A State-of-the-Science Review of Alcoholic Beverages and Polycyclic Aromatic Hydrocarbons

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BACKGROUND: The association between alcohol and certain cancers is well established, yet beyond ethanol and its metabolite acetaldehyde, little is known about the presence of other carcinogenic compounds in alcoholic beverages, including polycyclic aromatic hydrocarbons (PAHs), such as benzo[a]pyrene (a Group I carcinogen).

OBJECTIVES: We summarized the published literature on PAH levels in alcoholic beverages to identify potential gaps in knowledge to inform future research.

METHODS: Medline and Scopus were searched for primary research published from January 1966 to November 2023 that quantified PAH levels among various types of alcoholic beverages, including whisky, rum, brandy, gin, vodka, wine, and beer. Studies that were not primary literature were excluded; only studies that quantified PAH content in the specified alcoholic beverages were included.

RESULTS: Ten studies published from 1966 to 2019 met the criteria for review. Other than beverage type, no publication reported selection criteria for their samples of tested alcohol products. Studies used a variety of analytical methods to detect PAHs. Of the 10 studies, 7 were published after 2000, and 6 assessed <20 products. Of the studies, 7 examined spirits; 3, beer; and 4, wines. Benzo[a]pyrene was most prevalent among spirit products, particularly whisky, with values generally exceeding acceptable levels for drinking water. Some beer and wine products also contained PAHs, albeit at lower levels and less frequently than spirit products.

Discussion: PAHs are found in some alcohol products and appear to vary by beverage type. However, there is an incomplete understanding of their presence and levels among large, representative samples from the range of currently available alcohol products. Addressing this gap could improve understanding of alcohol–cancer relationships and may have important implications for public health and the regulation of alcohol products. In addition, novel methods, such as direct mass spectroscopy, may facilitate more thorough testing of samples to further investigate this relationship. https://doi.org/10.1289/EHP13506

Introduction

Alcohol consumption in much of the world is widely seen as a social norm, but it has serious health, social, and economic impacts. An area of great interest in the field of alcohol and substance use policy is the relationship between alcohol and certain cancers. There is an established, dose-response relationship between alcohol consumption and cancers of the oral cavity, pharynx, larynx, colon, rectum, liver, and breast.^{2,3} Carcinogenic effects of alcohol are largely related to the effects of ethanol and its primary metabolite, acetaldehyde, both of which have been classified by the International Agency for Research on Cancer (IARC) as Group I carcinogens (i.e., cause cancer in humans).^{5,6} Mechanisms of alcohol-induced carcinogenesis include genotoxic effects of acetaldehyde, generation of reactive oxidative species, cytochrome P450 induction, changes to retinoic acid and folate metabolism, DNA methylation, and increased estrogen levels.^{4,5}

Awareness of ethanol-cancer relationships is limited among the general population owing in part to a relative lack of knowledge translation in developed countries, such as the UK and Canada. The awareness of formal studies of other carcinogens

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No conflicts of interest to disclose.

Received 18 June 2023; Revised 8 December 2023; Accepted 19 December 2023; Published 19 January 2024.

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that may be present in alcohol products is unknown to the authors at this time, including aflatoxins, ethyl carbamate, and polycyclic aromatic hydrocarbons (PAHs).⁴ PAHs are a family of related compounds, many of which have been classified as Group IIA carcinogens (i.e., probably cause cancer in humans), with benzo [a]pyrene (BaP) being classified as Group I by the IARC, and which have been found to be present in a variety of alcoholic beverages.^{6,9,10}

PAH Structure, Function, and Carcinogenicity

PAHs are organic compounds produced during incomplete combustion of carbon products. 11 They are composed of fused aromatic rings that contain hydrogen and carbon, making them highly hydrophobic and lipophilic.¹¹ There are three main routes of PAH absorption in humans: a) inhalation through the respiratory tract, b) absorption through the dermal layer, and c) ingestion via the gastrointestinal tract (the route of absorption for ethanol).¹¹ Because of this lipophilicity, PAHs are sparingly soluble in aqueous solutions.¹¹ However, PAHs are far more soluble in ethanolbased solutions.¹² Although PAHs are a class comprised of hundreds of related compounds, there is substantial variation in their size and structure. ^{13,14} In addition, there is variability in their biological function and toxicity, with 16 being designated as highpriority pollutants by the US Environmental Protection Agency (EPA).^{6,15} These include naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, benzo[a]anthracene, chrysene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[a]pyrene, benzo[g,h,i]perylene, indeno[1,2,3-c, d]pyrene, and dibenz[a,h]anthracene. The IARC has further classified PAHs based on their carcinogenicity in humans, with most of the 16 US EPA high-priority PAHs classified as Group IIA and III carcinogens.⁶ BaP, however, is classified as a Group I carcinogen.6

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Formation of PAHs in Alcoholic Beverages

Spirits are produced through distillation to concentrate the beverage and increase its alcohol by volume (ABV); typically, spirits are in the range of $\sim 40\%$ ABV. To achieve this ABV, the raw ingredients of the spirits are first fermented, followed by alcohol concentration by fractional distillation and often maturation in charred barrels. All of these steps may introduce PAHs into the beverages. 16 Most studies in this review assessed different types of spirits.

Whisky is made from cereal grains, such as barley, malt, rye, wheat, and corn. Although whisky is often thought of as a single type of alcoholic beverage, it describes a class of alcoholic beverages that are differentiated based on the main grain used to produce them: scotch (malted barley), bourbon (corn), and rye (rye).¹⁷ Nonetheless, the general production process remains similar for all styles of whisky and consists of many steps, including malting, mashing, fermentation, distillation, maturation, and bottling.¹⁷ The introduction of PAHs into whiskies is primarily attributed to malting and maturation. During malting, the grain is heated or smoked, which introduces PAHs via the incomplete combustion to which the grain is exposed. 18 Maturation is considered to be the main driver of PAH exposure in whisky owing to the process of storage in wooden barrels that are smoked or charred before the aging process, resulting in PAH transfer from the barrel to the whisky. 10,19

Rum is a spirit that is produced from fermented sugar cane juice or molasses. Prior to harvesting of the sugar cane, the cane fields are burned to remove excess foliar material, as well as to concentrate the sugar weight and evaporate excess water. This process has been shown to introduce PAHs in the sugar cane, thereby contaminating the final rum product.²⁰ In addition, as with whisky products, some rum products are aged in charred wooden barrels, which can also cause PAHs to leech from the wood into the final product. However, rum is often aged for shorter periods compared with whisky, leading to lower PAH concentrations in the final products.⁹

Gin and vodka have been less extensively studied, possibly because maturation in barrels is not an essential step for these products. On the other hand, aging in charred wood barrels occurs for some brandy products.

Beer is produced from cereal grain, most commonly barley, and fermented with yeast to produce a typical ABV of $\sim 5.0\%$. In some cases, the barley, or other cereal grain, is roasted or toasted before the fermentation process, which has been found to introduce PAHs into the final product. 21,22 This roasting process is the most extreme in dark beer products, where the grain is roasted for a longer duration of time, leading to increased combustion and potential exposure to PAHs. 22 Consequently, research looking at PAH content in beer products has mainly focused on dark beer products, although limited publications have assessed this relationship.

Wine is produced from fermented grapes with a typical ABV of $\sim 12\%$, depending on the style and production process used. Although there is no initial burning or roasting process that occurs to wine grapes before fermentation, wine can be aged in toasted wooden barrels, or with burned wood chips, to introduce novel flavors. Both of these processes have been found to introduce PAHs into aging wine products. ^{19,23}

Permissible PAH Levels in Drinking Water

Per Canadian guidelines for drinking water quality, the maximum acceptable concentration of BaP in safe drinking water is $40\,\mathrm{ng/L}.^{24}$ Other countries have published similar guidelines for BaP contamination in drinking water, including the United States at $200\,\mathrm{ng/L},^{25}$ the UK at $10\,\mathrm{ng/L},^{26}$ and Australia at $10\,\mathrm{ng/L}.^{27}$

Although the United States has less stringent guidelines for BaP concentration in drinking water, US EPA guidelines surrounding clean drinking water in the United States were introduced in 1994 and have not been updated since. ²⁵ Given that BaP is the only IARC class I carcinogen of the 16 US EPA high-priority pollutant PAHs, researchers have assessed BaP levels, as well as total PAH levels, in alcoholic beverages. ^{9,28,29}

Objectives

Although some primary literature has examined the association between the presence of PAHs in alcoholic beverages, to our knowledge there has been no prior review of the topic to provide an overview of the existing science (e.g., across multiple types of alcoholic beverages). The objective of this review was to characterize the published literature about the presence and levels of PAHs in consumable alcohol products on a beverage-specific basis.

Methods

This review assessed literature using the Medline and Scopus electronic databases for manuscripts published from 1966 to November 2023. The initial search was conducted 7 May 2023, the updated search was conducted 18 August 2023, and the final search was conducted 23 November 2023. Searches were conducted using the following keywords: ("polycyclic aromatic hydrocarbons" OR "PAH" AND "alcohol") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "alcoholic beverages") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "whisky") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "whiskey") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "scotch") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "rum") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "brandy") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "gin") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "tequila") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "vodka") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "beer") OR ("polycyclic aromatic hydrocarbons" OR "PAH" AND "wine"). Both "polycyclic aromatic hydrocarbon" and "PAH" were included as search terms to reduce the possibility of missing a potential manuscript.

After the initial search, manuscripts were screened using specified inclusion and exclusion criteria. Only primary literature was considered; review articles, meta-analyses, textbooks, and other secondary or tertiary publications were excluded. In addition, PAH is also an acronym for pulmonary hypertension, thus all studies that investigated pulmonary hypertension were excluded. The inclusion criteria included the following: a) being a primary or original research article, b) analysis of one or more beverage alcohols, c) quantification of PAH content, d) publication in a peer-reviewed journal, and e) publication being available in the English language.

Results

Manuscript Characteristics

The initial search yielded 464 publications. After applying the above inclusion and exclusion criteria, 10 publications remained and were included in the final review. Table 1 reports the baseline characteristics of the included publications (n=10) in this review, by type of beverage alcohol. The majority of publications assessed PAH values in spirits (n=7), with wine (n=4) and beer (n=3) having fewer studies. Across all studies, whisky had the most total samples assessed (n=51), followed by rum (n=26), beer (n=19), wine (n=15), brandy (n=7), and gin (n=6). Only

Table 1. Characteristics of included manuscripts based on beverage alcohol type.

				Samples per alcoholic prod-			Bap lower analytical
	Studies		PAH compounds assessed	uct tested per study [mean;	Region of alcohol	Methods used	threshold [range
Alcohol product	(<i>n</i>)	Years of publication	per study $[mean; n (range)]$	n (range)]	production	(n studies)	(mean)]
Whisky	59,19,28–30	1966, 1996, 2007,	11.8 (7–15)	11.4 (1–18)	Scotland, Ireland,	HPLC-FLD (3), GC-	0.1-6.3 ng/L (4.1 ng/L)
		2009, 2016			USA, Japan	MS (1), column/	(not specified for
						paper chromatog-	2 studies)
						raphy with UV	
						absorption spec-	
						troscopy (1)	
Rum	49,28,29,31	2007, 2007, 2009,	12.3 (7–15)	6.5 (1–19)	Canada, Brazil,	HPLC-FLD (3) and	$0.1-6.3\mathrm{ng/L}\ (4.1\mathrm{ng/L})$
		2016			Mexico, Cuba,	GC-MS (1)	(not specified for
					Jamaica, Venezuela,		2 studies)
					Panama, Nicaragua		
Brandy	29,28	2007, 2016	9.5 (7–12)	3.5 (2–5)	Not specified	HPLC-FLD (1) and	$0.1-6.3\mathrm{ng/L}\ (3.2\mathrm{ng/L})$
						GC-MS (1)	
Gin	1^{28}	2016	12	9	Not specified	GC-MS (1)	$6.3\mathrm{ng/L}$
Vodka	1^{32}	2019	16	1	Spain	GC-MS (1)	Not quantified
Wine	49,32,33	1995, 2007, 2007,	12 (6–19)	3.5 (2–5)	Spain, Italy (not speci-	HPLC-FLD (2) and	0.1 - 6.0 ng/L (2.9 ng/L)
		2019			fied for all products)	GC-MS (2)	
Beer	322,32,34	1995, 2018, 2019	12.7 (6–19)	6.3 (4–9)	Spain, Italy (not speci-	HPLC-FLD (1), GC-	$0.2-5.0\mathrm{ng/L}\ (1.9\mathrm{ng/L})$
					fied for all products)	MS (1), and SFC-	
					(I	MS (1)	

Note: BaP, benzo[alpyrene; GC-MS, gas chromatography with mass spectrometry; HPL-FLD, high-performance liquid chromatography with fluorescence detection; PAH, polycyclic aromatic hydrocarbon; SFC-MS, supercritical fluid chromaography with 7 studies were published after 2000. By beverage type, the mean number of types of PAHs analyzed per study ranged from 10 to 13; all studies assessed BaP concentration. For any beverage type, no study assessed >20 products. Other than geographical location of beverage production, none of the studies reported the basis for their selection of samples (e.g., brand popularity, purchase location, price range). Of note, none of the included studies had a potential conflict of interest or funding source from trade groups or alcohol marketers. The majority of the included publications were based out of Brazil, Spain, and Japan; none were based in North America, the UK, or Australia or New Zealand. In addition, four different methods were used to test for PAHs across studies: high-performance liquid chromatography with fluorescence detection (HPLC-FLD), gas chromatography coupled with mass spectrometry (GC-MS), supercritical fluid chromatography with mass spectrometry (SFC-MS), and column/paper chromatography with ultraviolet (UV) absorption spectroscopy. The BaP detection threshold ranged from 0.1 to 6.3 ng/L. Direct mass spectrometry (DMS) was not used in any of the included publications.

Studies of Spirits Products

Whisky. Five previous studies have assessed the PAH content level in whisky products for either BaP levels or the sum of total PAHs $(\sum PAH)$ (Tables 1 and 2). Kleinjans et al. assessed 18 different whisky products, including scotch malt, scotch blend, American bourbon, and Irish whisky using HPLC-FLD and found that BaP equivalents ranged from 3.4 to 47.5 ng/L.¹⁹ The levels of PAHs and BaP equivalents were highest in the scotch malts, with some PAHs being present in concentrations from 4,000 to 8,000 ng/L.¹⁹ Another study by Masuda et al. examined 5 brands of bourbon, 8 scotch brands, and 2 Japanese whisky brands for PAH content and found that the scotch products contained BaP at a level of 40 ng/L. Although this study was done >50 y ago, and the analytical techniques used are outdated, it is still an important study in the field because it was one of the first to investigate the relationship between alcohol and PAHs. A more recent study by Cacho et al. assessed 5 whisky products for PAH content and determined that BaP levels ranged from 66 to 72 ng/L using GC-MS.²⁸ Furthermore, ∑ PAH was also quantified for the 5 whisky brands, ranging from 547 to 2,109 ng/L.²⁸ In a different study investigating whisky and PAHs by Galinaro and Franco, 18 whisky brands were sampled, and the mean BaP concentration was determined using HPLC-FLD to be 32 ng/L, with the highest BaP concentration being 48.5 ng/L.²⁹ Finally, García-Falcón and Simal-Gándara measured BaP and \sum PAH contents among 1 whisky brand, as well as other spirits, and found that it contained only 0.9 ng/L of BaP and 3.6 ng/L of \sum PAH using HPLC-FLD.

Rum. Compared with whisky, the relationship between rum and PAHs has been less comprehensively studied; however, some studies have investigated the PAH content in commonly consumed rum products (Tables 1 and 2). Galinaro and Franco assessed the BaP concentration in 19 rum products using HPLC-FLD. The mean BaP concentration in all the rum products was 7.02 ng/L, with concentrations ranging from undetectable levels to 93 ng/L in 1 product.²⁹ In a separate study, Galinaro et al. evaluated 4 rum products using HPLC-FLD to assess the mean BaP concentration and found that the average was 4.92 ng/L, a value similar to their other work.³¹ Two final publications have investigated the relationship between rum and PAHs. Cacho et al. tested 1 rum product using GC-MS and found that BaP was undetectable, but the \sum PAH was 996 ng/L.²⁸ García-Falcón and Simal-Gándara assessed 2 rum products using HPLC-FLD and determined that the BaP concentration ranged from undetectable to $0.7\,\text{ng}/\text{L},$ whereas the $\sum PAH$ ranged from 0.9 to $3.2 \, \text{ng/L.}^{9}$

Table 2. PAH and BaP content of beverage alcohols.

Samples/products		BaP equivalent range	∑PAH range	
(n)	Methods	(ng/L)	(ng/L)	Reference
Whisky				
18	HPLC-FLD	3.4-47.5	NQ	Kleinjans et al. 19
15	Column/paper chromatography with UV absorption spectroscopy	ND-40.0	NQ	Masuda et al. ³⁰
5	GC-MS	66.0-72.0	547-2,109	Cacho et al. ²⁸
18	HPLC-FLD	<5.9 to 48.5	NQ	Galinaro and Franco ²⁹
1	HPLC-FLD	0.9	3.6	García-Falcón and Simal-Gándara ⁹
Rum				
19	HPLC-FLD	ND-93.0	NO	Galinaro and Franco ²⁹
4	HPLC-FLD	Median BaP = 4.92	NQ	Galinaro et al. ³¹
1	GC-MS	ND	996	Cacho et al. ²⁸
2	HPLC-FLD	ND-0.7	0.9-3.2	García-Falcón and Simal-Gándara9
Gin				
6	GC-MS	ND	138.0-327.0	Cacho et al. ²⁸
Brandy				
5	HPLC-FLD	2.6-6.3	108.4–172.3	García-Falcón and Simal-Gándara ⁹
2	GC-MS	ND-55.0	592.0-2,308.0	Cacho et al. ²⁸
Vodka				
1	GC-MS	ND	3,100	Rascón et al. ³²
Beer				
4	GC-MS	ND	1,140.0-4,470.0	Rascón et al. ³²
9	HPLC-FLD	ND-70.0	ND-720.0	Moret et al. ³⁴
6	SFC-MS	ND	ND	Yoshioka et al. ²²
Wine				
3	GC-MS	< 6.0	42.0-326.0	Chatonnet and Escobessa ³³
5 2	GC-MS	ND	430.0–4,275.0	Rascón et al. ³²
2	HPLC-FLD	< 5.0	<5.0 to 50.0	Moret et al. ³⁴
5	HPLC-FLD	ND-3.1	ND-36.5	García-Falcón and Simal-Gándara ⁹

Note: BaP, benzo[a]pyrene; GC-MS, gas chromatography with mass spectrometry; HPLD-FLD, high-performance liquid chromatography with fluorescence detection; ND, not detected; NQ, not quantified; PAH, polycyclic aromatic hydrocarbon; SFC-MS, supercritical fluid chromatography with mass spectrometry.

Other spirits. There are very few studies of other types of spirits including gin, brandy, and vodka (Tables 1 and 2). Nevertheless, Cacho et al. assessed six gin products using GC-MS and did not detect any BaP in any of the samples, with ∑PAH levels ranging from 128 to 327 ng/L.²⁸ García-Falcón and Simal-Gándara investigated five brandy products using HPLC-FLD and detected BaP at levels ranging from 2.6 to 6.3 ng/L.⁹ In a separate study, two brandy products were evaluated using GC-MS and the BaP concentration was found to be nondetectable and 55 ng/L, respectively.²⁸ This finding highlights the variability between products of the same spirit family. Finally, one sample of vodka was assessed by Rascón et al., who found that that BaP was not identifiable in the sample.³²

Studies of Beer Products

Rascón et al. investigated four beer products using GC-MS to assess \sum PAH and BaP content and found that there was no BaP detected, whereas \sum PAH ranged from 1,140 to 4,470 ng/L.³² In a different study, Moret et al. used HPLC-FLD to assess PAH contamination in nine beer products and determined that BaP concentration ranged from not detectable to 70 ng/L, and \sum PAH ranged from not detectable to 720 ng/L.³⁴ Finally, Yoshioka et al. examined six dark beer products using SFC-MS and determined that no PAHs were present in any of the samples.²²

Studies of Wine Products

Research into wine and PAHs is limited thus far, with only four studies assessing PAH content (Tables 1 and 2). Chatonnet and Escobessa (Table 2) explored wines aged in different styles of barrels (French vs. American oak) for PAH content using GC-MS and discovered that the BaP content in all the samples was <6.0 ng/L (their analytical threshold for BaP), which is less than the permissible drinking water levels in various countries. ^{24–27,33}

Moreover, the \sum PAH in these samples was found to range from 42.0 to $326\,\text{ng/L}.^{33}$ In a different study, Rascón et al. used GC-MS to analyze five different wine products and found that although BaP was not detectable in any samples, \sum PAH ranged from 430 to 4,275 ng/L. 32 Moret et al. analyzed two wine products using HPLC-FLD and determined that BaP was only present in trace amounts below their analytical threshold of 5.0 ng/L. 34 Finally, García-Falcón and Simal-Gándara assessed five wine products with HPLC-FLD and determined that BaP content ranged from nondetectable to 3.1 ng/L, whereas \sum PAH ranged from nondetectable to 36.5 ng/L. 9

Discussion

Overall, the identified literature on the presence and levels of PAH in alcoholic beverages was sparse and dated, but it suggests that PAHs are prevalent across several beverage types, including at levels that may pose a risk to human health. However, since 1966 there were only 10 studies that met our criteria, including only 7 studies published since 2000. Although many leading products are produced or consumed internationally, the composition of leading brands may vary by country or region, and other popular products may be locally produced and consumed. In addition, other than selecting one or more beverage types, no study specified its sampling frame for products selected for testing, which should be addressed in future studies. Furthermore, few products were tested in any individual study, or even across all studies (e.g., a total of <20 product samples for beer or wine products were analyzed and reported in the literature since 1966).

The analytical techniques employed to assess PAH and BaP content in alcoholic beverages varied across publications. Thresholds for PAH detection also varied between studies, and some studies had insufficient detection limits to measure PAH levels associated with potential public health risks. Further, the

wide range of analytical methods used for the determination of PAHs (i.e., HPLC-FDC, GC-MS, SFC-MS, and column/paper chromatography with UV absorption spectroscopy) may introduce some variability in results across studies, but it is difficult to assess the extent to which this may occur. We suspect that the more recent literature using fluorescence- and MS-based detection with chromatography should be representative of the variability, and the older literature using UV absorption might suffer from insufficient detection limits for trace measurements.

Several analytical techniques have been employed for the determination of PAHs in complex matrixes, such as alcoholic beverages, including HPLC-FLD and GC-MS. Although these methods are widely used, challenges arise with the time-consuming preparation, analytical, and cleanup steps that may limit the number of samples that can be feasibly analyzed in a study. 9,28,29,31,32

Compared with previous techniques, an emerging technique that may facilitate testing larger numbers of samples is DMS, which eliminates the need for chromatography and greatly reduces sample preparation and cleanup steps. In addition, DMS satisfies several of the 12 Principles of Green Chemistry. Condensed phase membrane introduction MS (CP-MIMS) is a type of DMS that uses a semipermeable membrane directly immersed into a sample to measure analytes of interest. This technique, coupled with liquid electron ionization/chemical ionization, has been shown to successfully resolve and quantify isomeric PAHs in soil samples. Of note, no publication used DMS, which would facilitate PAH-level assessment of larger sample sets across all beverage types and could lead to better relative estimates of PAH levels, within or across various types of alcoholic beverages.

It is also important to address that environmental PAH exposures are not solely from alcoholic beverages but, rather, from a variety of sources, including air pollution, smoking, and open flame cooking, such as barbequing and gas stoves. This is of vast importance given that the aforementioned exposures can be far more constant and unavoidable in certain settings, such as air pollution in populated areas. It is unknown how the magnitude of PAH exposure in alcohol compares to environmental sources, but it is important to recognize that there are likely additive effects of prolonged exposure through different sources.³⁸ As such, future research that investigates the comparative magnitude of different sources of PAH exposure could help elucidate the relative carcinogenic effect of alcoholic beverages vs. other sources, particularly among those who regularly or heavily consume alcoholic beverages. In addition, future research could compare the relative carcinogenic magnitude of PAH exposures in alcohol in comparison with the effects of ethanol and acetaldehyde.

In terms of limitations of our review, only publications that were published in the English language were considered. In addition, the published literature may not accurately reflect the actual testing of PAHs in alcohol that may have been done in unpublished or gray literature; however, it is important to emphasize that only reported values in traditional scientific literature are likely to be widely available and thus subject to discussion and evaluation by health authorities.

This review highlights the knowledge gap that exists regarding the presence of PAHs in alcohol products. This is noteworthy given the carcinogenic risk that ethanol and its metabolite acetal-dehyde already pose for health, with PAHs potentially creating unmeasured additive or synergistic relationship with alcohol-associated cancers, although the extent of this is unknown at this time. Overall, to determine the estimates of human exposures to PAH contamination in alcohol products, more research is required to establish the prevalence and typical levels of PAHs among representative samples of alcohol products on a beverage-

specific basis. It is recommended that future studies assess PAH levels across a large number and wide variety of alcohol products within beverage categories, with priority given to products that account for the largest volumes of consumption in the populations that are to be studied. In addition to studies of PAH levels in alcohol products, future studies might also assess PAH levels in different organ systems in relation to total alcohol consumption and type (or even brands) of alcohol consumed to better assess the potential of PAH consumption to cause cancer in humans.

Acknowledgments

L.K. and T.N. conceived the study concept. L.K. performed the literature review and drafted the manuscript. L.K., T.N., R.A., and C.G. revised the manuscript. All authors reviewed the manuscript and approved the final submitted version.

The work was supported by Natural Sciences and Engineering Research Council of Canada (NSERC) discovery grant RGPIN-2021-02981 (to C.G.). We also graciously acknowledge the ongoing support of students from Vancouver Island University and the University of British Columbia.

References

- Gilmore W, Chikritzhs T, Stockwell T, Jernigan D, Naimi T, Gilmore I. 2016. Alcohol: taking a population perspective. Nat Rev Gastroenterol Hepatol 13(7):426–434, PMID: 27188823, https://doi.org/10.1038/nrgastro.2016.70.
- Boffetta P, Hashibe M. 2006. Alcohol and cancer. Lancet Oncol 7(2):149–156, PMID: 16455479, https://doi.org/10.1016/S1470-2045(06)70577-0.
- Connor J. 2017. Alcohol consumption as a cause of cancer. Addiction 112(2):222–228, PMID: 27442501, https://doi.org/10.1111/add.13477.
- Ratna A, Mandrekar P. 2017. Alcohol and cancer: mechanisms and therapies. Biomolecules 7(3):61, PMID: 28805741, https://doi.org/10.3390/biom7030061.
- Varela-Rey M, Woodhoo A, Martinez-Chantar ML, Mato JM, Lu SC. 2013. Alcohol, DNA methylation, and cancer. Alcohol Res 35(1):25–35, PMID: 24313162
- IARC (International Agency for Research on Cancer). 2022. List of classifications. https://monographs.iarc.who.int/list-of-classifications/ [accessed 21 July 2022].
- Buykx P, Li J, Gavens L, Hooper L, Lovatt M, Gomes de Matos E, et al. 2016. Public awareness of the link between alcohol and cancer in England in 2015: a population-based survey. BMC Public Health 16(1):1194, PMID: 27899099, https://doi.org/10.1186/s12889-016-3855-6.
- Vallance K, Stockwell T, Zhao J, Shokar S, Schoueri-Mychasiw N, Hammond D, et al. 2020. Baseline assessment of alcohol-related knowledge of and support for alcohol warning labels among alcohol consumers in northern Canada and associations with key sociodemographic characteristics. J Stud Alcohol Drugs 81(2):238–248, PMID: 32359055, https://doi.org/10.15288/jsad.2020.81.238.
- García-Falcón MS, Simal-Gándara J. 2005. Determination of polycyclic aromatic hydrocarbons in alcoholic drinks and the identification of their potential sources. Food Addit Contam 22(9):791–797, PMID: 16192065, https://doi.org/10.1080/02652030500198498.
- Da Porto C, Moret S. 2007. Comparison of polycyclic aromatic hydrocarbons (PAHs) between smoked marc spirits and whiskies. Food Chem Toxicol 45(10):2069–2071, PMID: 17566624, https://doi.org/10.1016/j.fct.2007.04.022.
- Ifegwu OC, Anyakora C. 2015. Polycyclic aromatic hydrocarbons: part I. Exposure. Adv Clin Chem 72:277–304, PMID: 26471085, https://doi.org/10.1016/bs.acc.2015.08.001.
- Yap CL, Gan S, Ng HK. 2012. Evaluation of solubility of polycyclic aromatic hydrocarbons in ethyl lactate/water versus ethanol/water mixtures for contaminated soil remediation applications. J Environ Sci (China) 24(6):1064–1075, PMID: 23505874, https://doi.org/10.1016/s1001-0742(11)60873-5.
- Huang M, Penning TM. 2014. Processing contaminants: polycyclic aromatic hydrocarbons (PAHs). In: Encyclopedia of Food Safety, vol 2. Motarjemi Y, Moy G, Todd ECD, eds. Amsterdam, the Netherlands: Elsevier/Academic Press, 416–423.
- Law RJ, Biscaya JL. 1994. Polycyclic aromatic hydrocarbons (PAH)—problems and progress in sampling, analysis and interpretation. Mar Pollut Bull 29(4–5): 235–241, https://doi.org/10.1016/0025-326X(94)90415-4.
- Zelinkova Z, Wenzl T. 2015. The occurrence of 16 EPA PAHs in food—a review. Polycycl Aromat Compd 35(2–4):248–284, PMID: 26681897, https://doi.org/10.1080/10406638.2014.918550.
- Peng PL, Lim LH. 2022. Polycyclic aromatic hydrocarbons (PAHs) sample preparation and analysis in beverages: a review. Food Anal Methods 15:1042–1061, https://doi.org/10.1007/s12161-021-02178-y.

- Wiśniewska P, Boqué R, Borràs E, Busto O, Wardencki W, Namieśnik J, et al. 2017. Authentication of whisky due to its botanical origin and way of production by instrumental analysis and multivariate classification methods. Spectrochim Acta A Mol Biomol Spectrosc 173:849–853, PMID: 27816884, https://doi.org/10. 1016/j.saa.2016.10.042.
- Mastanjević K, Krstanović V, Kovačević D, Kartalović B, Habschied K. 2021. Polycyclic aromatic hydrocarbons in malt. Beverages 7(3):58, https://doi.org/10. 3390/beverages7030058.
- Kleinjans JC, Moonen EJ, Dallinga JW, Albering HJ, van den Bogaard AE, van Schooten FJ. 1996. Polycyclic aromatic hydrocarbons in whiskies. Lancet 348(9043):1731, PMID: 8973440, https://doi.org/10.1016/S0140-6736(96)24051-6.
- Riachi LG, Santos A, Moreira RFA, De Maria CAB. 2014. A review of ethyl carbamate and polycyclic aromatic hydrocarbon contamination risk in cachaça and other Brazilian sugarcane spirits. Food Chem 149:159–169, PMID: 24295690, https://doi.org/10.1016/j.foodchem.2013.10.088.
- Anderson HE, Santos IC, Hildenbrand ZL, Schug KA. 2019. A review of the analytical methods used for beer ingredient and finished product analysis and quality control. Anal Chim Acta 1085:1–20, PMID: 31522723, https://doi.org/10.1016/j.aca.2019.07.061.
- Yoshioka T, Nagatomi Y, Harayama K, Bamba T. 2018. Development of an analytical method for polycyclic aromatic hydrocarbons in coffee beverages and dark beer using novel high-sensitivity technique of supercritical fluid chromatography/mass spectrometry. J Biosci Bioeng 126(1):126–130, PMID: 29499993, https://doi.org/10.1016/j.jbiosc.2018.01.014.
- Chinnici F, Natali N, Spinabelli U, Riponi C. 2007. Presence of polycyclic aromatic hydrocarbons in woody chips used as adjuvant in wines, vinegars and distillates. LWT-Food Sci Technol 40(9):1587–1592, https://doi.org/10.1016/j.lwt. 2006.11.005.
- Government of Canada. 2022. Guidelines for Canadian Drinking Water Quality: Guideline Technical Document – Benzo[a]pyrene. https://www.canada.ca/en/health-canada/services/publications/healthy-living/guidelines-canadian-drinking-water-quality-guideline-technical-document-benzo-pyrene.html [accessed 10 July 2022].
- U.S. EPA (U.S. Environmental Protection Agency). n.d. Consumer Factsheet on Benzo[a]pyrene. US EPA archive. https://archive.epa.gov/water/archive/web/ pdf/archived-consumer-factsheet-on-benzo.pdf [accessed 10 July 2022].
- Public Health England. 2018. Polycyclic aromatic hydrocarbons (benzo[a] pyrene) incident management. PHE publications gateway no. 2014790. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/737016/PAH_IM_PHE_030818.pdf [accessed 10 July 2022].
- NHMRC (National Health and Medical Research Council). 2011. Australian Drinking Water Guidelines. https://www.nhmrc.gov.au/about-us/publications/ australian-drinking-water-guidelines [accessed 10 July 2022].

- Cacho JI, Campillo N, Viñas P, Hernández-Córdoba M. 2016. Evaluation of the contamination of spirits by polycyclic aromatic hydrocarbons using ultrasoundassisted emulsification microextraction coupled to gas chromatography–mass spectrometry. Food Chem 190:324–330, PMID: 26212977, https://doi.org/10.1016/j. foodchem.2015.05.106.
- Galinaro CA, Franco DW. 2009. Polycyclic aromatic hydrocarbons (PAHS) in cachaça, rum, whiskey and alcohol fuel [in Portuguese]. Quím Nova 32(6):1447– 1451, https://doi.org/10.1590/S0100-40422009000600016.
- Masuda Y, Mori K, Hirohata T, Kuratsune M. 1966. Carcinogenesis in the esophagus. 3. Polycyclic aromatic hydrocarbons and phenols in whisky. Gan 57(5):549–557. PMID: 4165496.
- Galinaro CA, Cardoso DR, Franco DW. 2007. Profiles of polycyclic aromatic hydrocarbons in Brazilian sugar cane spirits: discrimination between cachaças produced from nonburned and burned sugar cane crops. J Agric Food Chem 55(8):3141–3147, PMID: 17381124, https://doi.org/10.1021/jf063671a.
- Rascón AJ, Azzouz A, Ballesteros E. 2019. Use of semi-automated continuous solid-phase extraction and gas chromatography—mass spectrometry for the determination of polycyclic aromatic hydrocarbons in alcoholic and non-alcoholic drinks from Andalucía (Spain). J Sci Food Agric 99(3):1117–1125, PMID: 30051478, https://doi.org/10.1002/jsfa.9279.
- Chatonnet P, Escobessa J. 2007. Impact of toasting oak barrels on the presence of polycyclic aromatic hydrocarbons in wine. J Agric Food Chem 55(25):10351–10358, PMID: 18001029, https://doi.org/10.1021/jf071665o.
- Moret S, Amici S, Bortolomeazzi R, Lercker G. 1995. Determination of polycyclic aromatic hydrocarbons in water and water-based alcoholic beverages. Z Lebensm Unters Forsch 201(4):322–326, PMID: 8525699, https://doi.org/10.1007/BF01192725.
- ATSDR (Agency for Toxic Substances and Disease Registry). 2022. Environmental Health and Medicine Education. Case studies accredited for CE. Page last reviewed 9 September 2022. http://www.atsdr.cdc.gov/csem/csem.asp?csem=13& po=11 [accessed 11 September 2022].
- Termopoli V, Famiglini G, Palma P, Cappiello A, Vandergrift GW, Krogh ET, et al. 2016. Condensed phase membrane introduction mass spectrometry with direct electron ionization: on-line measurement of PAHs in complex aqueous samples. J Am Soc Mass Spectrom 27(2):301–308, PMID: 26471041, https://doi.org/10.1007/s13361-015-1285-9.
- Vandergrift GW, Krogh ET, Gill CG. 2020. Direct, isomer-specific quantitation of polycyclic aromatic hydrocarbons in soils using membrane introduction mass spectrometry and chemical ionization. Anal Chem 92(23):15480–15488, PMID: 33076653, https://doi.org/10.1021/acs.analchem.0c03259.
- Staal YCM, Hebels DGAJ, van Herwijnen MHM, Gottschalk RWH, van Schooten FJ, van Delft JHM. 2007. Binary PAH mixtures cause additive or antagonistic effects on gene expression but synergistic effects on DNA adduct formation. Carcinogenesis 28(12):2632–2640, PMID: 17690111, https://doi.org/10.1093/carcin/bgm182.