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Electronic cigarettes and toxic substances, including arsenic species

Electronic cigarettes, or e-cigarettes, are battery-powered devices that heat a liquid and deliver an aerosolized product to the user via inhalation. Electronic cigarettes are also popularly called “e-cigs”, “vapes”, “e-hookahs”, “mods”, and “tank systems”. A large variety of e-cigarettes are commercially available. Some e-cigarettes look like regular cigarettes, cigars, or pipes while others look like USB drives, pens, and popular everyday items. The United States National Academies of Sciences, Engineering, and Medicine refer to e-cigarettes generally as “electronic nicotine delivery systems” (ENDS) (NAS, 2018).

Although “e-cigarettes may have the potential to benefit adult smokers if used as a complete substitute for regular cigarettes and other smoked tobacco products”, the available science is inconclusive on “whether e-cigarettes are effective for quitting smoking”. However, it is clear that “e-cigarettes are not safe for youth, young adults, and pregnant women, as well as adults who do not currently use tobacco products” (CDC, 2020a).

Extensive advertisements suggesting e-cigarettes as a “safer” alternative to the traditional tobacco cigarettes have been misleading for the general public, especially young adults. E-cigarettes were first introduced in the United States about fifteen years ago. Results from the National Youth Tobacco Survey showed that among high school students in the United States, the prevalence of current use of e-cigarettes increased from 1.5% in 2011 to more than 20% in 2018, and the growing trend continues (CDC, 2017; NAS, 2018; Gentzke et al., 2019).

More than 6400 publications on e-cigarettes are available (Fig. 1). These publications deal with diverse topics, such as environmental and occupational health, substance abuse and mental health, clinical medicine, toxicology and pharmacology, environmental sciences, and chemistry. Despite the large number of publications, there is an incomplete understanding of the chemical constituents of the inhaled aerosol, the health risk from “vaping” various aerosolized products, and even the effectiveness of smoking cessation using e-cigarettes as substitutes for conventional tobacco smoking (NAS, 2018).

1. Chemical constituents in e-liquids

E-cigarettes are commonly used to deliver nicotine. However, a variety of substances, ranging from flavors and additives to illicit drugs, have also been introduced. Typically, a solution known as e-liquid is aerosolized by a battery-operated heating device, and the aerosols are inhaled through a mouthpiece whereby the users puff. E-liquids in cartridges and refills contain a huge number of chemical compounds, e.g., more than 7000 unique e-liquid flavors are available to e-cigarette users (Zhu et al., 2014), and this list continues to grow. Most e-cigarette products do not list ingredients of flavoring components but use “natural or artificial flavors” as labeling.

While the most common vaporizing solvent carriers used in e-cigarettes are propylene glycol (PG) and glycerol (also called vegetable glycerin), e-liquids also contain a variety of flavors and additives, along with a variable percentage of nicotine. Many studies have identified diverse groups of chemicals in e-cigarettes (Table 1). More compounds are present in the aerosols than in their respective e-liquids because additional compounds are generated during the heating and vaporization processes. Many of these compounds are toxic and/or carcinogenic, and are known to cause respiratory and cardiovascular diseases. Compounds of particular health concerns include aldehydes, carbonyl compounds, endotoxins, heterocyclic compounds, metals, phenolic compounds, polycyclic aromatic hydrocarbons (PAHs), tobacco alkaloids, tobacco specific nitrosamines (TSNAs), ultrafine particles, and volatile organic compounds (VOCs).

2. Arsenic species

A number of studies have reported the presence of arsenic in e-cigarettes (Beauval et al., 2016; Mikheev et al., 2016; Olmedo et al., 2018; Palazzolo et al., 2017; Song et al., 2018; Williams et al., 2017; Zhao et al., 2019). Arsenic has been detected in e-liquids (˜1.5 μg/L) (Beauval et al., 2016), found captured on filters of e-cigarettes (0.01–1 ng arsenic per mg of particulate matter) (Mikheev et al., al.,2016), and in aerosols (Williams et al., 2017 and 2019; Palazzolo et al., 2017). For every 10 puffs of disposable e-cigarettes and e-hookahs, arsenic in the aerosols was in a range of 0.001 to 0.01 μg (Williams et al., 2017). Although the source of arsenic is not known, concentrations of arsenic in e-liquids ranged from 0.83 to 3.04 μg/kg from one study (Song et al., 2018), and the median concentration of arsenic in e-liquids was 26.7 μg/kg from another study (Olmedo et al., 2018).

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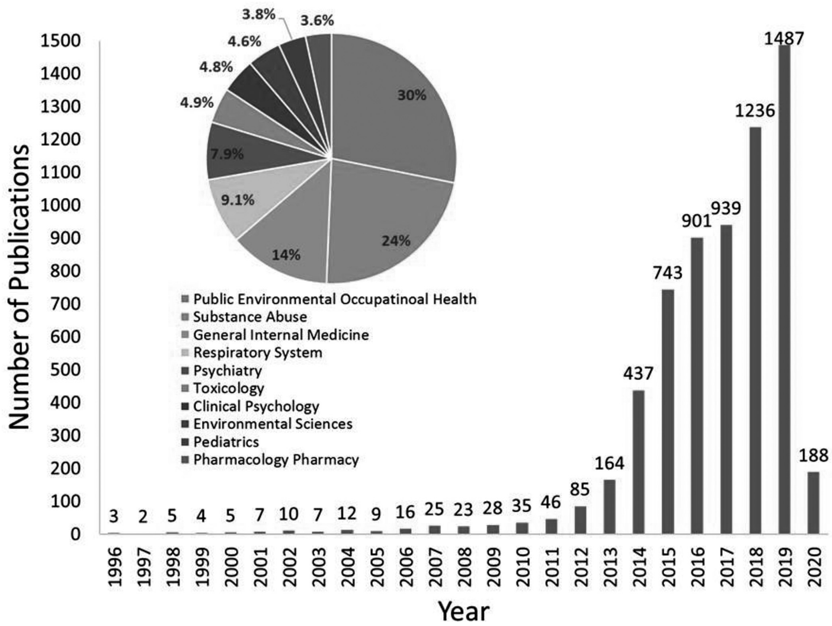

Fig. 1 – Publications by year on the topic of electronic cigarettes from 1996 to February 29, 2020. A basic search from Web of Science Core Collection, using Topic words "electronic cigarette" OR "e-cigarette", shows a total of 6430 publications as of February 29, 2020. The number on top of each bar indicates the number of publications in the respective year. The inset shows relative percentages of publications by science category. Top ten categories are summarized, with 30% publications in the area of Public Health, including Environmental and Occupational Health.

The assessment of arsenic in e-cigarettes to date has mainly focused on total arsenic concentration. None of the previous studies have investigated arsenic species in e-cigarettes. The toxicity of arsenic is highly dependent on its chemical species, varying by several orders of magnitude, e.g., in medium lethal concentration (LC_{50}) values (Cohen et al., 2016; Moe et al., 2016; Naranmandura et al., 2011; Shen et al., 2013; Styblo et al., 2000; Thomas and Bradham, 2016). Therefore, an appropriate assessment of potential health risks of arsenic exposure depends on the knowledge of the exact arsenic species, and the concentrations of each arsenic species present in the e-liquid and its corresponding aerosol samples.

Liu et al. (2020) recently reported the determination of arsenic species in e-liquids and discussed potential health risk from e-cigarette vaping. The authors purchased seventeen e-liquid samples of major brands, from local and online stores in Canada and China. They determined arsenic species in e-liquids using high-performance liquid chromatography (HPLC) and inductively coupled plasma mass spectrometry (ICPMS). They revealed the presence of seven arsenic species, including inorganic arsenate (iAs^{V}), arsenite (iAs^{III}), monomethylarsonic acid (MMA), and three new arsenic species not previously known. They found iAs^{III} in 59% of the e-liquid samples, iAs^{V} in 94% of the samples, and MMA in 47% of the samples. They also generated aerosols from the e-liquids, condensed the aerosols, collected the condensates, and carried out arsenic speciation analyses. They detected iAs^{III} in 100% of the aerosol condensate samples, iAs^{V} in 88% of the samples, and MMA in 13% of the aerosol condensate samples.

Liu et al. (2020) found that inorganic arsenic species were predominant in e-liquids and condensates of aerosols. The median concentration of iAs^{III} in the condensate of aerosols was 3.27 μg/kg, which was significantly higher than the median concentration of iAs^{III} in the e-liquid samples (1.08 μg/kg). These results suggest conversion of some arsenic species to iAs^{III} during the process of vaporization of the e-liquid and condensation of the aerosol.

On the basis of arsenic concentrations and the total volume of the puffed air from vaping the e-liquid, Liu et al. (2020) estimated that the concentration of inorganic arsenic in the vaping air was approximately 3.4 μg/m^3. This concentration is not far from the permissible exposure limit (10 μg/m^3) set by the United States Occupational Safety and Health Administration (OSHA). Using the Environmental Protection Agency's (EPA) unit risk factor (4.3×10^{-3} per μg/m^3) for inhalation exposure to inorganic arsenic and assuming e-cigarettes users inhale vaping air containing 3.4 μg/m^3 of inorganic arsenic at 1% of the time, the authors estimated that the excess lung cancer risk from lifetime exposure to inorganic arsenic in the e-cigarette vaping air (3.4 μg/m^3) is as high as 1.5×10^{-4}. This excess lung cancer risk is more than 150 times higher than the EPA's goal of one in a million. These results raise serious health concerns over the exposure to arsenic from electronic cigarettes.

Although the total number of e-liquid samples were small comparing to the vast varieties available, the seventeen samples were selected on the basis of monthly sales and market share information. They represent e-liquids matched with rechargeable USB-like and tank-type e-cigarette devices. Quantitative results of individual arsenic species in these

Table 1 – Known chemical components present in e-cigarette (vaping) products. From National Academies of Sciences, Engineering, and Medicine. Public Health Consequences of E-cigarettes. National Academies Press, Washington, DC. 2018.

Group	Compound examples	Comments
Delivery solvents	Propylene glycol (PG) Glycerol (Vegetable glycerin, VG) Ethylene Glycol (not always present and often not listed on labels)	E-cigarette users commonly experience dry mouth and throat, which may be due to the water-absorbing property of PG and glycerol. Chronic effects from e-cigarette exposure to PG and glycerol have not been investigated.
Alcohols (Flavoring)	Geraniol Menthol Thymol Eugenol	Floral flavor (sweet, fruity, etc.) Mentholic flavor (minty, cooling, etc.) Respiratory irritant. Respiratory irritant.
Acids (Flavoring)	Butyric acid Valeric acid 2-Methylbutyric acid	Cheesy flavor Cheesy Acidic
Esters (Flavoring)	Ethyl butyrate 2-Methylbutyrate Methyl cinnamate Methyl salicylate	Fruity flavor Fruity Balsamic Minty
Lactones (Flavoring)	g-nonalactone d-decalactone	Coconut flavor
Carbonyl compounds	Formaldehyde Acetaldehyde Acrolein Glyoxal Methylglyoxal Acrylamide Benzaldehyde Cinnamaldehyde Crotonaldehyde o-methylbenzaldehyde Propionaldehyde Butanal Geranial Propanal Vanilin	Formaldehyde is classified as a human carcinogen by the International Agency for Research on Cancer (IARC). Acetaldehyde is classified as possibly carcinogenic to humans, and glycidol is a probable carcinogen. Acrolein causes irritation of the nasal cavity and damages the lining of the lungs.
Ketones	Diacetyl, Acetyl propionyl (also known as 2,3—pentanedione), Acetoin	Diacetyl, acetyl propionyl, and acetoin are associated with adverse respiratory health outcomes, e.g., asthma.
Heterocycles	2-Acetylpyrazine 2,3,5-Trimethylpyrazine 2-Acetylpyrrole 2-Isopropyl-4-methylthiazole 2-Isobuthylthiazole	These nitrogen-containing and sulfur-containing heterocyclic compounds cause irritation to the respiratory system.
Sulfur compounds	Furfuryl mercaptan Thiomenthone p-Menthene-8-thiol Dimethyl sulfide (DMS) Tropathiane	Furfuryl mercaptan, DMS, and tropathiane cause irritation to the respiratory tract.
Minor tobacco alkaloids	Nornicotine Anatabine Anabasine Cotinine Nicotine N-oxides (*cis*- and *trans*-) Myosmine β-nicotyrine β-nornicotyrine Isonicoteine Nicotyrine	The main alkaloid in tobacco-derived products, including e-liquids, is nicotine. The minor tobacco alkaloids are nicotine-related impurities. These alkaloids are less toxic than nicotine, but their health effects to e-cigarette users are unknown.

(*continued on next page*)

Table 1 (*continued*)

Group	Compound examples	Comments
Tobacco-Specific Nitrosamines	*N*'-nitrosonornicotine (NNN) 4-(methylnitrosamino)−1-(3-pyridyl)-1-butanone (NNK) *N*'-nitrosoanabasine (NAB) *N*'-nitrosoanatabine	Tobacco-specific nitrosamines are potent carcinogens. They are derived from tobacco leaves and formed during the curing process. E-liquids typically contain μg/L levels of tobacco-specific nitrosamines.
Reactive Oxygen Species	Free radicals	Detected 10^{11}–10^{14} radicals per puff (Goel et al., 2015). ROS causes oxidative stress and affect a variety of biological processes.
Volatile organic compounds (VOCs)	Benzene Toluene Ethylbenzene *m*-xylene *p*-xylene *o*-xylene Styrene Ethyl acetate Ethanol Methanol Pyridine Acetylpyrazine 2,3,5-trimethylpyrazine Octamethylcyclotetrasiloxane	VOCs have been detected in flavored e-liquids, nicotine liquids, disposable cartridges, and e-cigarette aerosols. Benzene is classified as a human carcinogen (Group 1) by the International Agency for Research on Cancer (IRAC).
Furans	5-hydroxymethylfurfural Furfural	Both 5-hydroxymethylfurfural and furfural are mutagenic. Furfural causes irritation to the upper respiratory tract.
Phthalates	Diethyl phthalate (DEP) Diethylhexyl phthalate (DEHP)	DEP and DEHP are plasticizers. DEHP is classified by IARC as possibly carcinogenic to humans. Both estrogen-like compounds are antiandrogenic.
Other substances	Vitamin E acetate Caffeine Nitrate Catechol *m*-cresol *o*-cresol Phenol Residue solvents Endotoxins Microorganisms	Vitamin E acetate is linked to the 2800 hospitalized severe lung injury cases reported in the United States in summer 2019 (Blount et al., 2020; CDC, 2020). Very little is known about the effects of caffeine inhalation.
Illicit drugs and Pharmaceuticals	Tetrahydrocannabinol (THC) Cannabinoid (CBD) Rimonabant Amino tadalafil (analogue of Cialis)	THC is the psychoactive compound of marijuana. The use of THC and CBD has been associated with a wide range of health effects.
Metals and metalloids	Cadmium Chromium Copper Lead Nickel Arsenic Antimony Aluminum Boron Calcium Iron Manganese Potassium Silver Tin Titanium Zinc	Some of the metals and metalloids come from e-liquids. The coil and other parts of the e-cigarette device could be a source of metals, such as chromium, nickel, lead, manganese, aluminum, tin, and iron. Lead is associated with neurotoxicity and cardiovascular disease. Chromium(VI) and nickel are associated with respiratory diseases and lung cancer. Copper nanoparticles in e-cigarette aerosols increase mitochondrial oxidative stress and DNA fragmentation (Lerner et al., 2016)

representative e-cigarette samples provide important information and enable assessment of potential risks from e-cigarettes.

3. Future research needs and perspectives

Liu et al. (2020) detected inorganic arsenate (iAs^{V}), arsenite (iAs^{III}), monomethylarsonic acid (MMA), as well as three new arsenic species not previously reported. Toxicity of arsenic species varies greatly depending on the individual arsenic species (Moe et al., 2016; Styblo et al., 2000; Uppal et al., 2019). Future research should identify these new arsenic species and study their health effects (Cullen et al., 2016). Efficient chromatographic separation in combination with multiple types of mass spectrometric detection will be useful for the characterization and identification of new arsenic species (Liu et al., 2018; Peng et al., 2017; Reid et al., 2020).

E-cigarette vaping is not limited to the delivery of nicotine, but also includes flavoring, additives, and drugs, such as tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is the psychoactive, mind-altering component of marijuana. The use of THC has been associated with a wide range of health effects. In addition, cannabis products also contain pesticide residues and metals (Craven et al., 2019).

Some e-cigarette pods or cartridges marketed for single use can be refilled with illicit drugs or unknown substances. Some e-cigarette products are used for "dripping" (Talih et al., 2016), which involves dropping e-cigarette liquid directly onto the hot coils of an e-cigarette device which can result in high concentrations of these compounds (e.g., THC and CBD) in the aerosol.

Vaping is known to cause adverse respiratory effects, but the exact compounds responsible are not fully understood. For example, in response to a mysterious outbreak of severe lung injury that started in July 2019, the United States Center for Disease Control and Prevention (CDC) conduced a nationwide public health investigation into the "outbreak of lung injury associated with electronic cigarette, or vaping, products" (CDC, 2020b). In July 2019, the Wisconsin and Illinois state health authorities received unusually high number of reports of severe lung disease of unclear cause (Layden et al., 2020). The patients were users of e-cigarettes and related products. The number of cases continued to increase until late September 2019. As of February 18, 2020, a total of 2807 hospitalized cases of lung injury were reported, including 68 deaths. The deceased patients were 15–75 years old (median age 49.5 years). Although the CDC suggests that vitamin E acetate is linked to the e-cigarette vaping associated lung injury (Blount et al., 2020), evidence is not sufficient to rule out the contribution of other substances of concern. Among 2022 hospitalized patients who had data on substance use, 82% reported using THC-containing products. There may be more than one cause of the disease.

Many flavoring compounds and additives are intended for use in food products, and their toxicities may be lower when ingested. However, the toxicities of these compounds could be higher when they are heated, aerosolized, and inhaled. For example, saccharides used to make sweet e-liquid flavors can degrade and produce furans and aldehydes when heated. Aldehydes have been shown to cause irritation to the respiratory tract (Tierney et al., 2016). The safety of inhalation exposure to many other food flavors has not been tested and remains poorly understood. There is little information on how flavoring chemicals in e-cigarette products affect health during long-term exposure by inhalation.

The available science is inconclusive on whether e-cigarettes are an effective way to quit smoking. E-cigarettes are not currently approved by the Food and Drug Administration (FDA) as a smoke cessation aid. In addition to nicotine, most e-cigarette products contain many potentially toxic substances. The number, concentration, and characteristics of toxic substances emitted from e-cigarettes are highly variable and depend on the characteristics of e-liquids and the operation of the e-cigarette device. Although e-cigarettes may contain a smaller number of substances than tobacco smoke, e-cigarette vaping is also harmful. People who do not currently use tobacco products should not use e-cigarettes. A message to youth and young adults should be loud and clear: Do not smoke tobacco or vape e-cigarettes.

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REFERENCES

Beauval, N., Howsam, M., Antherieu, S., Allorge, D., Soyez, M., Garcon, G., et al., 2016. Trace elements in e-liquids - Development and validation of an ICP-MS method for the analysis of electronic cigarette refills. Regul. Toxicol. Pharmacol. 79, 144–148. doi:10.1016/j.yrtph.2016.03.024.

Blount, B.C., Karwowski, M.P., Shields, P.G., Morel-Espinosa, M., Valentin-Blasini, L., Gardner, M., et al., 2020. Vitamin E acetate in bronchoalveolar- lavage fluid associated with Evali. New Engl. J. Med. 382, 697–705.

Centers for Disease Control and Prevention (CDC), 2017. Tobacco use among middle and high school students—United States, 2011–2016. MMWR Morb. Mortal Wkly. Rep. 66 (23), 597–603. doi:10.15585/mmwr.mm6623a1.

Centers for Disease Control and Prevention (CDC). 2020a. Electronic cigarettes. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/index.htm (Accessed 12 March 2020).

Centers for Disease Control and Prevention (CDC). 2020b. Electronic cigarettes. outbreak of lung injury associated with the use of E-Cigarette, or vaping, products. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html (Accessed 12 March 2020).

Cohen, S.M., Chowdhury, A., Arnold, L.L., 2016. Inorganic arsenic: a non-genotoxic carcinogen. J. Environ. Sci. 49. doi:10.1016/j.jes.2016.04.015.

Craven, C.B., Wawryk, N., Jiang, P., Liu, Z.S., Li, X.-.F., 2019. Pesticides and trace elements in cannabis: analytical and environmental challenges and opportunities. J. Environ. Sci. 85, 82–93. doi:10.1016/j.jes.2019.04.028.

Cullen, W.R., Liu, Q.Q., Lu, X.F., McKnight-Whitford, A., Peng, H.Y., Popowich, A., et al., 2016. Methylated and thiolated arsenic species for environmental and health research—A review on synthesis and characterization. J. Environ. Sci. 49, 7–27. doi:10.1016/j.jes.2016.11.004.

Gentzke, A.S., Creamer, M., Cullen, K.A., Ambrose, B.K., Willis, G., Jamal, A., et al., 2019. Vital signs: tobacco product use among middle and high school students—United states, 2011–2018. MMWR Morb. Mortal. Wkly. Rep. 68 (6), 157–164. doi:10.15585/mmwr.mm6806e1.

Goel, R., Durand, E., Trushin, N., Prokopczyk, B., Foulds, J., Elias, R.J., et al., 2015. Highly reactive free radicals in electronic cigarette aerosols. Chem. Res. Toxicol. 28 (9), 1675–1677.

Layden, J.E., Ghinai, I., Pray, I., Kimball, A., Layer, M., Tenforde, M.W., et al., 2020. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin – Final report. N. Engl. J. Med. 382 (10), 903–916.

Lerner, C.A., Rutagarama, P., Ahmad, T., Sundar, I.K., Elder, A., Rahman, I., 2016. Electronic cigarette aerosols and copper nanoparticles induce mitochondrial stress and promote DNA fragmentation in lung fibroblasts. Biochem. Biophys. Res. Commun. 477 (4), 620–625.

Liu, Q., Lu, X., Peng, H., Popowich, A., Tao, J., Uppal, J.S., et al., 2018. Speciation of arsenic – a review of phenylarsenicals and related arsenic metabolites. TrAC - Trends Anal. Chem. 104, 171–182. doi:10.1016/j.trac.2017.10.006.

Liu, Q., Huang, C.Z., Le, X.C., 2020. Arsenic species in electronic cigarettes: determination and potential health risk. J. Environ. Sci. 91, 168–176. doi:10.1016/j.jes.2020.01.023.

Mikheev, V.B., Brinkman, M.C., Granville, C.A., Gordon, S.M., Clark, P.I., 2016. Real-time measurement of electronic cigarette aerosol size distribution and metals content analysis. Nicotine Tob. Res. 18 (9), 1895–1902. doi:10.1093/ntr/ntw128.

Moe, B., Peng, H., Lu, X., Chen, B., Chen, L.W.L., Gabos, S., et al., 2016. Comparative cytotoxicity of fourteen trivalent and pentavalent arsenic species determined using real-time cell sensing. J. Environ. Sci. 49, 113–124. doi:10.1016/j.jes.2016.10.004.

NAS. National Academies of Sciences, Engineering and Medicine, 2018. Public Health Consequences of E-cigarettes. National Academies Press, Washington, D.C http://nap.edu/24952.

Naranmandura, H., Carew, M., Xu, S., Leslie, E., Lee, J., Weinfeld, M., et al., 2011. Comparative toxicity of arsenic metabolites in human bladder cancer EJ-1 cells. Chem. Res. Toxicol. 24, 1586–1596. doi:10.1021/tx200291p.

Olmedo, P., Goessler, W., Tanda, S., Grau-Perez, M., Jarmul, S., Aherrera, A., et al., 2018. Metal concentrations in e-cigarette liquid and aerosol samples: the contribution of metallic coils. Environ. Health Perspect. 126 (2), 027010. doi:10.1289/EHP2175.

Palazzolo, D.L., Crow, A.P., Nelson, J.M., Johnson, R.A., 2017. Trace metals derived from electronic cigarette (ECIG) generated aerosol: potential problem of ecig devices that contain nickel. Front Physiol 7 (JAN), 663. doi:10.3389/fphys.2016.00663.

Peng, H., Hu, B., Liu, Q., Li, J., Li, X.-.F., Zhang, H.Q., et al., 2017. New methylated phenylarsenical metabolites discovered in chicken liver. Angew. Chem. Int. Ed. 56 (24), 6773–6777. doi:10.1002/anie.201700736.

Reid, M.S., Hoy, K.S., Uppal, J.S., Schofield, J.R.M., Lin, Y., Lu, X., et al., 2020. Arsenic speciation analysis: a review with an emphasis on chromatographic separations. TrAC - Trends Anal. Chem. 123, 115770. doi:10.1016/j.trac.2019.115770.

Shen, S., Li, X.-.F., Cullen, W.R., Weinfeld, M., Le, X.C., 2013. Arsenic binding to proteins. Chem. Rev. 113 (10), 7769–7792.

Styblo, M., Del Razo, L.M., Vega, L., Germolec, D.R., LeCluyse, E.L., Hamilton, G.A., et al., 2000. Comparative toxicity of trivalent and pentavalent inorganic and methylated arsenicals in rat and human cells. Arch. Toxicol. 74 (6), 289–299. doi:10.1007/s002040000134.

Talih, S., Balhas, Z., Salman, R., Karaoghlanian, N., Shihadeh, A., 2016. “Direct dripping”: a high-temperature, high-formaldehyde emission electronic cigarette use method. Nicotine Tob. Res. 18 (4), 453–459. doi:10.1093/ntr/ntv080.

Thomas, D.J., Bradham, K., 2016. Role of complex organic arsenicals in food in aggregate exposure to arsenic. J. Environ. Sci. 49, 86–96. doi:10.1016/j.jes.2016.06.005.

Tierney, P.A., Karpinski, C.D., Brown, J.E., Luo, W., Pankow, J.F., 2016. Flavour chemicals in electronic cigarette fluids. Tob. Control 25 (e1), e10–e15. doi:10.1136/tobaccocontrol-2014-052175.

Uppal, J.S., Zheng, Q., Le, X.C., 2019. An improved and simple method for removal of arsenic from drinking water. J. Environ. Sci. 76, 415–417. doi:10.1016/j.jes.2018.11.017.

Williams, M., Bozhilov, K., Ghai, S., Talbot, P., 2017. Elements including metals in the atomizer and aerosol of disposable electronic cigarettes and electronic hookahs. PLoS ONE 12 (4), e0175430. doi:10.1371/journal.pone.0175430.

Williams, M., Bozhilov, K.N., Talbot, P., 2019. Analysis of the elements and metals in multiple generations of electronic cigarette atomizers. Environ. Res. 175, 156–166. doi:10.1016/j.envres.2019.05.014.

Zhao, D., Navas-Acien, A., Iljevski, V., Slavkovich, V., Olmedo, P., Adria-Mora, B., et al., 2019. Metal concentrations in electronic cigarette aerosol: effect of open-system and closed-system devices and power settings. Environ. Res. 174, 125–134. doi:10.1016/j.envres.2019.04.003.

Zhu, S.H., Sun, J.Y., Bonnevie, E., Cummins, S.E., Gamst, A., Yin, L., et al., 2014. Four hundred and sixty brands of e-cigarettes and counting: implications for product regulation. Tob. Control 23 (Suppl 3), iii3–iii9. doi:10.1136/tobaccocontrol-2014-051670.