without UV exposure, showed dose-dependent WCG reactivity (6–60 %) but no Gly-pNA response, reinforcing the notion that amino-reactive species arose predominantly from UV-induced transformations of polymer constituents or additives not included in the mix. Together, these findings indicate that reactivity of leachates may arise from inherent material properties as well as UV-induced aging.

3.1.2. Cell line toxicity of plastic leachates

Exposure of five human cancer cell lines to UV plastic leachates revealed distinct cytotoxicity patterns upon UV aging, in contrast to their DCs, which were non-toxic at 1–20 % (v/v) concentrations (Fig. 1, Table S4). Notably, at 20 % concentration, PE1_UV reduced HepG2 viability by 99 %, while PE2_UV decreased it by 44 %. At the same concentration, PVC1_UV selectively reduced MDA-MB-231 viability by 27 %. These differential cytotoxic responses—ranging from moderate to near-complete inhibition—were clearly distinguishable from the much weaker or even negative inhibition values observed in the procedural blanks (ranging from +19 % to –40 %), reinforcing that the observed effects were attributable to the plastic leachates rather than to background matrix interference.

To probe higher exposures, the HepG2 cell line was treated with 50 % and 100 % leachates. PE1_DC and PVC1_UV exhibited cytotoxicity comparable to the positive control, doxorubicin. Hill model fitting revealed that PE1_UV had a 13-fold lower half-maximal activity concentration (AC_{50}) compared to PE1_DC (4 % vs. 53 %) (Figure S1).

Quality control measures confirmed assay integrity. Negative controls (deionized water, Milli-Q, Millipore water) showed no effects. The positive control reference systems—doxorubicin (100 μg/mL) and a 50-additive mix (0.02–0.4 μg/mL)—elicited dose-dependent responses across all cell lines. Inhibition values for procedural blanks across all cell lines were generally low, with most values ranging from –25–19 %, consistent with the expected variability of fluorescence-based assays like CellTiter-Blue. A notable outlier was observed for UVC-1 Blank DC at 20 % in HepG2 cells (–40 % inhibition; Table S4), but this was not

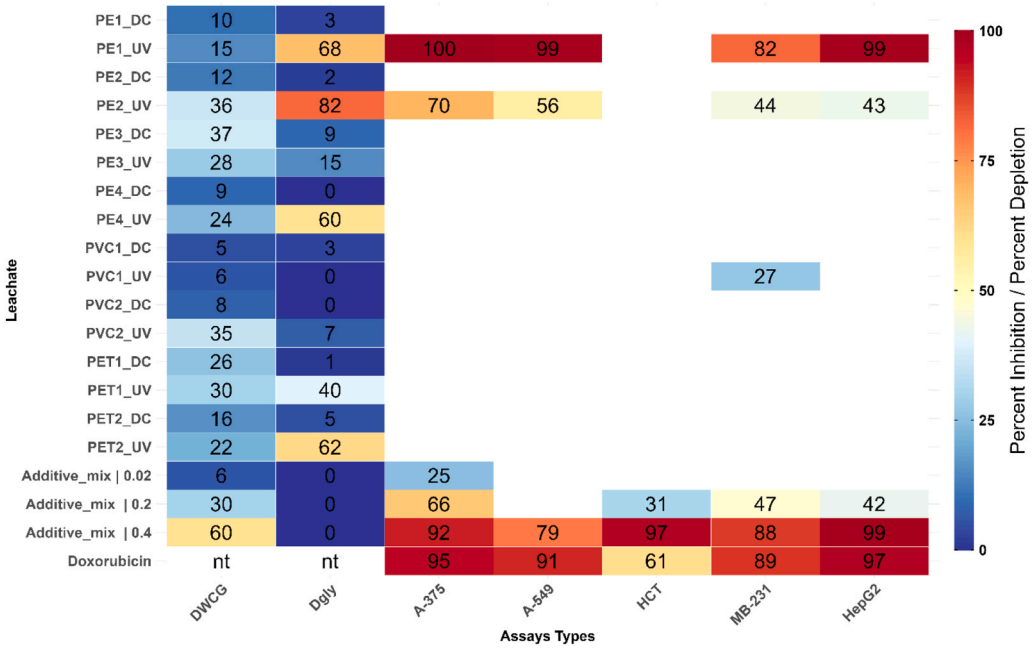


Fig. 1. Depletion and inhibition patterns of two chemoassay types and five cancer cell lines exposed to plastic leachates under UV-irradiated (UV) and dark control (DC) conditions. The percent depletion of the chemoassays tryptophan-cysteine-glycine tripeptide (DWCG) and glycine-para-nitroanilide (Dgly) is shown for plastic leachates at a concentration of 67 %. Similarly, the percentage inhibition of cellular metabolic activity (CellTiter-Blue; resazurin reduction) of skin (A-375), lung (A-549), colon (HCT-116), breast (MDA-MB-231), and liver (HepG2) cancer cell lines are depicted for plastic leachates at a concentration of 20 %. Results include exposures to an additive mixture of 50 components at concentrations ranging from 0.02 to 0.4 μg/mL, and the positive control doxorubicin (100 μg/mL; for cell lines only). nt, not tested. Color intensity, ranging from blue (0 % depletion/inhibition) to red (100 % depletion/inhibition), correlates with the level of reactive toxicity and cytotoxicity. Cell line growth inhibition values < 20 % are omitted in the heatmap as they were considered within the range of experimental variability and are not indicative of significant biological effects. For detailed protocols of the chemoassays and cell-based bioassays, see Section S1.

replicated in other batches or cell lines, suggesting an isolated event rather than a reproducible effect.

To statistically evaluate whether blank effects varied systematically with UV treatment, we conducted pairwise *t*-tests. Independent-sample *t*-tests comparing UV-treated versus dark control blanks revealed no statistically significant differences for any cell line (all $p > 0.05$), indicating that UV exposure alone did not affect cell viability. These results support that the observed trends in procedural blanks were within expected assay variability and not indicative of real cytotoxic or stimulatory effects.

To evaluate the reproducibility of leachate-induced cytotoxicity, we compared PE1 leachates from the UVC-1 batch with an independent replicate from the UVC-3 batch under matched UV and DC conditions across five human cell lines. Responses closely agreed between batches (Table S5). We then tested for batch effects using a two-way ANOVA with main effects Batch (UVC-1 vs UVC-3) and Concentration (1 %, 10 %, 20 %), omitting the interaction due to limited degrees of freedom ($n = 6$; residual df=2). Under UV, no batch differences were detected for any cell line (A-375 $p = 0.667$; A-549 $p = 0.275$; HCT $p = 0.099$; MB-231 $p = 0.197$; HepG2 $p = 0.423$). Under DC, some uncorrected batch *p*-values were small, but none remained significant after Benjamini–Hochberg correction across the ten batch tests (all $q \geq 0.0568$). As expected, concentration was a significant main effect in most panels (e.g., UV A-375 $p = 1.1 \times 10^{-4}$; UV MB-231 $p = 0.0048$; UV HepG2 $p = 0.0037$), confirming dose dependence. Collectively, these analyses indicate that PE1 leachates from UVC-1 and UVC-3 are statistically reproducible under both UV and DC conditions.

Cell-type-specific responses reflected known physiological susceptibilities. A-375 and A-549 were highly sensitive to PE2_UV, likely due to interference with melanin and surfactant pathways [61,62], while HCT-116 remained largely resistant [63,64]. HepG2, typically vulnerable to toxicants due to its detoxification role [65], showed variable responses, suggesting selective toxicity driven by leachate composition. These findings underscore the cell-specific nature of plastic leachate toxicity and its varied implications across different organ systems.

Notably, the PET1_DC exhibited pronounced negative inhibition values across several cell lines, most strongly in HepG2 (–82 %) and MDA-MB-231 (–63 %), indicative of apparent increased viability or metabolic activity. In contrast, the PET1_UV induced much less negative inhibition values (e.g., HepG2: –28 %; MDA-MB-231: –4 %), pointing to relatively greater inhibition following UV exposure. These viability-enhancing effects may be linked to specific leachate constituents present in the DC but lost after UV aging. These paradoxical trends—viability enhancement in DC and reduction in UV treatments—warrant further mechanistic investigation (cf. 3.3.1).

Comparison of the chemoassays and cell-based bioassays (Fig. 1, Table S4) revealed both similarities and differences in plastic leachate responses. PE1_UV showed high chemical reactivity (DWCG: 31 %, DGly: 68 %) and correspondingly strong cytotoxicity towards A-375, A-549, MDA-MB-231, and HepG2 cells. PVC1_UV showed no chemical reactivity but was toxic to HepG2 and MDA-MB-231 cell lines, indicating effects beyond detectability in chemoassays. Conversely, leachates that were active in the chemoassays, such as PE4_UV (DWCG: 24 %, DGly: 60 %) and PET2_UV (DWCG: 22 %, DGly: 62 %) displayed no cytotoxicity, highlighting that reactivity alone does not imply acute toxicity. Such differences highlight that cell assays quantify biological effects, while chemoassays uncover reactive mechanisms—together offering a broader toxicity profile.

The effects observed across various plastic leachates prompt a key question about their underlying causes: Are the effects driven by organic or inorganic plastic-associated chemicals, microplastics, or a combination thereof? Answering this question requires detailed compositional analysis to pinpoint the sources of toxicity. Although this study focused on the analysis of organic compounds (see following subchapter), the interpretation of results was informed by previously reported data on inorganic constituents and microplastics [39].

3.2. Chemical composition of the leachates

3.2.1. UV-induced shifts in chromatographic peaks of plastic leachates

A qualitative visual comparison of Base Peak Chromatograms (BPCs) offered a practical starting point for assessing compositional changes in plastic leachates due to UV treatment compared to the DCs. Under DC conditions, leachate composition varied by plastic types (Figure S2). For example, the BPC of PE2_DC appeared more complex than PE1_DC, likely due to PE2_DC being a multilayer material composed of both PE and PET. PE2_DC also showed more early retention peaks than PVC2_DC, indicating more polar, potentially bioavailable compounds. These differences align with findings by ref. [39] (Table S6), where PE2_DC leachates showed higher numbers of mass spectral features ($n = 189$, mean RT ~13 min) than PE1_DC ($n = 114$, RT ~12.5 min) and PVC2 ($n = 152$, RT ~14.5 min).

Following UV treatment, most leachates exhibited greater chromatographic complexity (Figure S3). PE1_UV, PE2_UV, and PE3_UV showed increases in the numbers of peaks and their intensity, while PE4_UV displayed only minor differences compared to its PE4_DC counterpart. Peak heights varied similarly: for example, in PVC1_UV, the peak at ~11.5 min increased approximately 1.5-fold compared to PVC1_DC, whereas PET1_UV and PET2_UV showed substantial reductions (10–15-fold) in peak intensity at ~13.5 min relative to their corresponding DC samples. These shifts suggest that UV exposure either enhanced or suppressed leaching from plastics, or that UV exposure produced transformation products from leached compounds. Such transformation products often elute at earlier retention times [66], pointing to a shift toward more hydrophilic constituents that potentially are more bioavailable and toxic.

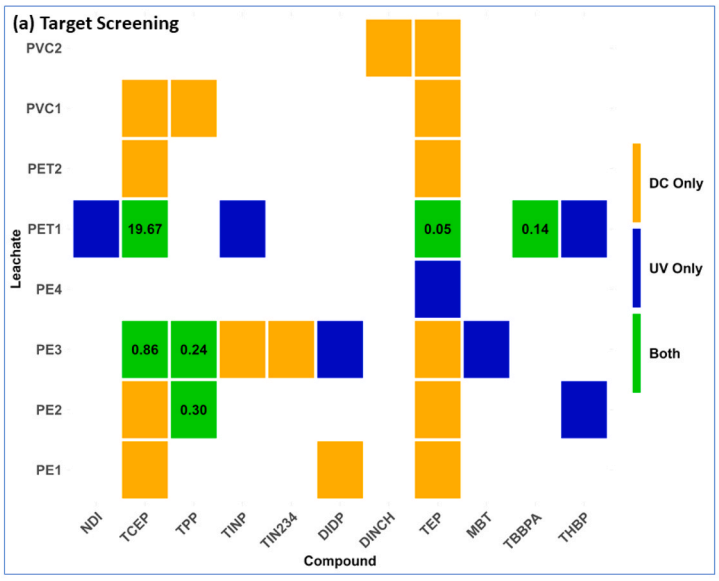
These qualitative observations are further supported by the number of mass spectral features reported in our recent study [39], while a detailed compound-level analysis using non-target screening is presented later in Subsection 3.2.3.

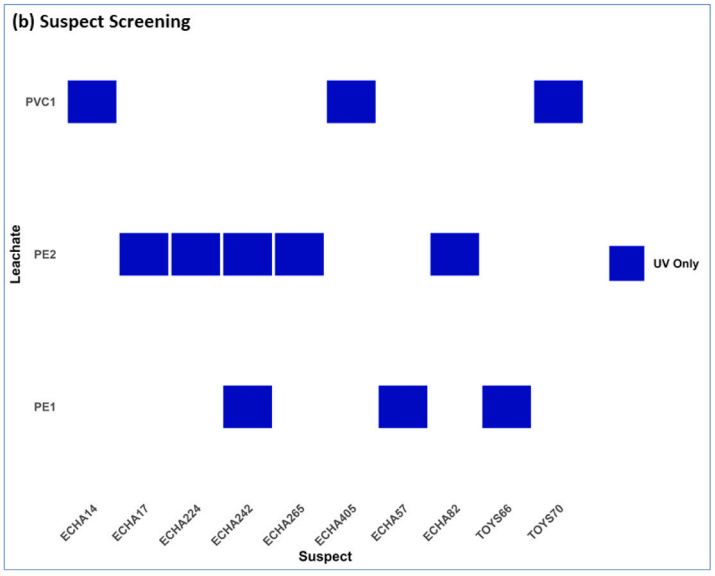
3.2.2. Target screening of plastic leachates

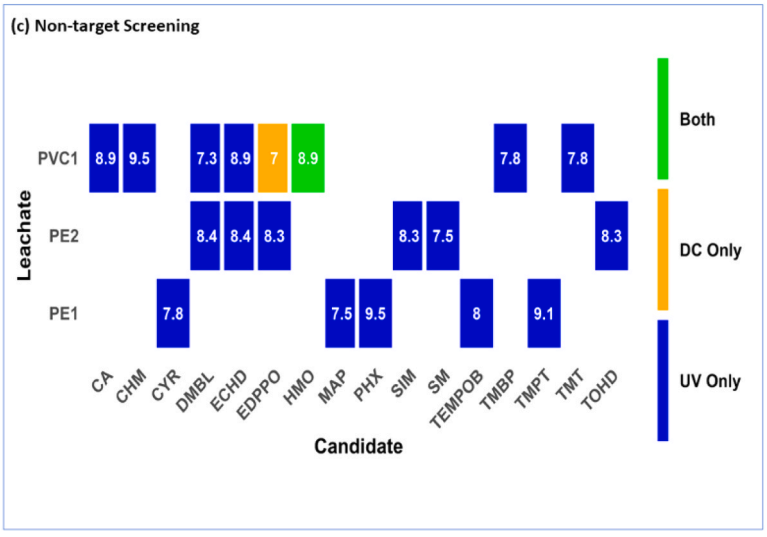
To move beyond qualitative shifts in chromatographic complexity, we conducted targeted screening using 77 analytical standards to identify specific chemicals. Target screening identified 11 additives (Fig. 2a): 1,5-naphthalene diisocyanate (NDI), tris(2-chloroethyl) phosphate (TCEP), tripropyl phosphate (TPP), Tinuvin P (TINP), Tinuvin 234 (TIN234), diisodecyl phthalate (DIDP), diisononylcyclohexane-1,2-dicarboxylate (DINCH), triethyl phosphate (TEP), 2-mercaptobenzothiazole (MBT), 2,2′,6,6′-tetrabromobisphenol A (TBBPA), 2,2′,4,4′-tetrahydroxybenzophenone (THBP). Of these, four (TCEP, TINP, DINCH, and TBBPA) were also covered by in a previous study using LC-MS/MS, [39] with concentrations ranging from below the method detection limit (0.05–1.5 ng/L) to > 5000 ng/L (Table S7).

The presence of these additives is expected in plastic leachates as they are used across various sectors of the plastic industry [9]. For example, NDI, TCEP, TINP, TIN234, DIDP, and TBBPA are widely used in industries such as automotives, construction, and electronics, serving as monomers, flame retardants, and stabilizers in various polymers. TEP is used globally on a scale of ~110,000 tons annually [9], stands out as a multipurpose flame retardant and plasticizer. DINCH, produced or imported at ≥ 10,000 tons per year in the EU [67], is used in food packaging and medical products for its low migration properties. Its presence in leachates indicates it does leach out of the polymer and may pose an exposure risk. MBT (~ 20,000 tons) and THBP (~ 100 tons) are used in smaller quantities compared to high-production additives such as TEP and TBBPA (both ~ 200,000 tons), but are important as antioxidants and light stabilizers in rubber manufacturing and textiles, respectively [9].

UV weathering may induce surface modifications in plastics, inducing the formation of cracks and shedding of smaller particles, and potentially affect leaching kinetics or cause photo-transformation of the additives [68,69]. The presence of additives in DC but not in UV-treated







(caption on next page)

Fig. 2. Occurrence patterns of plastic-associated chemicals in plastic leachates under UV-irradiated and dark control (DC) conditions, screened via (a) target, (b) suspect, and (c) non-target screening approaches. Plastic-associated chemicals detected exclusively in DC leachates are shown in orange, those only found in UV-treated leachates in blue, and those present in both conditions in green. Annotated values in (a) show UV/DC peak area ratios, while those in (c) indicate peak ratings, as assigned by Compound Discoverer. These ratings (scale 1–10) reflect a software-generated score based on multiple criteria including mass accuracy, isotopic pattern fit, and peak shape, with higher scores indicating higher confidence in the detected peak. See main text for full names of the abbreviated compounds and details.

leachates (Fig. 2a) suggests that UV may induce photo-transformation of these additives or reduce their leaching rates from the plastic matrix. Conversely, additives appearing only in UV-treated leachates may imply increased plastic leaching capacity under UV exposure. The differential response is further illustrated by the relative peak area of TCEP in PET1_UV, which increased by a factor of 20 compared to its DC counterpart — an observation consistent with LC-MS/MS quantification reported by Menger et al. [39], where TCEP levels increased from 32 ng/mL to 232 ng/mL following UV treatment (Table S7). In contrast, this increase was negligible in PE3, and TEP showed a marked decrease in PET1_UV.

The photo-transformation propensity of the detected additives was evaluated using the U.S. EPA Chemical Transformation Simulator (CTS) [42,70,71]) (Table S8) using the Direct Photolysis (ranked) and Abiotic Hydrolysis reaction libraries available under the category of Environmental Reaction System [42,71]. The observed 7-fold decrease in TBBPA levels in PET1_UV can be attributed to its high susceptibility to photo-transformation. CTS predicted eight photo-transformation products of TBBPA (log K_{ow} 7.2), several of which exhibit a three-orders-of-magnitude reduction in log K_{ow} compared to the parent compound, indicating substantially elevated solubility in aqueous media. To verify these predictions, we analyzed the HRMS data for TBBPA transformation products using their exact masses and identified two candidates: 4-[2-(3,5-dibromo-4-hydroxyphenyl)propan-2-yl]benzene-1,2-diol (log K_{ow} 4.94) and 2-bromo-4-[2-(3-bromo-4-hydroxyphenyl)propan-2-yl]phenol (log K_{ow} 5.42) (Table S9).

CTS suggested that these products are formed via aromatic photohydro dehalogenation, a characteristic transformation pathway for brominated compounds. Additionally, we tentatively identified monobromo-bisphenol A, a reported transformation product of TBBPA [72], in the UV-treated PET1 leachate (Table S9). The absence of these transformation products in the DC leachate further supports their formation as UV-induced transformation products of TBBPA. Similarly, the disappearance of TIN234 in the UV-treated PE3 leachate may result from its complete transformation into two highly bioavailable products, aniline and 2-aminophenol, as predicted by CTS. These two products, characterized by significantly lower log K_{ow} values than the parent compound, were not detected in the HRMS data due to their target masses falling below the MS scan range (150–2000 m/z) used in this study. In contrast, the decrease of TEP and TPP in UV treatments remained unexplained, as CTS did not predict any transformation products for these compounds.

The leaching behavior of these additives was consistent with their hydrophobic characteristics and partitioning tendencies (Table S10). Additives with log K_{ow} values below 3, such as TEP (log K_{ow} = 0.8), TCEP (log K_{ow} = 1.44), TPP (log K_{ow} = 1.87), MBT (log K_{ow} = 2.42), and THBP (log K_{ow} = 2.78), are likely to leach more readily from plastic materials due to their hydrophilic nature. Moderately hydrophobic additives (log K_{ow} range between 3 and 6), such as NDI (log K_{ow} = 4.37) and TINP (log K_{ow} = 4.31), are expected to leach from plastics at a moderate rate. Strongly hydrophobic additives (log K_{ow} >6), such as TIN234 (log K_{ow} = 7.67), TBBPA (log K_{ow} = 7.2), DINCH (log K_{ow} = 9.82), and DIDP (log K_{ow} = 10.36), are expected to largely remain sorbed to the plastic phases. However, log K_{ow} is not the sole determinant of leaching or partitioning behavior [73]. An analysis of experimental Abraham solute descriptors available on the UFZ-LSER website [74], which provide a more accurate description of chemical partitioning from plastics, reveals that certain very hydrophobic chemicals such as TBBPA and DIDP have significant hydrogen bonding capabilities, potentially enhancing their leachability into the water phase from the plastics.

3.2.3. *Suspect screening of UV transformation products in plastic leachates*

The suspect screening focused on leachate samples from PE1, PE2, and PVC1, which were prioritized due to the observed toxicological effects (see 3.1). The screening targeted peaks that were either uniquely formed or significantly increased in area (by more than 5-fold) in UV-treated samples compared to the respective DCs. This approach aimed to identify plastic-associated chemicals and their transformation products that were either released in greater quantities or newly formed due to UV exposure, potentially contributing to the observed effects.

Using a curated list of 287 plastic-associated chemicals, the suspect screening tentatively identified 11 plastic-associated compounds that exhibited increased leaching or possible formation in the respective UV samples (Fig. 2b, Table S11). The identified chemicals were ECHA14 (N,N′-1,6-hexanediylbis(N-(2,2,6,6-tetramethyl-piperidin-4-yl)formamide)), ECHA17 (Dibutyltin dilaurate), ECHA57 (Bis(2,2,6,6-tetramethyl-4-piperidyl) sebacate), ECHA82 (Tris(2,4-ditert-butylphenyl) phosphite), ECHA224 (N,N-bis(2-hydroxyethyl)dodecanamide), ECHA265 (1,3,5-triazine-2,4,6(1 H,3 H,5 H)-trione), ECHA405 (1,2,3-trihexyl 2-(butanoyloxy)propane-1,2,3-tricarboxylate), TOYS66 (4-Methoxyphenol), and TOYS70 (Dipentyl phthalate). Among these, Melamine (ECHA242) was identified at confidence level 2a, while all other suspects were identified at confidence level 3. The increase presence of compounds like N,N′-hexanediylbis(N-(2,2,6,6-tetramethylpiperidin-4-yl)formamide) and melamine underscores their potential role in the increased toxicological effects observed in UV-treated samples, as both have been associated with environmental persistence and toxicological concern [75,76].

These suspected chemicals, identified using the ECHA and TOYS lists, align with known functional roles in plastic manufacturing [8,75,77]. They span diverse additive categories, including plasticizers, antioxidants, stabilizers, flame retardants, and antistatic agents—each designed to enhance material performance and durability. For instance, ECHA14 (N,N′-1,6-hexanediylbis(N-(2,2,6,6-tetramethyl-piperidin-4-yl) formamide)) and ECHA57 (Bis(2,2,6,6-tetramethyl-4-piperidyl) sebacate) are hindered amine light stabilizers (HALS) commonly used to mitigate UV degradation. ECHA82 (Tris(2,4-ditert-butylphenyl) phosphite) acts as an antioxidant, while ECHA17 (Dibutyltin dilaurate) serves as a catalyst in polyurethane and silicone production. TOYS70 (Dipentyl phthalate) functions as a plasticizer to improve polymer flexibility, whereas TOYS66 (4-Methoxyphenol) acts as a polymerization inhibitor to prevent unwanted reactions during processing. ECHA224 (N,N-bis(2-hydroxyethyl)dodecanamide) serves as an antistatic agent, and ECHA405 is a triester-based non-phthalate plasticizer. ECHA265 (1,3,5-triazine-2,4,6(1 H,3 H,5 H)-trione) is employed as a cross-linking agent, and ECHA242 (Melamine), identified with higher confidence, functions as a nitrogen-based flame retardant.

The release of these additives in UV-treated leachates supports the hypothesis that photoaging mobilizes functionally diverse and potentially toxic substances into the aqueous environment.

3.2.4. *Non-target screening of plastic-associated chemicals in leachates*

Non-target screening (NTS) of plastic leachates resulted in the tentative identification of 99 distinct compounds across all leachate samples (Table S1 File 2). Among these, 92 were assigned high-

confidence level 2a identifications, while 7 were classified as tentative level 3. The distribution of these compounds, summarized in Figure S4, was dominated by transformation products, followed by industrial chemicals, additives, personal care products, and extractable/leachable substances. Notably, several additives detected through target screening—such as TCEP, TPP, TEP, TINP, and DIDP—were also identified in the NTS workflow, validating the NTS approach. All compound annotations were supported by high mass accuracy (±2 ppm) and verified using mzCloud, the high resolution accurate mass (HRAM) Compound Database, and ChemSpider.

In the subset of toxicologically relevant plastic leachates (PE1, PE2, PVC1), UV-treated samples exhibited greater chemical diversity and higher peak intensities than their corresponding DCs, reinforcing the role of UV radiation as a major driver of chemical release and transformation. The occurrence patterns of compounds with peak ratings ≥ 7 that were absent in blank samples revealed polymer-specific leaching profiles (Fig. 2c).

In PE1_UV, five unique compounds were identified: propylhexedrine (PHX), 5-methyl-1-(1,3,5-trimethyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole (TMPT), N-butyl-2,2,6,6-tetramethylpiperidin-4-amine (TEMPOB), cyromazine (CYR), and 4′-methoxyacetophenone (MAP). PE2_UV yielded seven unique hits, including degradation products such as β,β-dimethyl-γ-methylene-γ-butyrolactone (DMBL), 5-ethylcyclohexane-1,3-dione (ECHD), ethyldiphenylphosphine oxide (EDPPO), and simazine (SIM), as well as (1S,5 R,9 R,13 R)-1,5,9-trimethyl-11,14,15,16-tetraoxatetracyclo[10.3.1.0^{4},^{13}.0^{8},^{13}]hexadecan-10-one (TOHD) and sorbitan monolaurate (SM). PVC1_UV displayed the highest compound diversity, with ten compounds identified, including caffeic acid (CA), 6-(cyclohexylmethylidene)-6,7,8,9-tetrahydro-5H-benzo[*a*]cyclohepten-5-one (CHM), ECHD, 5-(6-hydroxy-6-methyloctyl)-2,5-dihydrofuran-2-one (HMO), trimethyl trimellitate (TMT), trihydroxy-methoxybenzopyranone (TMBP), and DMBL. Two compounds—ECHD and HMO—were also detected in PE2_UV, while EDPPO was observed in both PVC1_UV and PVC1_DC.

These occurrence patterns revealed polymer-specific degradation and leaching behaviors. PE1_UV was enriched in nitrogenous and heterocyclic transformation products; PE2_UV was characterized by polyether and plasticizer degradation products; and PVC1_UV featured a range of phenolic and oxygenated aromatic compounds. The overlap in identified chemicals between PE2_UV and PVC1_UV suggests potential mechanistic convergence in the leaching of parent compounds and degradation pathways of different polymers under UV exposure.

Collectively, these findings highlight the substantial influence of UV-induced weathering on the complexity and chemical composition of plastic leachates. The emergence of diverse transformation products under UV conditions has important implications for ecological exposure and toxicity, reinforcing the need for comprehensive chemical characterization in environmental risk assessments.

3.3. Correlation between toxic effects and chemical composition

3.3.1. Linking toxicity to organic composition in plastic leachates

As a first step toward identifying potential toxicity drivers, we analyzed the bioactivity profiles of plastic-associated chemicals identified through target, suspect, and non-target screening using the US EPA CompTox database [40]. The analysis showed that 10 out of 11 target analytes, 7 out of 11 suspect analytes, and 9 out of 16 non-target analytes that had activity data available exhibited measurable activity across diverse cellular assays (Figures S5–S7). These assays covered various biological effects, including endocrine disruption, cytotoxicity, enzyme inhibition, gene expression modulation, and impacts on liver metabolism. Complementing these results, toxicity annotations extracted from the PlasticMAP database [9] revealed that many of these analytes—particularly high-production-volume chemicals such as TCEP, TBBPA, and DIDP—exhibit characteristics of concern, including persistence, bioaccumulation, endocrine-disrupting potential, and aquatic toxicity (Table S11). These hazard traits, observed across analytes identified at different confidence levels, further substantiate the cytotoxic and oxidative stress-related effects measured in our chemoassays and cell line experiments (3.1), reinforcing the biological relevance of chemical mixtures leaching from consumer plastics.

To investigate whether these toxic effects could be linked to compositional changes in the leachates, we compared toxicity data with chromatographic patterns. Toxic effects in UV-treated PE1, PE2, and PVC1 leachates appeared to correlate with changes in chemical composition, as suggested by the emergence of new chromatographic peaks at earlier retention times (Figure S3)—indicative of more polar, bioavailable, and potentially toxic transformation products (see 3.1). PE1_UV showed the most pronounced shifts in features [39] and an increase in both chemical reactivity and cytotoxicity, with a 293 % increase in detected features (from 114 to 449) and a reduction in mean retention time from ~12.5 to ~11.2 min. PE2_UV, which showed the second highest toxicity, exhibited a comparable but less pronounced shift, with a 61 % increase in features (from 189 to 304) and a retention time shift from ~13.0 to ~12.0 min. PVC1_UV showed limited cytotoxicity (27 % inhibition in MDA-MB-231cells at 20 % concentration) and minimal reactivity in both chemoassays (0–6 % depletion at 66.7 % concentration). However, pronounced cytotoxicity was observed at 100 % concentration (96 % inhibition in HepG2). Chromatographic analysis revealed a moderate rise in new peaks, including a marked increase at ~11.5 min compared to the DC (Figure S3). Feature analysis indicated a 264 % increase in features (from 123 to 448) and a decrease in mean retention time from ~14.0 to ~12.5 min [39].

A notable exception was observed in PET1 leachates. PET1_DC exhibited strong negative inhibition values (i.e., apparent viability enhancement) in HepG2 (–82 %) and MDA-MB-231 (–63 %), while PET1_UV showed much less negative inhibition (–28 % and –4 %, respectively), indicating relatively greater inhibition following UV exposure. LC-HRMS data for PET1 leachates showed that additives such as TEP and TBBPA—both known toxicants with endocrine or proliferation-related activity [78,79]—were strongly depleted upon UV irradiation, with UV/DC peak area ratios of 0.05 and 0.14, respectively. These changes suggest that PET1_DC may have contained bioactive compounds capable of promoting cell proliferation or metabolic activity, which were diminished or transformed by UV exposure. Although these findings are intriguing, further validation using mechanistic endpoints (e.g., apoptosis, ROS, or proliferation assays) is required to confirm any such proliferative effects.

Taken together, UV exposure increased chemical complexity in PE1, PE2, and PVC1, as indicated by the appearance of more chromatographic peaks or a higher number of detected features, and earlier retention times, indicating a shift to more polar compounds. While target, suspect, and non-target screenings (3.2.2) uncovered a range of potentially relevant compounds, many of the complex UV-induced features remained uncharacterized, highlighting the analytical limitations of predefined lists and the inherent complexity of plastic leachates.

3.3.2. Linking toxicity to microplastics and inorganic compounds in leachates

The most toxic leachate, PE1_UV, did not contain high concentrations of microplastics and metal(loid)s (Table S13; [39]). Notably, the leachate from UV-treated PE1 exerted higher reactivity and cell line toxicity than the DC, but for PE1, UV exposure had no observable impact on the leaching of microplastics and metal(loid)s, as their concentrations remained unchanged or decreased compared to the dark control (Table S13). This discrepancy suggests that the observed toxicity for PE1 was likely exclusively due to organic plastic-associated chemicals and their potential transformation products caused by UV treatment, as supported by UV-induced shifts in the chromatographic peaks of PE1 leachates (see 3.2.1).

In contrast, the PE2 leachate after UV treatment exhibited a substantial increase in activity towards the cancer cell lines, especially the

human skin (melanoma) A-375 cell line, which is more sensitive to reactive toxicants [80], as well as in the chemoassays. This increase correlated with a significant rise in both microplastic particles (from 430 particles per mL to 3440 particles per mL) and metal concentrations (e.g., Sb: 20 μg/L in DC vs. 630 μg/L in UV) [33].

The UV-treated PVC1 leachate, which exhibited weak toxicity (27 % inhibition) toward MDA-MB-231 cells at 20 % concentration and strong cytotoxicity (96 % inhibition) in HepG2 cells at 100 % concentration, showed a negligible change in microplastic concentrations but a significant increase in certain metal(loid)s, such as Zn (from 10 μg/L in DC to 930 μg/L in UV). While the elevated metal(loid) levels may have contributed to the observed toxicity at higher concentrations, chromatographic analysis also revealed a 264 % increase in detected features and a reduction in mean retention time, indicating the formation of more polar transformation products. These results suggest that the cytotoxic effects may stem from both inorganic constituents and UV-induced organic compounds.

4. Conclusions

The toxicity of consumer plastic leachates in the current study was closely linked to their chemical complexity, which was notably altered by UV exposure. UV treatment not only increased the peak areas of the leached plastic-associated chemicals but also promoted the formation of more polar transformation products—likely more bioavailable and toxic.

The most toxic effects observed, particularly in PE1_UV, PE2_UV, and PVC1_UV, were primarily associated with organic substances and their transformation products. However, in some cases, such as PE2_UV and PVC1_UV, microplastic particles and metal(loid)s likely also contributed to the observed toxicity. These results emphasize that no single class of chemicals — whether organic substances, microplastics, or metal(loid)s — can fully explain the observed toxic effects. Instead, toxicity outcomes are an interplay among diverse chemical species, including many still unknown transformation products. Target, suspect, and non-target screening approaches revealed several known and suspected compounds, but many newly formed features remained uncharacterized. This highlight both the chemical complexity of plastic leachates and the analytical limitations of predefined chemical lists. At the same time, it underscores the value of combining chemical screening with bioanalytical profiling to capture biologically relevant effects.

This study is subject to the following limitations. First, the absence of quantitative concentration data for the detected compounds limited the ability to establish more robust correlations between chemical profiles and observed toxic effects. Nonetheless, prior studies [81–83] have demonstrated that even with quantified analytes, only a small fraction of observed toxicity is typically explained. Second, the focus on LC-amenable compounds likely excluded relevant (semi-)volatiles or non-polar substances better suited for gas chromatography (GC)-based analysis. Third, the UV exposure conditions in this study may not fully reflect real-world plastic aging scenarios. Fourth, while multiple chemo- and cell-based bioassays were applied, they represent a limited set of biological endpoints, tested at short exposure durations (targeting acute toxicity) and working at rather low levels of biological organization. Fifth, while technical replicates were employed for all chemo- and cell-based assays, independent replication of leachate preparations was conducted only for the most cytotoxic sample (PE1). For all other plastic types, only single leachate batches were analyzed, limiting our ability to assess variability arising from the leaching process itself. Nonetheless, this design is consistent with several previous studies [29,44,49,50], which also relied on single leachate preparations or complex environmental mixtures tested in technical replicates. While our approach ensures reproducibility at the assay level, it does not capture inter-sample variation in chemical composition or toxicity. Such a screening-level approach—though suitable for identifying leachates with strong cytotoxic potential—may not detect more subtle inhibitory effects, particularly at lower concentrations. As such, the current study may underestimate weak or sub-cytotoxic responses that could still hold biological relevance. Finally, all cell-based assays were conducted using immortalized cancer cell lines, which — although standard in screening studies [25–30] — may not fully represent the behavior or sensitivity of healthy human tissues [84]. As such, results should be interpreted with caution when extrapolating to normal physiological responses. Overall, the results presented here should be interpreted as conservative, first-tier hazard signals rather than definitive measures of toxicity thresholds.

Building on current efforts, the further integration of advanced analytical and predictive tools could enhance future studies. Non-targeted analytical strategies that incorporate comprehensive two-dimensional liquid/gas chromatography (LC×LC, GC×GC) and high-resolution mass spectrometry, combined with advanced data analytics and modeling — such as spectral deconvolution algorithms, chemometric tools [32], and plastic-specific predictive toxicology models [85] — can be pivotal for identifying and prioritizing previously unknown toxicants. Complementing these approaches with targeted quantification of key tentatively identified compounds could further strengthen causal links between chemical features and observed toxic effects. In parallel, future confirmatory studies should include biological replication of the leachate preparations to capture inter-sample variability in chemical release and enable probabilistic interpretation. Additionally, applying finer concentration spacing, expanded assay endpoints, and longer exposure durations will improve sensitivity to low-level effects and better resolve subtle toxicological responses. To enhance physiological relevance, future work may also consider complementing cancer-derived models with primary human cell lines or advanced tissue-derived systems. Effect-directed analysis could provide a critical link between chemical composition and biological effects, enabling the isolation and identification of toxic compounds within complex leachate mixtures [86], but its resource-intensive nature placed it beyond the scope of this study. By facilitating a next-level integrative strategy for characterizing the plastic-associated chemical universe, this approach supports more accurate risk assessments, guides the development of safer plastic materials, and ultimately informs sustainable environmental management. Such efforts align with emerging multisectoral frameworks that emphasize chemical safety as a prerequisite for achieving a circular economy for plastics [87].

Environmental implication

UV weathering transforms consumer plastics into potent sources of toxic, bioavailable chemicals, increasing risks to aquatic ecosystems. Our findings show that these transformations elevate the reactivity and cytotoxicity of plastic leachates, driven largely by organic compounds, with minor to no contribution from leached microplastics or metal(loid)s. As these leachates enter freshwater and marine environments, they may impair key biological functions across trophic levels. Current environmental risk assessments underestimate the impact of weathered plastics by overlooking transformation-driven toxicity. This study underscores the need to integrate chemical aging and mixture effects into regulatory frameworks to better protect ecosystem health.

CRediT authorship contribution statement

Deedar Nabi: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Eric Carmona:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation. **Frank Menger:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation. **Mara Römerscheid:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Stefan Lips:** Writing – review & editing, Formal analysis. **Aaron J. Beck:** Writing – review & editing, Investigation, Funding acquisition, Conceptualization. **Alexander Böhme:**

Writing – review & editing, Methodology, Investigation, Formal analysis. **Hanna Joerss:** Writing – review & editing, Funding acquisition, Formal analysis. **Annika Jahnke:** Writing – review & editing, Visualization, Project administration, Funding acquisition. **Deniz Tasdemir:** Writing – review & editing, Resources, Methodology, Funding acquisition. **Eric P. Achterberg:** Writing – review & editing, Resources, Funding acquisition.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

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Data availability

attached as supplementary material

References

[1] Thompson, R.C., Courtene-Jones, W., Boucher, J., Pahl, S., Raubenheimer, K., Koelmans, A.A., 2024. Twenty years of microplastic pollution research—what have we learned? Science 386, 1979. https://doi.org/10.1126/science.adl2746.

[2] Zhu, X., Huang, W., Fang, M., Liao, Z., Wang, Y., Xu, L., Mu, Q., Shi, C., Lu, C., Deng, H., Dahlgren, R., Shang, X., 2021. Airborne microplastic concentrations in five megacities of Northern and southeast China. Environ Sci Technol 55. https://doi.org/10.1021/acs.est.1c03618.

[3] Issac, M.N., Kandasubramanian, B., 2021. Effect of microplastics in water and aquatic systems. Environ Sci Pollut Res 28, 19544–19562.

[4] Guo, J.J., Huang, X.P., Xiang, L., Wang, Y.Z., Li, Y.W., Li, H., Cai, Q.Y., Mo, C.H., Wong, M.H., 2020. Source, migration and toxicology of microplastics in soil. Environ Int 137.

[5] Sun, A., Wang, W.X., 2023. Human exposure to microplastics and its associated health risks. Environ Health 1.

[6] Li, Y., Tao, L., Wang, Q., Wang, F., Li, G., Song, M., 2023. Potential health impact of microplastics: a review of environmental distribution, human exposure, and toxic effects. Environ Health 1.

[7] Barnett A.N., Arshad M., Nabi D. 2023. A Snapshot into the Invasion of Plastics in Human Urine. https://chemrxiv.org/engage/chemrxiv/article-details/64bd357cb605c6803b38ab17.

[8] Wagner M., Monclús L., Arp H.P.H., Groh K.J., Løseth ME, Muncke J., Wang Z., Wolf R., Zimmermann L., 2025. State of the science on plastic chemicals - Identifying and addressing chemicals and polymers of concern.

[9] Wiesinger, H., Wang, Z., Hellweg, S., 2021. Deep dive into plastic monomers, additives, and processing aids. Environ Sci Technol 55, 9339–9351. https://doi.org/10.1021/acs.est.1c00976.

[10] Leslie, H.A., Jahnke, A., Rojo-Nieto, E., Arp, H.P.H., 2025. Plastic-Associated chemicals: late lessons from early equilibrium partitioning science. Environ Sci Technol 59, 10707–10710. https://doi.org/10.1021/acs.est.5c04383.

[11] Jahnke, A., Arp, H.P.H., Escher, B.I., Gewert, B., Gorokhova, E., Kühnel, D., Ogonowski, M., Potthoff, A., Rummel, C., Schmitt-Jansen, M., Toorman, E., MacLeod, M., 2017. Reducing uncertainty and confronting ignorance about the possible impacts of weathering plastic in the marine environment. Environ Sci Technol Lett 4, 85–90. https://doi.org/10.1021/acs.estlett.7b00008.

[12] He, W., Liu, S., Zhang, W., Yi, K., Zhang, C., Pang, H., Huang, D., Huang, J., Li, X., 2023. Recent advances on microplastic aging: identification, mechanism, influence factors, and additives release. Sci Total Environ 889.

[13] Andrady, A.L., Barnes, P.W., Bornman, J.F., Gouin, T., Madronich, S., White, C.C., Zepp, R.G., Jansen, M.A.K., 2022. Oxidation and fragmentation of plastics in a changing environment; from UV-radiation to biological degradation. Sci Total Environ 851.

[14] Cai, L., Wang, J., Peng, J., Wu, Z., Tan, X., 2018. Observation of the degradation of three types of plastic pellets exposed to UV irradiation in three different environments. Sci Total Environ 628629 740–747. https://doi.org/10.1016/j.scitotenv.2018.02.079.

[15] Duan, L., Qin, Y., Meng, X., Liu, Y., Zhang, T., Chen, W., 2023. Sulfide- and UV-induced aging differentially affect contaminant-binding properties of microplastics derived from commercial plastic products. Sci Total Environ 869. https://doi.org/10.1016/j.scitotenv.2023.161800.

[16] Bridson, J.H., Abbel, R., Smith, D.A., Northcott, G.L., Gaw, S., 2023. Impact of accelerated weathering on the leaching kinetics of stabiliser additives from microplastics. J Hazard Mater 459. https://doi.org/10.1016/j.jhazmat.2023.132303.

[17] Ainali, N.M., Bikiaris, D.N., Lambropoulou, D.A., 2021. Aging effects on low- and high-density polyethylene, polypropylene and polystyrene under UV irradiation: an insight into decomposition mechanism by Py-GC/MS for microplastic analysis. J Anal Appl Pyrolysis 158. https://doi.org/10.1016/j.jaap.2021.105207.

[18] Suhrhoff, T.J., Scholz-Böttcher, B.M., 2016. Qualitative impact of salinity, UV radiation and turbulence on leaching of organic plastic additives from four common plastics - a lab experiment. Mar Pollut Bull 102, 84–94. https://doi.org/10.1016/j.marpolbul.2015.11.054.

[19] Sun, B., Hu, Y., Cheng, H., Tao, S., 2019. Releases of brominated flame retardants (BFRs) from microplastics in aqueous medium: kinetics and molecular-size dependence of diffusion. Water Res 151, 215–225. https://doi.org/10.1016/j.watres.2018.12.017.

[20] Groh, K.J., Backhaus, T., Carney-Almroth, B., Geueke, B., Inostroza, P.A., Lennquist, A., Leslie, H.A., Maffini, M., Slunge, D., Trasande, L., Warhurst, A.M., Muncke, J., 2019. Overview of known plastic packaging-associated chemicals and their hazards. Sci Total Environ 651, 3253–3268. https://doi.org/10.1016/j.scitotenv.2018.10.015.

[21] Simoneit, M., Langer, H., Ulrich, N., Böhme, A., 2025. Refining the amino Reactivity-Based identification of respiratory sensitizers. Chem Res Toxicol. https://doi.org/10.1021/acs.chemrestox.4c00545.

[22] Böhme, A., Laqua, A., Schüürmann, G., 2016. Chemoavailability of organic electrophiles: impact of hydrophobicity and reactivity on their aquatic excess toxicity. Chem Res Toxicol 29. https://doi.org/10.1021/acs.chemrestox.5b00398.

[23] Bohme, A., Moldrickx, J., Schuurmann, G., 2021. Amino reactivity of glutardialdehyde and Monoaldehydes—Chemoassay profile vs skin sensitization potency. Chem Res Toxicol 34, 2353–2365. https://doi.org/10.1021/acs.chemrestox.1c00266.

[24] Böhme, A., Ulrich, N., Schüürmann, G., 2023. Amino chemoassay profiling of aromatic Aldehydes-Unraveling drivers of their skin sensitization potency. Chem Res Toxicol 36, 1055–1070. https://doi.org/10.1021/acs.chemrestox.3c00013.

[25] Savva, K., Borrell, X., Moreno, T., Pérez-Pomeda, I., Barata, C., Llorca, M., Farré, M., 2023. Cytotoxicity assessment and suspected screening of PLASTIC ADDITIVES in bioplastics of single-use household items. Chemosphere 313, 137494. https://doi.org/10.1016/J.CHEMOSPHERE.2022.137494.

[26] Klein, K., Hof, D., Dombrowski, A., Schweyen, P., Dierkes, G., Ternes, T., Schulte-Oehlmann, U., Oehlmann, J., 2021. Enhanced in vitro toxicity of plastic leachates after UV irradiation. Water Res 199, 117203. https://doi.org/10.1016/J.WATRES.2021.117203.

[27] Schwarz, W., Wegener, S., Schertzinger, G., Pannekens, H., Schweyen, P., Dierkes, G., Klein, K., Ternes, T.A., Oehlmann, J., Dopp, E., 2023. Chemical and toxicological assessment of leachates from UV-degraded plastic materials using in-vitro bioassays. PeerJ 11. https://doi.org/10.7717/peerj.15192.

[28] Zimmermann, L., Göttlich, S., Oehlmann, J., Wagner, M., Völker, C., 2020. What are the drivers of microplastic toxicity? Comparing the toxicity of plastic chemicals and particles to daphnia magna. Environ Pollut 267. https://doi.org/10.1016/j.envpol.2020.115392.

[29] Zimmermann, L., Dierkes, G., Ternes, T.A., Völker, C., Wagner, M., 2019. Benchmarking the in vitro toxicity and chemical composition of plastic consumer products. Environ Sci Technol 53. https://doi.org/10.1021/acs.est.9b02293.

[30] Judson, R., Houck, K., Martin, M., Richard, A.M., Knudsen, T.B., Shah, I., Little, S., Wambaugh, J., Woodrow Setzer, R., Kothya, P., Phuong, J., Filer, D., Smith, D., Reif, D., Rotroff, D., Kleinstreuer, N., Sipes, N., Xia, M., Huang, R., Crofton, K., Thomas, R.S., 2016. Analysis of the effects of cell stress and cytotoxicity on in vitro assay activity across a diverse chemical and assay space. Toxicol Sci 152, 323–339. https://doi.org/10.1093/toxsci/kfw092.

[31] Albergamo, V., Wohlleben, W., Plata, D.L., 2024. Tracking dynamic chemical reactivity networks with High-Resolution mass spectrometry: a case of Microplastic-Derived dissolved organic carbon. Environ Sci Technol. https://doi.org/10.1021/acs.est.3c08134.

[32] Siddiqui, M.U., Sibtain, M., Ahmad, F., Zushi, Y., Nabi, D., 2024. Screening disinfection byproducts in Arid-Coastal wastewater: a workflow using GC×GC-TOFMS, passive sampling, and NMF deconvolution algorithm. J Xenobiot 14, 554–574. https://doi.org/10.3390/jox14020033.

[33] Tisler, S., Kristiansen, N., Christensen, J.H., 2024. Chemical migration from reusable plastic bottles: silicone, polyethylene, and polypropylene show highest hazard potential in LC-HRMS analysis. J Hazard Mater 480, 136391. https://doi.org/10.1016/j.jhazmat.2024.136391.

[34] Fries, E., Sühring, R., 2023. The unusual suspects: screening for persistent, mobile, and toxic plastic additives in plastic leachates. Environ Pollut 335, 122263. https://doi.org/10.1016/j.envpol.2023.122263.
[35] Meng, W., Chen, Q., Zhang, Y., Sun, H., Li, J., Sun, H., Liu, C., Fang, M., Su, G., 2024. Tracking chemical feature releases from plastic food packaging to humans. J Hazard Mater 480, 135897. https://doi.org/10.1016/j.jhazmat.2024.135897.
[36] Omidoyin, K.C., Jho, E.H., 2024. Environmental occurrence and ecotoxicological risks of plastic leachates in aquatic and terrestrial environments. Sci Total Environ 954, 176728. https://doi.org/10.1016/J.SCITOTENV.2024.176728.
[37] Fries, E., Sühring, R., 2023. The unusual suspects: screening for persistent, mobile, and toxic plastic additives in plastic leachates. Environ Pollut 335, 122263. https://doi.org/10.1016/J.ENVPOL.2023.122263.
[38] Li, Y., Lu, Z., Abrahamsson, D.P., Song, W., Yang, C., Huang, Q., Wang, J., 2022. Non-targeted analysis for organic components of microplastic leachates. Sci Total Environ 816, 151598. https://doi.org/10.1016/J.SCITOTENV.2021.151598.
[39] Menger F., Römerscheid M., Lips S., Klein O., Nabi D., Gandrass J., Joerss H., Wendt-Potthoff K., Bedulina D., Zimmermann T., Schmitt-Jansen M., Huber C., Böhme A., Ulrich N., Beck A.J., Pröfrock D., Achterberg E.P., Jahnke A., Hildebrandt L. 2024. Screening the release of chemicals and microplastic particles from diverse plastic consumer products into water under accelerated UV weathering conditions. J Hazard Mater 135256. https://doi.org/10.1016/j.jhazmat.2024.135256.
[40] US EPA, 2023. CompTox Chemicals Dashboard. https://comptox.epa.gov/dashboard. Accessed 1 May 2023.
[41] Williams, A.J., Grulke, C.M., Edwards, J., McEachran, A.D., Mansouri, K., Baker, N. C., Patlewicz, G., Shah, I., Wambaugh, J.F., Judson, R.S., Richard, A.M., 2017. The CompTox chemistry dashboard: a community data resource for environmental chemistry. J Chemin 9. https://doi.org/10.1186/s13321-017-0247-6.
[42] US EPA, 2024. CTS: Chemical Transformation Simulator 1.3.2.2. https://qed.epa.gov/cts/. Accessed 18 Dec 2024.
[43] Li, H.X., Getzinger, G.J., Ferguson, P.L., Orihuela, B., Zhu, M., Rittschof, D., 2016. Effects of toxic leachate from commercial plastics on larval survival and settlement of the barnacle amphibalanus amphitrite. Environ Sci Technol 50. https://doi.org/10.1021/acs.est.5b02781.
[44] Zimmermann, L., Bartosova, Z., Braun, K., Oehlmann, J., Völker, C., Wagner, M., 2021. Plastic products leach chemicals that induce in vitro toxicity under realistic use conditions. Environ Sci Technol 55, 11814–11823. https://doi.org/10.1021/acs.est.1c01103.
[45] Peng, X., Yang, T., Guo, S., Zhou, J., Chen, G., Zhu, Z., Tan, J., 2024. Revealing chemical release from plastic debris in animals' digestive systems using nontarget and suspect screening and simulating digestive fluids. Environ Pollut 348. https://doi.org/10.1016/j.envpol.2024.123793.
[46] Peng, X., Li, X., Zhou, J., Tan, J., Chen, G., Zhu, Z., Yang, T., 2024. Beyond plastic pollution: unveiling chemical release from plastic debris in river water and seawater using non-target screening. Water Res 267, 122515. https://doi.org/10.1016/J.WATRES.2024.122515.
[47] Gewert, B., Plassmann, M., Sandblom, O., MacLeod, M., 2018. Identification of chain scission products released to water by plastic exposed to ultraviolet light. Environ Sci Technol Lett 5, 272–276. https://doi.org/10.1021/acs.estlett.8b00119.
[48] Fan, X., Tao, J., Zhou, Y., Hou, Y., Wang, Y., Gu, D., Su, Y., Jang, Y., Li, S., 2019. Investigations on the effects of ginsenoside-Rg1 on glucose uptake and metabolism in insulin resistant HepG2 cells. Eur J Pharm 843, 277–284. https://doi.org/10.1016/J.EJPHAR.2018.11.024.
[49] Blackwell, B.R., Ankley, G.T., Bradley, P.M., Houck, K.A., Makarov, S.S., Medvedev, A.V., Swintek, J., Villeneuve, D.L., 2019. Potential toxicity of complex mixtures in surface waters from a nationwide survey of United States streams: identifying in vitro bioactivities and causative chemicals. Environ Sci Technol 53. https://doi.org/10.1021/acs.est.8b05304.
[50] Kim, S., Kang, K., Kim, H., Seo, M., 2024. In vitro toxicity screening of fifty complex mixtures in HepG2 cells. Toxics 12, 126. https://doi.org/10.3390/toxics12020126.
[51] Riss T.L., Niles A.L., Minor L., Moravec R.A., Benink H.A., Worzella T.J. 2013. Assay Guidance Manual: Cell Viability Assays. In: Assay Guidance Manual.
[52] Shenoy, N., Stenson, M., Lawson, J., Abeykoon, J., Patnaik, M., Wu, X., Witzig, T., 2017. Drugs with anti-oxidant properties can interfere with cell viability measurements by assays that rely on the reducing property of viable cells. Lab Investig 97. https://doi.org/10.1038/labinvest.2017.18.
[53] Gruber, S., Nickel, A., 2023. Toxic or not toxic? The specifications of the standard ISO 10993-5 are not explicit enough to yield comparable results in the cytotoxicity assessment of an identical medical device. Front Med Technol 5. https://doi.org/10.3389/fmedt.2023.1195529.
[54] Biological evaluation of medical devices —Part 5: Tests for in vitro cytotoxicity, 2009. In: ANSI/AAMI/ISO 10993-5:2009/(R)2014; Biological evaluation of medical devices —Part 5: Tests for in vitro cytotoxicity.
[55] Longhin, E.M., El Yamani, N., Rundén-Pran, E., Dusinska, M., 2022. The alamar blue assay in the context of safety testing of nanomaterials. Front Toxicol 4. https://doi.org/10.3389/ftox.2022.981701.
[56] Larsson, P., Engqvist, H., Biermann, J., Werner Rönnerman, E., Forssell-Aronsson, E., Kovács, A., Karlsson, P., Helou, K., Parris, T.Z., 2020. Optimization of cell viability assays to improve replicability and reproducibility of cancer drug sensitivity screens. Sci Rep 10. https://doi.org/10.1038/s41598-020-62848-5.
[57] Taha, M.H., Aalizadeh, R., Alygizakis, N., Antignac, J.-P., Arp, H.P.H., Bade, R., Baker, N., Belova, L., Bijlsma, L., Bolton, E.E., Brack, W., Celma, A., Chen, W.-L., Cheng, T., Chirsir, P., Čirka Ľ, D'Agostino, L.A., Djoumbou Feunang, Y., Dulio, V., Fischer, S., Gago-Ferrero, P., Galani, A., Geueke, B., Głowacka, N., Glüge, J., Groh, K., Grosse, S., Haglund, P., Hakkinen, P.J., Hale, S.E., Hernandez, F., Janssen, E.M.-L., Jonkers, T., Kiefer, K., Kirchner, M., Koschorreck, J., Krauss, M., Krier, J., Lamoree, M.H., Letzel, M., Letzel, T., Li, Q., Little, J., Liu, Y., Lunderberg, D.M., Martin, J.W., McEachran, A.D., McLean, J.A., Meier, C., Meijer, J., Menger, F., Merino, C., Muncke, J., Muschket, M., Neumann, M., Neveu, V., Ng, K., Oberacher, H., O'Brien, J., Oswald, P., Oswaldova, M., Picache, J.A., Postigo, C., Ramirez, N., Reemtsma, T., Renaud, J., Rostkowski, P., Rüdel, H., Salek, R.M., Samanipour, S., Scheringer, M., Schliebner, I., Schulz, W., Schulze, T., Sengl, M., Shoemaker, B.A., Sims, K., Singer, H., Singh, R.R., Sumarah, M., Thiessen, P.A., Thomas, K.V., Torres, S., Trier, X., van Wezel, A.P., Vermeulen, R.C.H., Vlaanderen, J.J., von der Ohe, P.C., Wang, Z., Williams, A.J., Willighagen, E.L., Wishart, D.S., Zhang, J., Thomaidis, N.S., Hollender, J., Slobodnik, J., Schymanski, E.L., 2022. The NORMAN suspect list exchange (NORMAN-SLE): facilitating european and worldwide collaboration on suspect screening in high resolution mass spectrometry. Environ Sci Eur 34, 104. https://doi.org/10.1186/s12302-022-00680-6.
[58] Musatadi, M., Baciero-Hernández, I., Prieto, A., Olivares, M., Etxebarria, N., Zuloaga, O., 2024. Development and evaluation of a comprehensive workflow for suspect screening of exposome-related xenobiotics and phase II metabolites in diverse human biofluids. Chemosphere 351, 141221. https://doi.org/10.1016/J.CHEMOSPHERE.2024.141221.
[59] Schymanski, E.L., Jeon, J., Gulde, R., Fenner, K., Ruff, M., Singer, H.P., Hollender, J., 2014. Identifying small molecules via high resolution mass spectrometry: communicating confidence. Environ Sci Technol 48.
[60] Wondrousch, D., Böhme, A., Thaens, D., Ost, N., Schüürmann, G., 2010. Local electrophilicity predicts the Toxicity-Relevant reactivity of michael acceptors. J Phys Chem Lett 1, 1605–1610. https://doi.org/10.1021/jz100247x.
[61] Chodurek, E., Orchel, A., Orchel, J., Kurkiewicz, S., Gawlik, N., Dzierzewicz, Z., Stępień, K., 2012. Evaluation of melanogenesis in A-375 cells in the presence of DMSO and analysis of pyrolytic profile of isolated melanin. Sci World J 2012. https://doi.org/10.1100/2012/854096.
[62] Cooper, J.R., Abdullatif, M.B., Burnett, E.C., Kempsell, K.E., Conforti, F., Tolley, H., Collins, J.E., Davies, D.E., 2016. Long term culture of the a549 cancer cell line promotes multilamellar body formation and differentiation towards an alveolar type II pneumocyte phenotype. PLoS One 11. https://doi.org/10.1371/journal.pone.0164438.
[63] De Angelis, P.M., Kravik, K.L., Tunheim, S.H., Haug, T., Reichelt, W.H., 2004. Comparison of gene expression in HCT116 treatment derivatives generated by two different 5-fluorouracil exposure protocols. Mol Cancer 3. https://doi.org/10.1186/1476-4598-3-11.
[64] Morshneva, A.V., Gnedina, O.O., Kindt, D.N., Igotti, M.V., 2022. Establishment and characterization of human Colon-Cancer cells resistant to cisplatin. Cell Tissue Biol 16. https://doi.org/10.1134/S1990519X22060037.
[65] Ren Z., Chen S., Ning B., Guo L. 2018. Use of liver-derived cell lines for the study of drug-induced liver injury. In: Methods in Pharmacology and Toxicology.
[66] Kern, S., Fenner, K., Singer, H.P., Schwarzenbach, R.P., Hollender, J., 2009. Identification of transformation products of organic contaminants in natural waters by computer-aided prediction and high-resolution mass spectrometry. Environ Sci Technol 43. https://doi.org/10.1021/es901979h.
[67] European Chemicals Agency. Substance Infocard. https://echa.europa.eu/de/substance-information/-/substanceinfo/100.103.017. Accessed 12 Jun 2025.
[68] Bridson, J.H., Masterton, H., Theobald, B., Risani, R., Doake, F., Wallbank, J.A., Maday, S.D.M., Lear, G., Abbel, R., Smith, D.A., Kingsbury, J.M., Pantos, O., Northcott, G.L., Gaw, S., 2024. Leaching and transformation of chemical additives from weathered plastic deployed in the marine environment. Mar Pollut Bull 198, 115810. https://doi.org/10.1016/j.marpolbul.2023.115810.
[69] Henkel, C., Hüffer, T., Peng, R., Gao, X., Ghoshal, S., Hofmann, T., 2024. Photoaging enhances the leaching of di(2-ethylhexyl) phthalate and transformation products from polyvinyl chloride microplastics into aquatic environments. Commun Chem 7, 218. https://doi.org/10.1038/s42004-024-01310-3.
[70] Weber E., C., Stevens M, Koopmans J., Olmstead N, Pope K., Wolfe, C. Yuan, 2019. User's Guide for the Chemical Transformation Simulator (CTS), Version 1.0. Washington, DC.
[71] Wolfe, K., Pope, N., Parmar, R., Galvin, M., Stevens, C., Weber, E., Flaishans, J., Purucker, T., 2016. Chemical transformation system: cloud based cheminformatic services to support integrated environmental modeling. Environmental Modelling and Software for Supporting a Sustainable Future, Proceedings - 8th International Congress on Environmental Modelling and Software. iEMSs 2016.
[72] Chu, S., Haffner, G.D., Letcher, R.J., 2005. Simultaneous determination of tetrabromobisphenol A, tetrachlorobisphenol A, bisphenol a and other halogenated analogues in sediment and sludge by high performance liquid chromatography-electrospray tandem mass spectrometry. J Chromatogr A 1097, 25–32. https://doi.org/10.1016/J.CHROMA.2005.08.007.
[73] Khawar, M.I., Nabi, D., 2021. Relook on the linear free energy relationships describing the partitioning behavior of diverse chemicals for polyethylene water passive samplers. ACS Omega 6, 5221–5232. https://doi.org/10.1021/acsomega.0c05179.
[74] Ulrich N., Endo S., Brown T.N., Watanabe N., Bronner G., Abraham M.H., Goss K.-U., 2018. UFZ-LSER database v 3.2.1. Helmholtz Centre for Environmental Research-UFZ, Leipzig, Germany. http://www.ufz.de/lserd.
[75] Deng, Q., He, B., Shen, M., Ge, J., Du, B., Zeng, L., 2024. First evidence of hindered amine light stabilizers as abundant, ubiquitous, emerging pollutants in dust and air particles: a new concern for human health. Environ Sci Technol 58. https://doi.org/10.1021/acs.est.3c08884.

[76] Cocchi, M., Vascellari, M., Gallina, A., Agnoletti, F., Angeletti, R., Mutinelli, F., 2010. Canine nephrotoxicosis induced by melamine-contaminated pet food in Italy. J Vet Med Sci 72.
[77] Monclús, L., Arp, H.P.H., Groh, K.J., Faltynkova, A., Løseth, M.E., Muncke, J., Wang, Z., Wolf, R., Zimmermann, L., Wagner, M., 2025. Mapping the chemical complexity of plastics. Nature 643, 349–355. https://doi.org/10.1038/s41586-025-09184-8.
[78] Liao, Y., Wang, Y., Lin, Y.J., Xiao, Y., Mohan, M., Jaman, R., Dong, H., Zhu, J., Li, X., Zhang, C., Chen, G., Zhou, J., 2024. Molecular mechanisms of tetrabromobisphenol a (TBBPA) toxicity: insights from various biological systems. Ecotoxicol Environ Saf 288, 117418. https://doi.org/10.1016/J.ECOENV.2024.117418.
[79] Li, J., Xu, Y., Li, N., Zuo, R., Zhai, Y., Chen, H., 2022. Thyroid hormone disruption by organophosphate esters is mediated by Nuclear/Membrane thyroid hormone receptors: in vitro, in vivo, and in silico studies. Environ Sci Technol 56. https://doi.org/10.1021/acs.est.1c05956.
[80] Hoh A., Maier K. 1993. Comparative Cytotoxicity Test with Human Keratinocytes, HaCaT Cells, and Skin Fibroblasts to Investigate Skin-Irritating Substances. In: Cell and Tissue Culture Models in Dermatological Research.
[81] Rummel, C.D., Escher, B.I., Sandblom, O., Plassmann, M.M., Arp, H.P.H., Macleod, M., Jahnke, A., 2019. Effects of leachates from UV-Weathered microplastic in Cell-Based bioassays. Environ Sci Technol 53, 9214–9223. https://doi.org/10.1021/acs.est.9b02400.
[82] Reiter, E.B., Escher, B.I., Rojo-Nieto, E., Nolte, H., Siebert, U., Jahnke, A., 2023. Characterizing the marine mammal exposome by iceberg modeling, linking chemical analysis and in vitro bioassays. Environ Sci Process Impacts 25. https://doi.org/10.1039/d3em00033h.
[83] Kienle, C., Vermeirssen, E.L.M., Schifferli, A., Singer, H., Stamm, C., Werner, I., 2019. Effects of treated wastewater on the ecotoxicity of small streams - unravelling the contribution of chemicals causing effects. PLoS One 14. https://doi.org/10.1371/journal.pone.0226278.
[84] Li, H., Yin, N., Yang, R., Faiola, F., 2024. Advancing environmental toxicology in vitro: from immortalized cancer cell lines to 3D models derived from stem cells. Environ Health 2.
[85] Nabi, D., Beck, A.J., Achterberg, E.P., 2024. Assessing aquatic baseline toxicity of Plastic-Associated chemicals: development and validation of the target plastic model. J Chem Inf Model 64, 6492–6505. https://doi.org/10.1021/acs.jcim.4c00574.
[86] Hong, S., Lee, J., Cha, J., Gwak, J., Khim, J.S., 2023. Effect-Directed analysis combined with nontarget screening to identify unmonitored toxic substances in the environment. Environ Sci Technol 57.
[87] Jahnke, A., Beck, A.J., Becker, R.L., Bedulina, D., Braun, U., Gerdts, G., Hildebrandt, L., Joerss, H., Klein, O., Korduan, J., Laforsch, C., Lannig, G., Leslie, H.A., Lips, S., Menger, F., Nabi, D., Oberbeckmann, S., Primpke, S., Pröfrock, D., Ramsperger, A.F.R.M., Römerscheid, M., Schmitt-Jansen, M., Scholz-Böttcher, B.M., Tröppner, O., Wendt-Potthoff, K., Kühnel, D., 2025. Perspective article: multisectoral considerations to enable a circular economy for plastics. J Hazard Mater 496, 139326. https://doi.org/10.1016/J.JHAZMAT.2025.139326.