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Comparison of product safety data sheet ingredient lists with skin irritants and sensitizers present in a convenience sample of light-curing resins used in additive manufacturing

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Abstract

Material jetting and vat photopolymerization additive manufacturing (AM) processes use liquid resins to build objects. These resins can contain skin irritants and/or sensitizers but product safety data sheets (SDSs) might not declare all ingredients. We characterized elemental and organic skin irritants and sensitizers present in 39 commercial products; evaluated the influence of resin manufacturer, system, color, and AM process type on the presence of irritants and sensitizers; and compared product SDSs to results. Among all products, analyses identified 23 irritant elements, 54 irritant organic substances, 22 sensitizing elements, and 23 sensitizing organic substances; SDSs listed 3, 9, 4, and 6 of these ingredients, respectively. Per product, the number and total mass (an indicator of potential dermal loading) of ingredients varied: five to 17 irritant elements (8.32–4756.65 mg/kg), one to 17 irritant organics (3273 to 356,000 mg/kg), four to 17 sensitizing elements (8.27–4755.63 mg/kg), and one to seven sensitizing organics (15–382,170 mg/kg). Median numbers and concentrations of irritants and sensitizers were significantly influenced by resin system and AM process type. The presence of undeclared irritants and sensitizers in these

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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.

Appendix A. Supplementary data

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resins supports the need for more complete information on product SDSs for comprehensive dermal risk assessments.

Keywords

3D printing; Photopolymer; Photoinitiator; Irritant contact dermatitis; Allergic contact dermatitis

1. Introduction

Occupational dermatitis is a costly problem, with an annual economic burden of US $1.5 billion (Milam et al., 2020). Skin exposure to certain chemicals can cause irritant contact dermatitis (ICD) or allergic contact dermatitis (ACD) (Novak-Bilíc et al., 2018). ICD is inflammation of the skin from exposure to an exogenous substance but does not require prior sensitization to the substance (Novak-Bilíc et al., 2018; Bains et al., 2019). Skin sensitizers are substances that can induce a delayed T-cell mediated immune response. Once sensitized, subsequent skin exposure to a sufficient dose of the offending substance can elicit a skin reaction, referred to as ACD (Martin et al., 2018; Novak-Bilíc et al., 2018). Once sensitized, avoidance and/or substitution are the best ways to prevent further exposure to the offending substance and elicitation of an allergic reaction (Martin et al., 2018). Some chemicals encountered in the workplace are both irritants and sensitizers (Sasseville, 2008).

Additive manufacturing (AM) describes a family of processes that join materials, usually layer-by-layer, to make objects from a computer aided design file (ISO/ASTM, 2015). Material jetting (MJ) and vat photopolymerization (VP) are types of AM that use liquid photopolymer resins that can contain skin irritants and/or sensitizers as feedstock to build objects. These resins are composed of binders, monomers, and photoinitiators (Short et al., 2014). In MJ, resin is dispensed onto a build platform via hundreds of micronozzles; photoinitiators are activated using an ultraviolet laser to harden the resin and the process is repeated layer-by-layer to build an object. For VP, a light source (ultraviolet or multi-wavelength light) is shone in a pattern on the surface of a vat that contains resin, which activates the photoinitiators to harden the resin, and the process is repeated layer-by-layer.

The U.S. Occupational Safety and Health Administration (OSHA) Hazard Communication Standard (§1910.1200) requires that employers, employees, and emergency responders be informed of hazards associated with chemicals used in the workplace. This information is conveyed via globally harmonized safety data sheets (SDSs). Note that under this standard, if an ingredient is present at $< 1\%$ by wt., it does not have to be listed on a product SDS, unless the ingredient will affect the product hazard classification (OSHA, 2012). Available literature indicates that SDSs might not convey all relevant information for health protection. For example, discrepancies have been reported in particle size and elemental composition of powders used for fusion-based AM processes compared with what was declared in the SDSs (Graff et al., 2017; Du Preez et al., 2018). Another study reported the presence of 2, 3-pentanedione and diacetyl (both associated with debilitating lung disease) in coffee flavorings that were not listed on SDSs (LeBouf et al., 2019). A third example is the conclusion that SDSs contained insufficient data to communicate the potential hazards of engineered nanomaterials (Eastlake et al., 2012).

To our knowledge, the first report of a skin disease among AM workers was ACD from a VP resin (Chang et al., 2004). Subsequently, more cases of ACD were reported among AM workers who had skin contact with photopolymer resins (Creytens et al., 2017). Based on this known risk of ACD among AM workers and the precedence that SDSs could lack relevant information for health protection, we evaluated whether VP and MJ feedstock resins contained skin irritants or sensitizers that were not declared on product SDSs. While the current study focuses on the dermal exposure pathway, it is important to understand that the inhalation pathway is also relevant for VP and MJ processes (Stefaniak et al., 2019; Väisänen et al., 2019, 2022). For example, numerous resin ingredients such as acrylates (2-hydroxypropyl methacrylate, methyl methacrylate, methacrylic acid, etc.) and carbonyls (e.g., acetone) are released into air during MJ and VP processes (Väisänen et al., 2019, 2022). When breathed in, these compounds can present inhalation hazards such as eye, nose, and throat irritation and respiratory sensitization (NIOSH, 2022).

2. Materials and methods

Thirty-nine resin products used in VP (29/39) and MJ (10/39) AM processes were obtained from an automotive manufacturer during a National Institute for Occupational Safety and Health (NIOSH) walk-through survey (see Table S1). The products were made by seven different manufacturers. For the VP resins, 17 were a one-part resin (not mixed with another component before use) and 12 were two-part resin systems (components are mixed just prior to use so that ingredients do not react and harden during storage). All MJ resins were one-part.

2.1. Quantification of elements

A sample of each product was digested and screened for 31 elements using inductively coupled plasma-optical emission spectrometry (ICP-OES) using a modified NIOSH Method 7303 by Bureau Veritas (Novi, MI) (NIOSH, 2003). If chromium (Cr) was quantified in a sample, the resin was further analyzed to speciate Cr(VI) using ion chromatography with ultraviolet–visible detection in accordance with a modified OSHA Method ID 215 (version 2) (OSHA, 2006). Details of the analytical method are provided in the Supplemental File. Table S2 lists the elements and their respective limits of detection (LOD) and quantification (LOQ).

2.2. Identification of organic constituents

Samples of each product were quantitatively analyzed for 10 target irritants and/or sensitizers and qualitatively analyzed to identify other organic compounds present using gas chromatography-mass spectrometry (GC-MS) by Bureau Veritas. The target substances (acetone, isopropyl alcohol, n-hexane, benzene, methyl methacrylate, toluene, ethylbenzene, styrene, *m,p*-xylene, *o*-xylene) were selected based on their presence in resins (unpublished data) used in a study of VP printer emissions (Stefaniak et al., 2019). Details of the analysis are provided in the Supplemental File. Target compounds were quantified by comparing the mass spectral patterns and retention times to authentic standards. Other organic substances in the samples were qualitatively identified from the remaining chromatographic peaks (tentatively identified compounds [TICs]) by the analyst based on the mass spectral matches with mass spectral library software (Wiley Registry 8th Edition/NIST, 2008 Mass Spectral Library, Wiley-Blackwell) and a manual review. The semi-quantitative mass concentration of each TIC was estimated from the total area response of the identified compound compared with the total area response of the closest internal standard assuming a 1:1 response ratio. The reporting limit for TICs was 2.5 ng/μL.

2.3. Review of literature and product documentation

For all elements and organic substances present, currently available literature was searched to determine whether each was a skin irritant and/or sensitizer. Product SDSs were reviewed for whether they listed individual ingredients, their Chemical Abstract Services (CAS) number, and product classification as a sensitizer and/or irritant in accordance with the European Commission regulation No. 1272/2008 on Classification, Labelling and Packaging of Substances and Mixtures (CLP Regulation). This regulation provides a decision logic by which manufacturers use set criteria and a weight-of-evidence approach to categorize a product based on types of hazards (e.g., skin sensitizer). Under the CLP regulation, products that are skin sensitizers can be classified into one of three categories (Category 1 = skin sensitizer, Category 1A = high frequency of skin sensitization in humans and/or a high potency in animals, and Category 1B = low to moderate frequency of skin sensitization in humans and/or a low potency in animals). Products that cause skin irritation (reversible damage) are assigned to CLP regulation Category 2 (skin irritation) or Category 3 (mild skin irritation).

2.4. Data analysis

The exact compositions of resin products were not declared on some product SDSs so there was no *a priori* expectation that the numbers and concentrations of elements and organic substances followed a normal distribution or had equal variances. As such, statistical analyses were performed only using the products in which the elements and organic substances were present. Results from characterization of the 39 products (herein designated 1, 2, …39) were compared by manufacturer (A – G), one- or two-part system (VP resins only), AM process type (MJ or VP), and color (clear, white, black, grey, yellow, green, and purple). The footnote in Table 1 lists the number of samples by factor (e.g., AM process type) and level (e.g., MJ or VP). Supplemental Table S1 lists the inventory of resin samples by product number and their properties. For each factor, the median number of sensitizers or irritants and the median mass concentration of sensitizers or irritants were compared in JMP (v13.5.1, SAS Institute Inc., Cary, NC) using the non-parametric Steel-Dwass test with multiple comparisons, which preserves the overall error rate ($\alpha = 0.05$). Data were plotted using SigmaPlot (version 13.0, Systat Software, Inc., San Jose, CA).

3. Results

Fig. 1 summarizes the literature review and screening measurements. The Supplemental File provides details of the literature review for the 31 elements (Tables S3 and S4) and

89 organic substances (Tables S5 and S6). Based on the analytical results and available literature, the final data set for elements consisted of 23 irritants and 22 sensitizers (19 were both an irritant and sensitizer) and for organic substances there were 54 irritants and 23 sensitizers (19 were both an irritant and sensitizer). The Excel format supplementary files give the analytical results for all resin samples.

3.1. Review of SDS information

Approximately 40% (15/39) of SDSs listed ingredients by name and included their CAS number. Thirty-three percent (13/39) of SDSs listed at least one ingredient as a generic class (e.g., photoinitiators) without a CAS number; three (products 18, 19, 20) listed all ingredients using generic classes without CAS numbers. Approximately 20% (8/39) of SDSs listed at least one ingredient as proprietary (trade secret) and did not provide its CAS number; of these eight products, two (numbers 16, 24) listed all ingredients as proprietary. Finally, 7% (3/39) of SDSs listed at least one ingredient as a generic class without a CAS number and at least one ingredient as proprietary without a CAS number (numbers 13, 22, 32). In accordance with the CLP regulation, manufacturers categorized 5% (2/39) of products as an irritant only, 18% (7/39) as a sensitizer only, 72% (28/39) as both an irritant and sensitizer, and 5% (2/39) as neither an irritant nor a sensitizer.

3.2. Skin irritants in resin products

Of the 23 elements and 54 organic substances that were categorized as irritants (Fig. 1), product SDSs listed only three of these elements and nine of these organic substances.

3.2.1. Irritant elements—From Fig. S1, the number of elements with propensity to cause skin irritation (i.e., irritant, or irritant and sensitizer) ranged from five (products 1, 10, 15) to 17 (product 32) per product. As shown in Fig. 2, the total concentration of these quantified elements ranged from 8.32 (product 10) to 4756.65 mg/kg (product 26) per product. From Fig. 3, four elements were categorized as irritants only, i.e., barium (0.05–14.00 mg/kg), lithium (1.20–1.60 mg/kg), magnesium (0.39–3.90 mg/kg), and yttrium (0.09–0.34 mg/kg). The median number and concentration of irritant elements per sample were used for all statistical comparisons. As shown in Table 1, one-part resins had significantly greater median mass concentration of irritant elements compared with two-part resins ($p < 0.05$).

3.2.2. Irritant organic substances—As shown in Fig. S2, per product, the number of organic substances with irritant properties ranged from one (product 10) to 17 (product 35). From Fig. 4, per product, the summed semi-quantitative concentrations of these substances ranged from 3273 (product 3) to 356,000 mg/kg (product 22). Fig. 5 illustrates that among organic substances categorized as irritants only, the highest concentrations were for 3,3′-sulfonyldianaline (product 7) at 39,000 mg/kg and tetramethoxymethane (products 1 and 4, both from manufacturer A) at 18,000 mg/kg. From Table 1, the median numbers of irritant organics were higher for manufacturer D compared with manufacturer F, for one-part resins compared with two-part resins, and for MJ resins compared with VP resins (all $p < 0.05$).

3.2.3. Comparison of irritant data to product safety data sheets—

For seven resins (products 5, 14, 15, 17, 21, 24, and 26), the CLP regulation classification for the skin irritant category on SDSs was "not applicable" (all were categorized as skin sensitizers). These resins contained from five (product 15) to 14 (product 26) irritant elements per product (Fig. S1) at total concentrations of 212.28 (product 24) to 4756.65 mg/kg (product 26) per product (Fig. 2). Additionally, these resins contained from three (products 5, 26) to seven (product 24) irritant organics (Fig. S2) per product with summed concentrations of 8087 mg/kg (product 14) to 100,755 mg/kg (product 15) per product (Fig. 4).

SDSs listed only 3/23 irritant elements quantified among products. Phosphorous was listed on SDSs for 15 products, antimony on SDSs for three products, and antimony and copper were both listed on the SDS of one product. Of the 54 irritant organics identified in products, nine (triethanolamine, toluene, 2-hydroxyethyl acrylate, hexamethylene diacrylate, propylene carbonate, glycerin, 3,3′-sulfonyldianaline, butylated hydroxytoluene, or acrylic acid) were listed on product SDSs. Twelve SDSs listed one of these organic substances, one SDS listed both 2-hydroxyethyl acrylate and butylated hydroxytoluene, and one SDS listed both 2-hydroxyethyl acrylate and acrylic acid.

3.3. Skin sensitizers in resin products

Of the 22 elements and 23 organic substances that were categorized as skin sensitizers, product SDSs only listed four of these elements and six of these sensitizing organic substances.

3.3.1. Sensitizing elements—

As summarized in Fig. S1, the number of elements with propensity to cause sensitization ranged from four (product 10) to 17 (products 28 and 32) per product. From Fig. 2, the summed concentration of sensitizing elements quantified in resins ranged from 8.27 (number 10) to 4755.63 mg/kg (number 26) per product. Three elements were categorized as sensitizers only (Fig. 3): iron (13.00–140.00 mg/kg), lead (0.33–0.83 mg/kg), and titanium (0.23–81.00 mg/kg). As summarized in Table 1, one-part resins had a significantly higher median number and greater median concentration of sensitizing elements per product compared with two-part resins (both $p < 0.05$). The median number of sensitizing elements per product in MJ resins was higher compared with VP resins ($p < 0.05$).

Chromium was quantified in 19 products. From Table S9, among the 12 products with detectable Cr(VI), the proportion of Cr(VI) was 0.05% (product 32) to 23.6% (product 25) by wt.

3.3.2. Sensitizing organic substances—

No organic sensitizers were identified in products 2, 3, 14, 26, and 27. From Fig. S2, among the remaining 34 resins, the number of organic substances with sensitizing properties ranged from one (products 1, 8–10, 16, 25, 28–30) to seven (products 32, 35) per product. As shown in Fig. 4, semi-quantitative concentrations of organic sensitizers ranged from 15 (product 1) to 382,170 mg/kg (product 7) per product. Four organic substances were sensitizers only (Fig. 5): 2-hydroxypropyl methacrylate (84,000 to 170,000 mg/kg), bisphenol-A (520–97,000 mg/kg), ethylene glycol dimethacrylate (790–1800 mg/kg), and *N,N*-dimethylacrylamide (37,000 to 360,000 mg/kg).

From Table 1, the median number of organic sensitizers per product was significantly higher for one-part resins compared with two-part resins and the median concentration was significantly greater for VP resins compared with MJ resins (all $p < 0.05$).

3.3.3. Comparison of sensitizer data to product safety data sheets—For products 12 and 18, the CLP regulation classification for the skin sensitizer category on their SDSs was "not applicable" (both were Category 2 skin irritants). Product 12 contained 11 sensitizing elements (Fig. S1) with a summed concentration of 573.55 mg/kg (Fig. 2) and four sensitizing organics (2-hydroxyethyl methacrylate, butylated hydroxytoluene, methyl methacrylate, and triethylene glycol dimethacrylate) (Fig. S2) with a summed concentration of 151,000 mg/kg (Fig. 4). Product 18 contained eight sensitizing elements (Fig. S1) at 375.33 mg/kg (Fig. 2) and three organic sensitizers (2-hydroxethyl acrylate, butyl isocyanate, and methyl acrylate) (Fig. S2) at a total concentration of 17,350 mg/kg (Fig. 4).

From ICP analysis, 22 unique sensitizing elements were quantified among products; however, only phosphorous (15 products), antimony (four products), titanium (two products) and copper (one product) were listed on SDSs. GC analysis identified 23 organic sensitizers; six were listed on SDSs: 2-hydroxyethyl acrylate (three products), *N,N*-dimethylacrylamide (two products), and hexamethylene diacrylate, triethanolamine, butylated hydroxytoluene, and glycerin (one product each).

3.4. Products not classified as an irritant or sensitizer

Products 3 and 10 were neither classified as a skin irritant nor as a sensitizer on their SDSs. Product 3 contained 3525.98 mg/kg of skin irritants and/or sensitizers. Specifically, it contained five elements that were irritants and sensitizers (cadmium, calcium, cobalt, phosphorous, and zinc) at a summed concentration of 251.42 mg/kg, two elements that were irritants only (barium and magnesium) at a sum of 1.33 mg/kg, and one element that was a sensitizer only (titanium) at 0.23 mg/kg. This product also contained four irritant organic substances (acetone, toluene, 2,4,6-trimethylbenzoic acid, and 2,4-bis(1,1-dimethylethyl) phenol) at a summed concentration of 3273 mg/kg. Product 10 contained 4308.32 mg/kg of skin irritants and sensitizers (irritant and sensitizing elements arsenic, phosphorous, selenium, and tin at a summed concentration of 8.27 mg/kg, irritant only element barium at 0.054 mg/kg, and the irritant and sensitizing organic substance triethanolamine at 4300 mg/kg).

3.5. Completeness of SDSs

ICP and GC analyses revealed that all SDS were incomplete with regard to ingredients that were skin irritants and/or sensitizers. Overall, the total number of skin irritant and/or sensitizer ingredients that were not listed on SDSs ranged from 5 (product 10) to 32 (product 32); corresponding mass concentrations were 8.32 mg/kg and 3521.41 mg/kg, respectively. For elements, the mass concentration of skin irritant and/or sensitizer ingredients that were not listed on SDSs ranged from 2.32 mg/kg (product 4) to 978.73 mg/kg (product 22). For organic substances, the mass concentration of skin irritant and/or sensitizer ingredients that were not listed on SDSs ranged from zero (product 10) to 356,000 mg/kg (product 22).

The SDSs for products 16 and 24 listed all ingredients as proprietary. Product 16 contained aluminum, arsenic, calcium, molybdenum, phosphorous, potassium, selenium, tin, and zinc (irritants and sensitizers) at a summed concentration of 534.78 mg/kg and barium and magnesium (irritants only) at a summed concentration of 3.43 mg/kg. Additionally, this product contained tetraethylene glycol diacrylate at 3800 mg/kg (irritant and sensitizer) and toluene, acetic acid, 1-methoxy-2-propanol, and propylene glycol methyl ether acetate (irritants only) at a summed concentration of 2305 mg/kg. Product 24 contained arsenic, calcium, chromium, nickel, phosphorous, potassium, selenium, tin, and zinc (irritants and sensitizers) with a summed concentration of 212.21 mg/kg and barium (irritant only) at 0.07 mg/kg. Isopropyl alcohol, methyl methacrylate, methyl acrylate, 2-hydroxyethyl methacrylate, and butylated hydroxytoluene (irritants and sensitizers) were present at 62,638 mg/kg and acetone and methacrylic acid (irritants only) were identified at a summed concentration of 335 mg/kg.

3.6. Ingredients present at greater than 1% by weight

From Fig. 3, no single element was quantified at a concentration that exceeded 1% by weight (10,000 mg/kg). As shown in Fig. 5, there were 12 irritant and/or sensitizing organic substances present at concentrations above 1% by wt. in one or more products in which the substance was detected (in mg/kg): 2-hydroxyethyl acrylate in 5/14 products (13,000 to 29,000), 2-hydroxyethyl methacrylate in 11/12 products (39,000 to 350,000), 2-hydroxypropyl methacrylate in 5/5 products (84,000 to 170,000), 3,3′-sulfonyldianiline in 1/1 product (39,000), bisphenol A in 1/3 products (97,000 mg/kg), bisphenol A diglycidyl ether in 2/2 products (24,000 to 110,000), glycerin in 1/1 product (75,000), hexamethylene diacrylate in 2/2 products (13,000 to 83,000), methyl methacrylate in 3/14 products (37,000 to 190,000), *N,N*-dimethylacrylamide in 2/2 products (37,000 to 360,000), tetramethoxymethane in 2/2 products (18,000 in both), and triethylene glycol dimethacrylate in 1/1 product (91,000).

4. Discussion

Despite the known risk of ACD (Chang et al., 2004; Creytens et al., 2017), data on the bulk composition of AM resins are scarce. The Danish Environmental Protection Agency (DEPA) screened the composition of objects made from three commercially available resin products using a VP process. Their ICP analysis quantified antimony (69 mg/kg), arsenic (0.2 mg/kg), chromium (0.7 mg/kg), copper (0.2 mg/kg), tin (3.6–78 mg/kg), and zinc (0.6–2.7 mg/kg), which were similar to the concentrations of these elements in VP resins measured in the current study. Chromium is one of the most common inducers of occupational ACD and irritant dermatitis worldwide (Bregnbak et al., 2015). Workers are exposed to the metal in one of its two major valence states: Cr(III) or Cr (VI). In the current study, for 12 products, speciation of chromium revealed that up to approximately one-fourth of chromium by wt. was in the Cr(VI) form, which is recognized as the most biologically-relevant oxidative state of the metal (Bregnbak et al., 2015). It is associated with greater oxidative potential within biological systems, as well as enhanced bioavailability due to its capacity to readily pass through epidermal barriers and cellular membranes (Buters and Biedermann, 2017). Consequently, Cr(VI) is a more potent skin sensitizer and dermal irritant than Cr(III).

Though Cr(III) is less frequently implicated in chromium allergy, it is still immunologically-relevant in some cases, as it can be transformed to Cr(VI) in the skin, and it has been shown in some reports to elicit ACD responses in Cr-sensitive individuals (Hansen et al., 2003).

GC screening by DEPA identified 19 organic substances in VP printed parts; five were in common with the current study: cyclohexanone (440–1030 mg/kg), propylene carbonate (340 mg/kg), 1,1′-thiobisbenzene (reported by DEPA using synonym diphenyl sulfide; 4100 mg/kg), bisphenol A diglycidyl ether (reported by DEPA using synonym 4,4′-isopropylidene-diphenyl-diglycidyl ether; 670 mg/kg), and 2-hydroxyethyl methacrylate (300 mg/kg). In the current study, for VP resins, the concentration of cyclohexanone (27 mg/kg in one product) was lower, concentrations of 1,1′-thiobisbenzene (3800 to 6700 mg/kg) were similar, and concentrations of propylene carbonate (3800 to 5200 mg/kg), 2-hydroxyethyl methacrylate (7500 to 350,000 mg/kg), and bisphenol A diglycidyl ether (110,000 mg/kg in one product) were higher compared with DEPA results (Fig. 5). Multiple factors could explain the differences in results between studies, including the product manufacturer and specific resin formulation.

The median number and/or concentration of skin irritants and sensitizers were influenced by resin parts and AM process type, and to a lesser degree by manufacturer, though resin color was not significant in any comparisons (Table 1). The observed influence of resin parts and AM process type suggest that controls can be used to minimize dermal exposures. Specifically, two-part resin systems could be substituted for one-part systems when feasible because they contained lower median numbers and concentrations of skin irritants and sensitizers and VP processes (lower median number of sensitizing elements and irritant organics) could be substituted for MJ processes when technically feasible; however, some caution is warranted as VP resins contained a higher median concentration of sensitizing organic substances. Note that some manufacturers of VP machines now offer build platforms that permit operators to release printed objects without using any tools; this engineer control potentially minimizes opportunity for skin contact with uncured resins (Formlabs, 2022).

4.1. Comparison of product SDSs to ICP and GC results

Under the OSHA Hazard Communication Standard, relevant ingredients (excluding carcinogens and reproductive toxins) in a mixture are defined as those present at greater than or equal to 10,000 mg/kg or 1% by wt. (OSHA, 2012). Disclosure of an individual chemical ingredient in a mixture at a concentration of <1% by wt. on a product SDS depends upon whether that ingredient affects the hazard classification (OSHA, 2012). Thus, if an ingredient is present at < 1% by wt., it does not have to be listed on a product SDS, unless the person interpreting the standard considers that the ingredient will affect the product hazard classification (LeBouf et al., 2019). Products 3 and 10 were neither classified as a skin irritant nor as a skin sensitizer under the CLP regulation, despite both containing ingredients that possess these properties. No individual ingredient identified in product 3 exceeded 1% by wt., so none were required to be reported (nor were they voluntarily listed) on the product SDS, despite their potential skin hazard. The concentration of each irritant and sensitizer identified in product 10 was below 1% so none were required to be reported on the product SDS, though triethanolamine (0.43%), both an irritant and sensitizer, was voluntarily listed for this product.

The OSHA Hazard Communication Standard does not require that a chemical constituent be listed on a product SDS regardless of its percent concentration by weight if a mixture is designated by the manufacturer as proprietary (OSHA, 2012). Though the proprietary designation protects intellectual property, it can obscure chemical hazards posed by products used in workplaces. The SDSs for products 16 and 24 listed all ingredients as proprietary, but they contained many known irritants and/or sensitizers. The incompleteness of ingredient listings on product SDSs was not limited to these products. In fact, all product SDSs, regardless of the amount of ingredient information given, did not list from 5 to 32 irritants and/or sensitizers. In accordance with the CLP regulation, product 16 was categorized as a skin sensitizer and irritant and product 24 was categorized as a skin sensitizer. Among the remaining resin products, all but two were categorized as an irritant only, as a sensitizer only, or as both an irritant and sensitizer. Though these designations under the CLP regulation provided some warning to users that precautions should be taken to protect skin when working with these products, under-reporting of ingredients could inadvertently infer a “false-safe” impression to users (i.e., the hazard is not as severe as communicated on the SDS). Additionally, it is difficult to properly select types of skin protection (e.g., gloves, aprons, arm covers) and specific product materials (e.g., nitrile or vinyl, disposable or reusable) without knowledge of specific product ingredients.

Twelve organic substances were present at concentrations that exceeded the 1% reporting threshold of the Hazard Communication Standard (see Fig. 5). Three of these 12 substances (3,3′-sulfonyldianiline, glycerin, and *N,N*-dimethylacrylamide) were listed on their respective product SDSs. Hexamethylene diacrylate was identified in two products but only listed on the SDS for one product. 2-Hydroxyethyl acrylate exceeded 1% by wt. in five products; however, this substance was only listed on the SDS for one product. None of the remaining substances (2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, bisphenol A, bisphenol A diglycidyl ether, methyl methacrylate, tetramethoxymethane, and triethylene glycol dimethacrylate) were listed on SDSs. The reason why these skin hazards were not reported on product SDSs is unknown but highlights that product SDSs alone might not be sufficient for understanding health risks.

Seven products were categorized as sensitizers though they also contained irritants; it is possible that sensitization was considered by the manufacturer to be a more severe endpoint because avoidance or substitution are the best ways to prevent further exposure and elicitation of an allergic reaction (Martin et al., 2018) whereas irritation is considered to be temporary and reversible (Novak-Bilíc et al., 2018; Bains et al., 2019). Products 12 and 18 were categorized as irritants, but they contained sensitizers. The rationale for categorizing these products as irritants but not sensitizers is unclear. Product 12 contained the irritants and sensitizers 2-hydroxyethyl methacrylate at 5.6% and triethylene glycol dimethacrylate at 9.1% and product 18 contained the irritant and sensitizer 2-hydroxyethyl acrylate at 1.7%.

It is important to have both transparency and completeness of ingredients on SDSs of resin products to permit accurate hazard assessments. If an employee develops dermatitis, a complete list of ingredients and concentrations on product SDSs can help facilitate the identification of the offending agent. For example, patch testing with standard "series" of common causative agents such as fragrances, metals, etc. is often used to inform the diagnosis of ACD in persons with skin disorders (Bourke et al., 2009); however, these series might not include a specific allergen present in a workplace. Rømyhr et al. followed industrial painters and conducted patch testing using standard allergen series and a special study series based on known or suspected sensitizers present in their workplaces. Several workers had positive patch tests to chemicals only in the special study series, which indicated that it was useful to test with known and suspected skin sensitizers specific to patients' workplaces (Rømyhr et al., 2006). Creytens et al. reported two cases of ACD among workers exposed to light curing resins in an AM facility and noted that they could not fully evaluate potential allergens in these products because some SDSs did not specify all ingredients, did not include concentrations of ingredients, or listed only a generic substance class (e.g., diacrylate esters) without a CAS number (Creytens et al., 2017). Note that under the Hazard Communication Standard, a health care professional can request disclosure of specific chemicals and amounts of proprietary ingredients for exposure assessment and medical treatment purposes (OSHA, 2012).

4.2. Study limitations

Firstly, we characterized a convenience sample of 39 commercial products, though it is unknown how many more MJ and VP resins are currently on the market, which could limit the generalizability of the results. Secondly, analysis of organic substances was done by methanol extraction followed by GC screening; however, it is possible that extractions were incomplete (recoveries not determined) and/or more organic irritants and sensitizers not amenable to this analytical technique were present in the products, so values presented herein should be considered underestimates. Volatilization or aerosolization of resin constituents could present an inhalation hazard such as irritation, sensitization, or cancer (Väisänen et al., 2019, 2022). Though the current study focused on the dermal exposure pathway, risk assessments should not neglect potential adverse health effects for the inhalation pathway. Additionally, 79 of the organic substances were TICs, so their identities were based on manual matching with spectral libraries by the analyst and concentration values were semi-quantitative based on the total area response of the identified compound compared with the total area response of the closest internal standard assuming a 1:1 response ratio. None-the-less, presentation of their concentration provided valuable information for future studies to quantify these substances using authentic standards. Thirdly, we categorized elements and organic substances as irritants and/or sensitizers. This simplified approach could overestimate risk because it gives equal probability to all elements and substances, though some are more common irritants and sensitizers than others. On the other hand, this approach could underestimate risk because it assumes all elements and organic substances have equal potency. Additionally, it ignores the possibility of effects from co-exposure to irritants and sensitizers, such as a 'danger' model, whereby an antigenic signal in the presence of a non-specific danger signal (e.g., irritancy) is needed to activate the immune system (Nagtegaal et al., 2012) and the possibility of multiple sensitivity from cross-reactivity or multiple sensitization (Thyssen and Menne, 2010) or permissive effects from other non-irritant and non-allergen components.

5. Conclusions

The median numbers and concentrations of irritants and sensitizers in products was influenced by resin system (one- or two-parts) and AM process type. Potential for dermatitis from working with light curing resins might be minimized by implementing substitution controls (two-part resin systems could be used to replace one-part systems when feasible and VP processes could be substituted for MJ processes when technically feasible). Screening of commercially available products revealed that not all ingredients that could cause dermatitis were reported, i.e., 20/23 irritant elements, 46/54 irritant organics, 18/22 sensitizing elements, and 17/23 sensitizing organics present were not listed on their respective product SDSs. Given the presence of undeclared irritants and sensitizers in these products, consideration should be given to enhanced transparency in reporting all resin ingredients on SDSs, regardless of concentration, to facilitate exposure and hazard assessments and diagnoses of occupational skin diseases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability statement

Anonymized data in Excel format are available upon request from the corresponding author.

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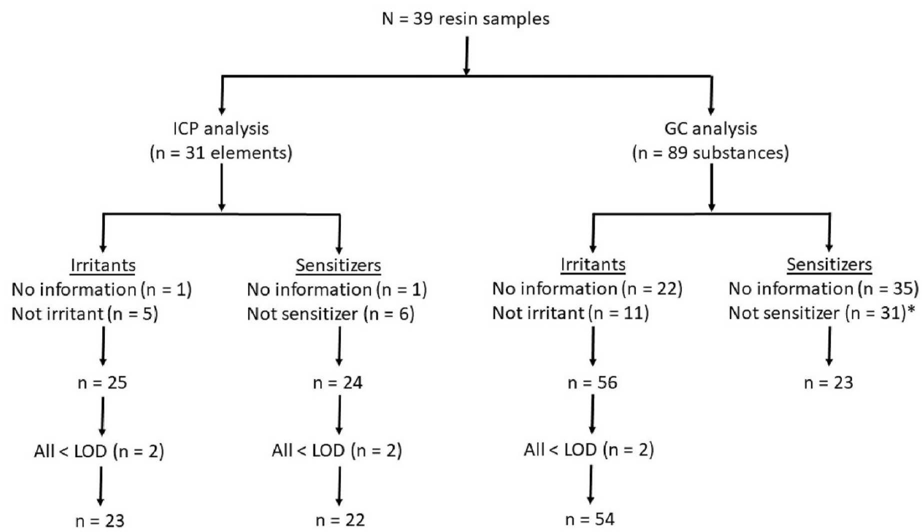

Fig. 1.

Categorization of elements and substances in resin products as skin irritants and/or sensitizers (< LOD = below the analytical limit of detection). *Includes benzene and n-hexane (not sensitizers) that were <LOD in all samples.

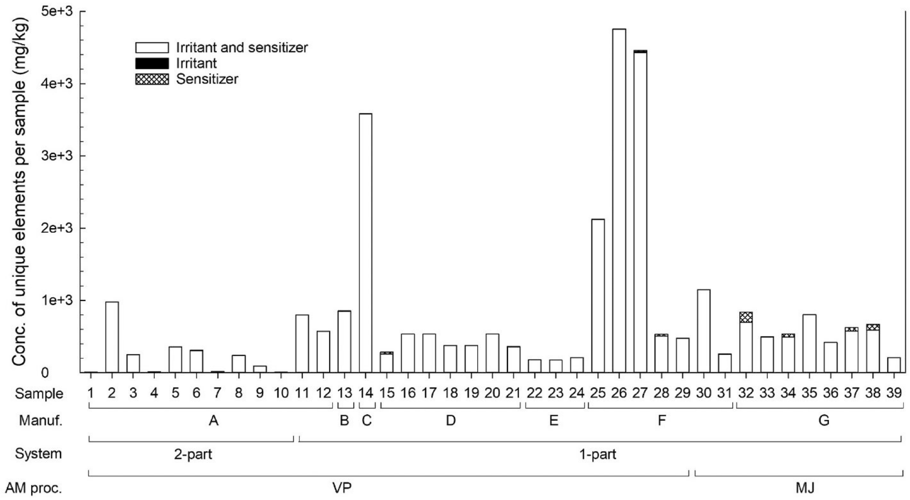

Fig. 2.
Sum of the mass concentration of elements that were categorized as skin irritants and/or sensitizers per resin product (see Table S7 for data). White infill = element is both irritant and sensitizer, black infill = element is irritant only, patterned infill = element is sensitizer only.

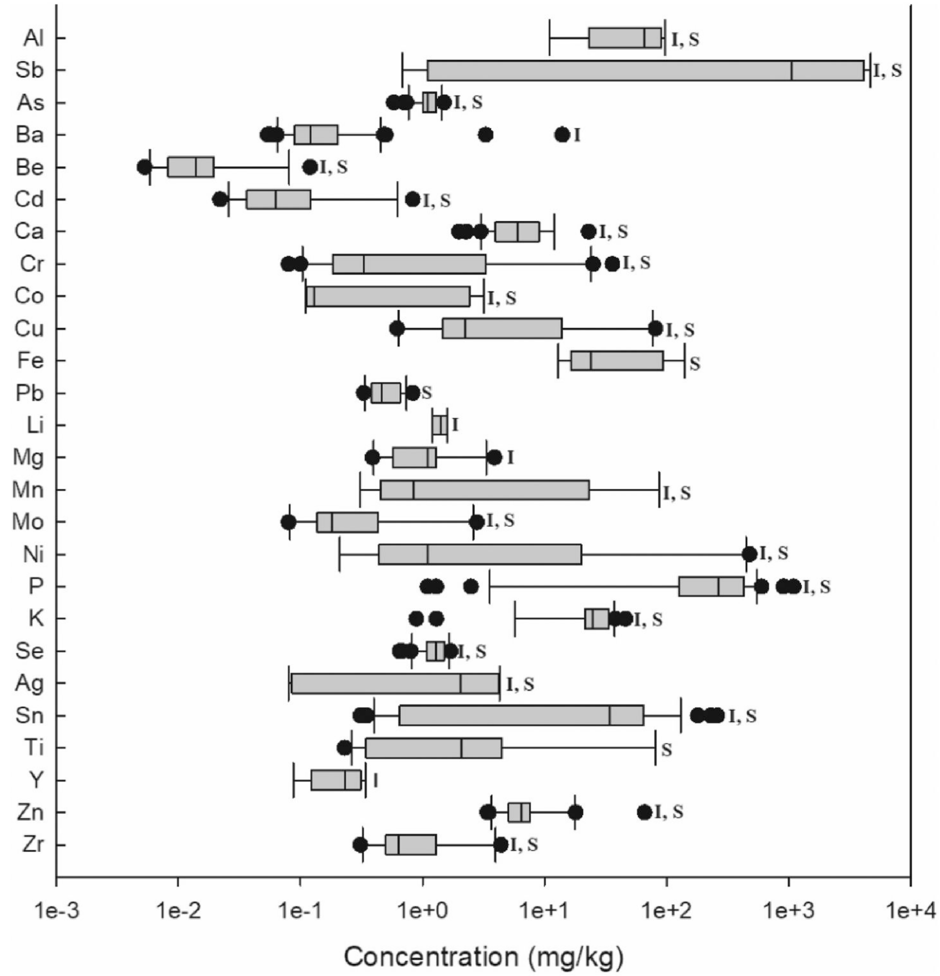

Fig. 3.

Range of mass concentrations of elements categorized as skin irritants (I) and/or sensitizers (S). The lower boundary of a box is the 25th percentile, the line within a box is the median, and the upper boundary of a box is the 75th percentile. Whiskers (error bars) below and above a box indicate the 10th and 90th percentiles.

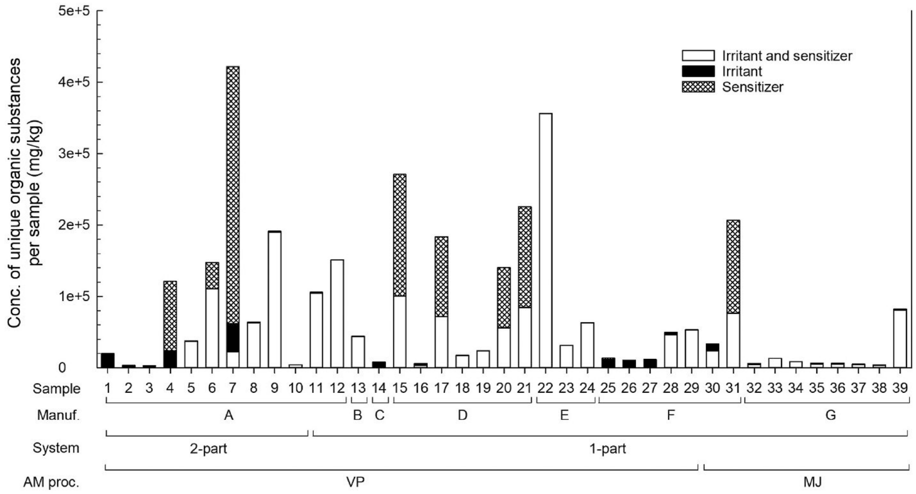

Fig. 4.

Sum of the mass concentration of organic substances that were categorized as skin irritants and/or sensitizers per resin product (see Table S8 for data). White infill = element is both irritant and sensitizer, black infill = element is irritant only, patterned infill = element is sensitizer only.

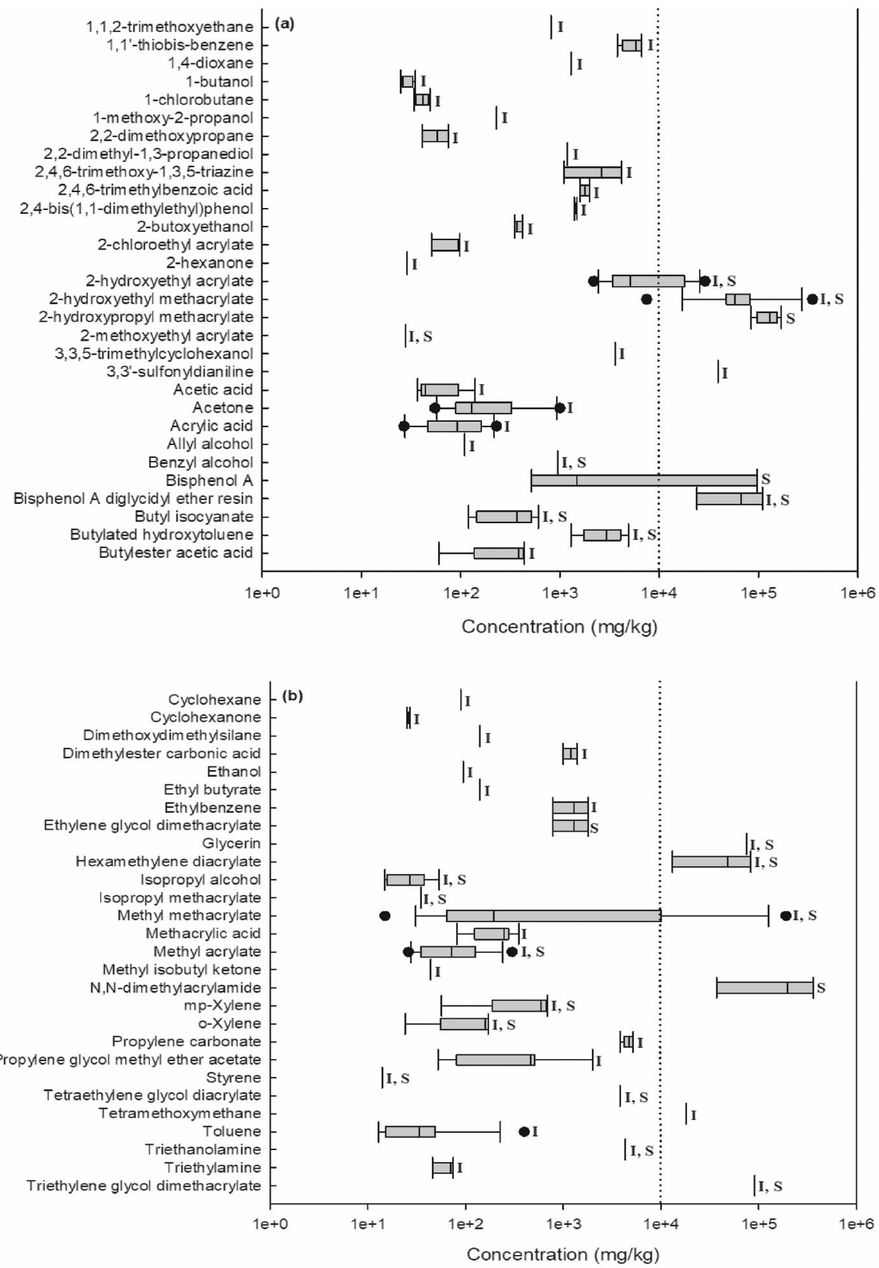

Fig. 5.

Range of mass concentrations of organic substances that were categorized as skin irritants (I) or sensitizers (S). Substances were arbitrarily divided between two panels, (a) and (b), for clarity. Vertical dotted line at 10,000 mg/kg denotes 1% w/w. The lower boundary of a box is the 25th percentile, the line within a box is the median, and the upper boundary of a box is the 75th percentile. Whiskers (error bars) below and above a box indicate the 10th and 90th percentiles.

Table 1

Summary of non-parametric comparisons of the influence of four factors on the median number and median concentration of irritants and sensitizers per product (">" indicates directionality of difference at a significance level of $\alpha = 0.05$).

	Elements[a]		Organic substances[b]	
Factor	**Irritants**	**Sensitizers**	**Irritants**	**Sensitizers**
Manufacturer				
Number	n.s.	n.s.	D > F	n.s.
Concentration (mg/kg)	n.s.	n.s.	n.s.	n.s.
Parts[c]				
Number	n.s.	1-part > 2-part	1-part > 2-part	1-part > 2-part
Concentration (mg/kg)	1-part > 2-part	1-part > 2-part	n.s.	n.s.
AM process category				
Number	n.s.	MJ > VP	MJ > VP	n.s.
Concentration (mg/kg)	n.s.	n.s.	n.s.	VP > MJ
Color				
Number	n.s.	n.s.	n.s.	n.s.
Concentration (mg/kg)	n.s.	n.s.	n.s.	n.s.

n.s. = not significant at $p < 0.05$.

[a] Manufacturer: A (n = 12), B (n = 1), C (n = 1), D (n = 7), E (n = 3), F (n = 7), and G (n = 8); Parts: 1-part (n = 29), 2-part (n = 10); AM process category: MJ = material jetting (n = 10), VP = vat photopolymerization (n = 29); Color: black (n = 8), clear (n = 12), green (n = 3), grey (n = 4), purple (n = 1), white (n = 6), and yellow (n = 5).

[b] Sensitizing organic substances were not identified by gas chromatography analysis in five products. Therefore, Manufacturer: A (n = 10), B (n = 1), C (n = 0), D (n = 7), E (n = 3), F (n = 5), and G (n = 8); Parts: 1-part (n = 26), 2-part (n = 8); AM process category: MJ = material jetting (n = 10), VP = vat photopolymerization (n = 24); Color: black (n = 8), clear (n = 10), green (n = 3), grey (n = 3), purple (n = 1), white (n = 6), and yellow (n = 3).

[c] VP resins only (all MJ resins are one-part system).