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Polycyclic aromatic hydrocarbons as a potential source of carcinogenicity of mate

Ebele Oranuba^a, **Hua Deng**^b, **Jiangnan Peng**^b, **Sanford M Dawsey**^c, and **Farin Kamangar**^{a,d} ^aASCEND Center for Biomedical Research, Morgan State University, Baltimore, MD, USA

^bDepartment of Chemistry, School of Computer, Mathematical, and Natural Sciences, Morgan State University, Baltimore, MD, USA

^cMetabolic Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

^dDepartment of Biology, School of Computer, Mathematical, and Natural Sciences, Morgan State University, Baltimore, MD, USA

Abstract

Drinking mate, an infusion of the herb *ilex paraguariensis*, is very common in several South American countries, and has been associated with an increased risk of esophageal cancer. This increased risk may be attributed to drinking mate very hot, or to mate's potentially carcinogenic contaminants, such as polycyclic aromatic hydrocarbons (PAHs). Mate leaves are often dried via smoking, and therefore commercial samples may have high amounts of PAHs. We found 10 original articles that had measured PAHs in commercial dry samples, and nearly all found very high mass fractions. Most studies found benzo[*a*]pyrene mass fractions to be over 25 ng/g, and some found levels up to 600 ng/g. However, carcinogenic PAHs are often hydrophobic, and may not readily transfer into infusions. Seven articles studied transfer rates, and these rates varied from 1 to 50%, depending on the methods employed. Further careful studies of transfer rates in situations that mimic real life drinking of mate are recommended. Also, further studies of biological indicators of PAH exposure, particularly in randomized experiments, and analyzing DNA from tumor samples of mate drinkers are recommended.

Keywords

mate; PAH; benzo[a]pyrene; esophageal cancer; hot drinks

CONTACT Farin Kamangar, farin.kamangar@morgan.edu Department of Biology, School of Computer, Mathematical and Natural Sciences, Morgan State University, Baltimore, Maryland, USA.

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1.

Introduction

Mate, a traditional nonalcoholic drink, is an aqueous infusion prepared from dried leaves of the herb *ilex paraguariensis*, commonly called *yerba mate* or *erva mate*. The leaves are harvested; dried using sunshine, smoking, traditional wood fires, or modern heating technologies; and chopped and ground into a powdery mixture, which is steeped in hot water and is served with a metal straw as "hot mate tea." This is the traditional way to prepare and consume mate tea, and the steeping process can be repeated 10–15 times. Nowadays, bottled mate beverages are also commonly available in the market.

Mate is a source of caffeine and is widely consumed in South American countries (Uruguay, Paraguay, Argentina, and parts of Brazil), in lieu of tea or coffee, sometimes in copious amounts. For example, in Uruguay, over 90% of cases and controls in a study consumed mate.¹ Another study in Brazil showed that the average consumption in mate drinkers was 1.8 L/day.² Nevertheless, the literature on health effects of mate is not nearly as extensive as that of tea or coffee.³ While some positive effects on blood sugar and lipid profile have been shown in human and animal studies³—leading to advertising mate as a health drink multiple studies have suggested that drinking mate is associated with increased risk of several cancers, particularly cancer of the esophagus,⁴⁻⁶ as well as cancers of lung and bladder.⁷ The association of mate with esophageal cancer has been partly attributed to repeated thermal injury to the esophageal mucosa; the International Agency for Research on Cancer (IARC) has classified very hot beverages such as hot mate infusion as a probable carcinogen (Class 2A).⁸ However, association of mate with other cancers, e.g. cancers of the lung and bladder, cannot be explained by the hot temperature of mate. The higher risk of these cancers among mate drinkers may potentially be because of confounding effect of tobacco use, as mate drinkers are more likely to be smokers. Alternatively, this higher risk may be because mate may have some carcinogenic contaminants—in particular polycyclic aromatic hydrocarbons (PAHs) such as benzo[a]pyrene (class 1 carcinogen), benzo[a]anthracene (class 2B carcinogen), benzo[b]fluoranthene (class 2B carcinogen), and chrysene (class 2B carcinogen)-that increase the risk of these cancers.

Several studies have indeed shown that commercially prepared yerba mate leaves have significant amounts of PAHs.^{9,10} A small amount may be accumulated in the unprocessed green leaves due to soil and atmospheric contamination. The majority of the PAHs in the dried leaves is introduced during processing, especially the blanching (sapeco) and smokedrying steps in commercial preparation.¹¹ Some researchers have argued that the high PAH concentrations in mate leaves does not translate into high levels of exposure to carcinogenic PAH exposure in consumers: mate infusions may contain insignificant amounts of PAHs, as carcinogenic PAHs are typically hydrophobic. The heavier, more carcinogenic PAHs (e.g. Benzo[a]pyrene) have very low water solubility and tend not to transfer from dry leaves into infusions. However, some studies have argued that the repeated soaking of the leaves, as it is done in daily life, will release substantial amounts of PAHs.¹⁰

The purpose of this paper is to conduct a review of studies that have measured the PAH content of commercial yerba mate leaves and mate infusions, and to discuss: (1) whether

commercial dry yerba mate contains significant levels of PAHs; (2) whether mate infusions have significant levels of PAHs; (3) how much humans are exposed to PAHs via drinking mate; (4) what additional studies need to be conducted to further explore this hypothesis; (5) how mate can be a healthier drink.

2. Literature search and data extraction

2.1. Literature search

We conducted a systematic search for articles that measured the concentration of PAHs in yerba mate leaves or mate infusions. Since the total number of such papers was relatively low, we used broad search terms to capture all potential papers. We searched PubMed for the terms "(mate OR *ilex paraguariensis*) AND (PAH OR polycyclic aromatic hydrocarbon)," which resulted in 89 articles. Reviewing the titles and abstracts, we found 19 potentially relevant articles. After reviewing the full text of the 19 articles, we found 13 that measured PAHs, alkylated PAHs, or nitro-PAHs in yerba mate leaves or mate tea. We searched the Wiley Library and Science Direct using the same terms as for PubMed, but found no new articles. In addition, we searched the references of the selected articles, and found two new articles. Therefore, a total of 15 articles were included in this review.

2.2 Data extraction

For dry material, we extracted data on the type of *Ilex paraguariensis* studied (fresh leaves or twigs, roasted, or smoke-dried), number of PAHs measured in each study, methods of extraction and measurement, and mass fractions (nanograms per gram, ng/g) for total PAHs and the four polycyclic aromatic hydrocarbons with the highest probability of being carcinogenic. These four PAHs, also known as PAH4, are benzo[*a*]pyrene (B[*a*]P), benzo[*a*]anthracene (B[*a*]A), benzo[*b*]flouranthene (B[*a*]F), and chrysene.¹² For infusions, we extracted data on the grams of leaf and water used for the experiment, water-to-leaf ratio, infusion time, infusion temperature, and either concentration (ng/mL) or amount and percentage of PAH mass fractions transferred to the infusions. Where multiple samples were measured, or one sample was measured several times, we report averages.

3. Mate in dry samples

Table 1 summarizes data from 10 studies, $9^{-11,13-19}$ published between 1985 and 2018, which measured values of individual PAHs in dry yerba mate leaves.

3.1 Mate samples

The material used for these studies were primarily commercial samples, prepared after drying. Most studies measured several samples, either from the same commercial brand or from various brands. One study¹¹ had fresh, dried, and commercial brands. Another study⁹ had 11 commercial samples that were prepared using traditional methods (including perhaps smoking), and one sample that was dried without exposure to smoke.

3.2. Extraction methods

To evaluate mass fractions in dry yerba mate leaves, PAHs were extracted and then made into a solution that could be injected into measurement instruments. This process involved three steps: extraction, purification, and solvent exchange. Dry leaves were often quartered and crushed in a hammer mill or similar device. Since PAHs are highly lipophilic, the crushed leaves were processed with organic solvents to extract the PAHs. The most common solvents used for this process were hexane, hexane/acetone, and dichloromethane, volatile and non-polar solvents with boiling points of 50 and 70 OC, which are easily removed using a rotary evaporator. Extraction by sonicating for 15 or 30 min at 30 or 60OC was most often used.^{11,13,16,18} Alternatively, pressurized fluid extraction or accelerated solvent extraction was used for quick and automatic extraction of PAHs from the dry yerba mate leaves.^{9,10,18} Soxhlet extraction was also used to thoroughly extract PAHs from mate.¹⁴ The extract solution was then put through a filtration or centrifugation step to separate the solution from the residues. Because other soluble organic species (impurities) may exist in the crude extract, the sample generally needed to be purified to remove or reduce interferences in further chromatographic analysis. A normal phase silica solid phase extraction (SPE) was often used for this purpose.^{9,13} Gel permeation chromatography (GPC) using a Bio Beads S-X3 was also used.¹⁸ Finally, the purified solution was concentrated to a small volume for GC analysis. To prevent the loss of PAHs with low boiling points during evaporation, dryness (total evaporation of solvent) should be avoided. A solvent exchange was performed to prepare the solution for HPLC analysis.

3.3. Measurement methods

Several studies used gas chromatography-mass spectrometry (GC-MS) while others used high-performance lipid chromatography (HPLC)-based methods to measure PAHs. In addition to the high lipophilicity, PAHs are a large class of compounds, many of which are isomers with very similar partition coefficients. These properties make the quantitative and qualitative measurement of PAHs difficult. Chromatographic separation of PAHs requires the utilization of either a PAH-specific HPLC column^{11,20} or a long GC column.^{10,16} Since PAHs are UV active, some studies used a UV detector to detect PAHs in mate.¹¹ However, considering the low concentration of PAHs and complex background in the mate, as well as the low sensitivity and selectivity of this method, a UV detector is not commonly used for the analysis of PAHs in mate. Mass spectrometry coupled with HPLC or GC are commonly used for detecting PAHs.^{11,13,14,16,18} Selected ion monitor mode is used to reduce background interference and increase the sensitivity of detection. Fluorescence detection (FLD) is highly sensitive, which is suitable for detection of relatively low concentrations of PAHs in mate.²⁰ By carefully selecting excitation and detection wavelengths, FLD can selectively detect PAHs, resulting in cleaner baseline and less requirement for sample purity. Although most PAHs are fluorescence active, PAHs without fluorescence activity, such as nitro-PAHs, require derivation before analysis. Alternatively, Du'sek et al. combined Soxhlet extraction, GPC and SPE purification, and GC-MS/NCI as quantitation technique to reach the specificity and sensitivity detection of nitro-PAHs.²¹ Internal standard references using deuterium or ¹³C isotope labeled PAHs are required to achieve better accuracy and recovery for complex analyses of PAHs.

While extraction and measurement methods vary by study, the extraction and measurement technologies used in these studies should only result in limited variations of the detected PAHs level. Therefore, differences in analytical methods are not the main reason for variations seen across the studies.

3.4. PAH mass fractions

For each study, we calculated and reported mean (or median) values and range of the PAH mass fractions obtained from the samples. Most studies measured between 4 and 21 types of PAHs, so the total of PAH mass fractions are not comparable across studies. By contrast, B[a]P and PAH4 mass fractions are comparable across studies. The studies typically found over 25 ng/g (and up to over 600 ng/g) of B[a]P and over 150 ng/g of PAH4 (up to over 2200 ng/g) (Table 1). These numbers are substantially higher than the mass fractions set by the European Union Commission for PAH4, which is 10–35 ng/g for different foodstuff.²² To put these numbers further into perspective, smoking each cigarette introduces about 10 ng of B[a]P into the body.^{23,24} Therefore, assuming that a typical user consumes 20 g of mate per day, and each gram of mate has 40 ng of B[a]P, the total amount of B[a]P in the daily consumed mate would be 800 ng, or equivalent to 80 cigarettes (four packs of cigarettes). However, only a small and insignificant fraction of this amount may be transferred into the infusion (see the next section).

While average PAHs mass fractions were high, there was substantial variations across the samples. For example, in the study by Kamangar et al.¹⁰ on eight commercial samples, the total PAHs mass fraction ranged from 536 to 2906 ng/g across the samples. These variations are most likely due to differences in methods of drying, as much of the PAHs are introduced when the leaves are dried using smoke exposure. A study by Vieira¹¹ found substantially higher levels of PAHs in dried samples than in fresh leaves. Another study by Golozar⁹ measured PAH mass fractions in 11 traditionally prepared commercial samples, and compared it with a sample that never touched smoked. In this study,⁹ the average total PAHs mass fraction in the 11 traditionally prepared commercial samples was 1703 ng/g, compared to only 621 ng/g for the nonsmoked sample.

In addition to the studies mentioned above, at least three papers evaluated the mass fractions of nitro-PAHs in mate samples.^{19,21,25} Notably, nitro-PAHs are highly mutagenic. In two studies, the mass fractions of nitro-PAHs were all below the detection limit of GC-MS and 2-D GC-MS methods.^{21,25} By contrast, in one study,¹⁹ appreciable amounts of nitro-PAHs (such as 1-nitropyrene and 3-nitrofluoranthene) were found, particularly in roasted mate leaves.

4. Mate in infusions

Table 2 summarizes data from seven studies, $^{10,15-17,20,26,27}$ published between 1985 and 2018, that measured the release of PAHs into infusions.

4.1 Methods of preparing infusions

Methods for preparing infusions varied substantially across studies (Table 2), which may be an important source for variation of results. A study by Lin et al.²⁸ found several factors that were associated with percentage of PAHs transferred into the infusions: lower leaf-to-water ratio resulted in higher percentage of transfers; when water was poured over the leaves for the first time, a relatively large percentage was transferred but there was a diminishing pattern of transfer when water was added a second or third time; washing tea prior to brewing naturally resulted in lower PAH transfers; and covering the infusions allowed more PAHs, particularly volatile ones, to remain in the infusion. Some of these factors varied substantially across studies. For example, leaf-to-water ratio ranged from 1 to 17 g/ 100 mL across studies. Likewise, infusion times varied from 20 sec to 30 min. Perhaps the most important source of variation was the number of times water was poured over the dry samples. Some studies made infusions by immersing dry mate in a large quantity of boiling water only one time, similar to tea.^{16,26,27} By contrast, two reports tried to mimic the way mate is prepared and consumed in daily life,^{10,20} which is repeatedly adding small quantities of hot or cold water into commercial dry mate, and letting the mate immerse for a short time. Temperature of infusions also varied. Two studies measured PAHs released into both hot and cold solutions,^{10,20} while others did not.

In some studies, the infusion solution was filtered,^{16,26,27} but in others it was not filtered^{10,20} before the back extraction of PAHs by partitioning with hexane, cyclohexane, or toluene. A stir bar sorptive extraction (SBSE) technique, utilizing a polydimethylsiloxane coated bar to absorb PAHs with higher recovery, was also used to extract PAHs in the infusions.²⁷

4.2 Measurement methods

After back extraction and purification, PAH measurements were done using methods similar to those described for dry mate samples. The actual PAH concentrations detected in infusions are normally very low. Thus, internal standards, normally isotope-labeled PAHs, are added to improve detection accuracy.

4.3. Transfer rate of PAHs into infusions

Table 2 shows characteristics of the studies that attempted to quantify either concentrations of PAHs, or their transfer from dry material to infusions. The grams of mate and volumes of water used, the infusion times, whether cold and hot infusions were used, and whether the study measured transfer after only a one-time addition of water or multiple times are shown in the table.

Due to major differences in methods, the findings are not comparable. While some studies have suggested that the amounts of PAHs transferred into the infusions are appreciable, others have found these amounts to be low or even negligible. A study by Kamangar¹⁰ found very high rates of transfer. In this study, the investigators added 30 mL of solution to 5 g of commercial mate leaves, allowed the leaves to steep for 5 min at either 5 or 80 °C, discarded the infusions and measured its PAH content, and then added more water to the leaves. This process was done to mimic real life drinking of mate, in which water is added to leaves,

drunk, and then more water is added. While 9% of B[a]P was released into the first infusion, only 2% was released into the final infusion. The investigators estimated that, over 12 infusions, approximately 50% of the total B[a]P was transferred. Similar amounts were released into the cold infusions. Therefore, temperature of the water appeared to not make a difference. Assuming that a transfer rate of 50% is correct, consuming 20 g of mate per day infuses into body as much B[a]P as smoking two packs of cigarettes per day, which may result in a significant increase in cancer risk. The study by Thea et al.²⁰ also simulated real life situations. As shown in Table 2, in Thea's study, only an estimated 1–10% of the B[a]P was transferred. If one assumes that the best estimate is 5%, then the amount of B[a]P infused into the body by using 20 g of mate per day is equivalent to smoke only four cigarettes, which is associated with only a modest increase in cancer risk. The amount released into cold infusions was several-fold lower than in the hot infusions. While the two studies by Kamangar and Thea have some methodological similarities, they have substantial differences, too. For example, Kamangar et al.¹⁰ allowed for the leaves to steep for 5 min, while Thea et al.²⁰ only allowed for only 20 sec of steeping time. In Kamangar's study, 5 g of mate was infused with 30 mL of water, while in Thea's study, much more mate (50 g) was infused with the same amount of water. Clearly, the differences in treatment methods resulted in quite different outcomes.

Except for Kamangar and Thea, other studies typically steeped the dry samples with water only one time. In Ruschenburg's study,¹⁵ an estimated 2–10% of the B[*a*]P in dry material was transferred. The studies by Tfouni¹⁷ and Schulz,¹⁶ which had both found very high amount of PAHs in dry mate, found negligible amounts in the infusions.

Some estimates for transfer of PAHs in mate can be obtained from studies of other drinks, such as tea and coffee. Duedahl-Olesen and colleagues²⁹ showed that up to 2 and 14% of PAH4 were detected in the ready-to-drink tea and coffee, respectively. They estimated that tea and coffee consumption was responsible for approximately 29% total PAH4 exposure in Danish consumers. Similarly, Lin et al.³⁰ showed that depending on the duration of the tea infusion, about 3–8% of total PAH in dry tea samples were detected in tea infusions.

5. Human exposure to PAHs via drinking mate

Human exposure to PAHs via drinking mate is a function of at least five factors: the mass fraction of PAHs in dry material, transfer of PAHs from dry material into the infusions, the mass of mate used to make the drinks, the volume of mate drinks consumed by each person, and the absorption into the body via the drink. Table 1 of this paper clearly shows that commercially dried mate has significant mass fractions of PAHs, and the mass and volume of mate consumed for many users are fairly large. As discussed earlier, the daily consumption of 20 g of mate, with 800 ng of B[a]P, in 1 L of water is not uncommon. What is less known is the percentage of PAHs transferred into the infusions. As discussed in Section 4.3 of this paper, transfer rates vary substantially across studies, between 1% (8 ng of B[a]P) to 50% (400 ng of B[a]P), depending on the method of extraction. These figures can be higher or lower in real life situations. The release of PAHs as suspension along with

small lipid particles or with crushed mate in the infusions that passes through the filters in household preparation can result in higher amounts of ingested PAHs in real life.

These levels may be perceived to pose a threat to human health if one compares them with PAH levels received from smoking cigarettes, but relatively low compared to what causes cancer in animals. As discussed earlier, humans receive approximately 10 ng of B[a]P from each cigarette. However, the absorption of B[a]P from inhalation may be different from drinking, and thus this comparison may not be entirely justified. Therefore, safe levels in drinks should ideally be determined in epidemiologic studies. But unfortunately, safe levels of exposure to B[a]P and other potentially carcinogenic PAHs in drinks have not been determined using epidemiologic data in humans. Based on rat studies, Kroese et al.³¹ suggested that an exposure of 5 ng B[a]P per kg body weight daily (350 ng/ day for a 70 kg person), is "virtually safe" in humans. Likewise, calculations by Okaru and colleagues, 32 based on studies conducted in mice and using margin of exposure method, show that any human exposure of <7 ng/kg (490 ng/day for a 70 kg person) of B[a]P is highly unlikely to cause alimentary tract cancers. Limits set by regulatory agencies are close to these numbers. The United States Environmental Protection Agency (USEPA) has set a limit of 200 ng/L,³³ and the World Health Organization has set a maximum of 700 ng/L for safe B[a]P levels.34 Only with transfer rates of 50%, the drinks may exceed some limits. But one might argue that extrapolations from animal studies to humans is less than ideal, and these amounts may still be dangerous. Furthermore, Kroese et al.³¹ suggest that animal studies with B[a]P may not capture the total carcinogenicity of all PAHs. These authors suggest that B[a]P may account for only 10% of the entire carcinogenicity of all consumed PAHs, and as such the true safe levels of B[a]P may be as low as 0.5 ng/kg (35 ng for a 70 kg person). If this latter assumption is correct, then a transfer rate of even 5% may pose a risk.

While the data is inconclusive as to whether enough PAHs are released into infusions to pose a threat, measurement of PAH metabolites in urine samples of mate drinkers suggests that the exposure may indeed be appreciable. Fagundes et al.³⁵ found a direct correlation between urinary concentrations of 1-hydroxypyrene glucuronide (1-OHPG), a PAH metabolite, and consumption of mate. The concentration of urinary 1-OHPG was four times higher in people who consumed greater than 1000 mL of mate per day, when compared to those who drank less than 100 mL per day. In fact, mate drinkers who did not smoke cigarettes had as much 1-OHPG in their urine as smokers who did not drink mate. In other words, mate drinking was associated with as much urine 1-OHPG as smoking cigarettes. A recent study of 244 adults³⁶ has confirmed these findings: recent mate consumption was associated with higher urinary concentrations of several PAH metabolites in a dose-response manner, and the sum of the urinary concentrations of the phenanthrene metabolites was similar or higher among mate drinkers who did not smoke than among smokers who did not drink mate. Notably, 1-OHPG concentrations have been found to be very high in urine samples of residents in regions in Iran and China that have very high incidence rates of esophageal cancer.^{37,38}

6. Future studies

Future studies should include a combination of chemical analyses of PAHs quantity in dry mate and infusions under different conditions, measurements of biomarkers of exposure to PAHs in biological samples from mate drinkers, and DNA mutation studies in tumors of mate drinkers.

6.1. Chemical analyses

While at least 10 studies have been published on the mass fraction of PAHs in dry mate leaves, there are relatively few that have carefully examined PAH mass fractions in different stages of drying. Repeating such a study will be valuable, particularly under controlled conditions, when some samples are smoked, and some are not. More importantly, previous studies measuring PAHs in infusions are not convincing, the main problem being that the measurements may not reflect real life concentrations and consumption. Careful studies that mimic real life concentrations of PAHs released into infusions are essential.

6.2. Measurement of biomarkers of exposure to mate

Further studies of 1-OHPG and other PAH metabolites in urine samples of mate drinkers is of interest, particularly under controlled conditions. For example, one can measure urinary metabolites of PAH exposure in a crossover trial, when some participants drink mate for a few days—while the control members do not—and then switch the mate drinking of the two groups and repeat the measurements. These measurements should indicate whether mate consumers are exposed to significant amounts of PAHs.

6.3. DNA mutation studies in tumors of mate drinkers

Exposure to B[a]P produces *P53* signature mutations in humans. It is worthwhile collecting tissue samples, particularly those of esophageal, lung, and bladder tumors from mate users who are not smokers to look for such mutations.

7. Conclusions

Mate is consumed in large amounts in South America, and it is also becoming more popular in other areas of the world. Therefore, it is very important to assess the health benefits and hazards of drinking mate. Although there are data from several epidemiological studies showing that drinking mate is associated with higher risks of esophageal cancer and perhaps other cancers, it is yet unclear whether this increased risk is only due to thermal injury, or also due to the consumption of PAHs via drinking mate.

The current literature is inadequate in determining whether humans receive high enough amounts of carcinogenic PAHs to increase their risk of cancer. In particular, data on PAHs dissolved in infusions are inadequate. Therefore, further studies of mate infusions, determination of biomarkers of PAH exposure in mate drinkers, and studies of tumor DNAs in mate drinkers are needed. The latter studies provide more direct evidence from humans, which will supersede animal studies. If mate drinkers are at higher risk of various cancers, the safe levels of B[*a*]P and other PAH4 in drinks may need to change. In the interim,

producers can be advised to dry mate leaves using methods other than smoking, and consumers may be advised to drink mate in moderation, and at slightly lower temperatures.

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Table 1.

PAHs measured in dry mass.

Author (year)	Analytical method	Mate source	Number of PAHs	Total PAH (range, ng/g)	PAH4 (ng/g)	B[a]P (range, ng/g)	B[a]A (range, ng/g)	B[b]F (range, ng/g)	Chrysene (range, ng/g)
Tfouni (2018) ¹⁷	QuEChERS;	3 CS	4	946 (194–1795)	946	208 (39–423)	231 (41–434)	177 (30–383)	329 (84–555)
	HPLC-FLD								
Rolle (2016) ¹⁴	GC-MS	1 CS	8	4065	2073	603	507	519	444
Schulz (2014) ¹⁶	GC-MS	3 CS	16	1967 (1600–2500)	1036	273 (200–380)	250 (200–310)	193 (110–250)	320 (260–420)
Londo~no (2014) ¹³	HPLC-FLD/DAD	50 CS	16	1664 (225–4450)	145	26.9 (1.3–125.2)	28.7 (2.2–108.8)	21.9 (1.7–85.3)	67.6 (3.1–210.5)
Golozar (2012) ⁹	GC-MS	8 CS (2008)	20	1500 (625–3710)	227	32.8 (11.9–99.3)	63.5 (46.3–206)	53.7 (27.9–190)	77.0 (30.5–271)
		3 CS (2010)		1394 (808–1993)	243	16.4 (12.3–21)	102 (84.8–122)	71.3 (45.4–113)	53.1 (11.3–112)
		1 CS		621	173	5.1	111	23.6	33.1
		(not smoked)							
Vieira (2010) ¹¹	HPLC-UV; PAHC18 column	18 CS	16	506 (443–593)	2.5	NP	1.6 (1.23–1.91)	NP	0.9 (0.65–1.13)
		6 fresh		5758 (5336–6095)	138	NP	32.5 (19.6–40.3)	36.4 (15.1–60.5)	69.3 (7.4–95.3)
		6 partially dried			375	34.1 (18.9–54.7)	131.7 (89.2–162)	88.9 (81.2–93.1)	120.3 (105–145)
		6 dried		8307 (7614–9001)					
Ziegenhals (2008) ¹⁸	Fast-GC-HRMS;	8 CS	16	1101 (326–2662)	635	106.5 (75.8–236.5)	147.1 (83.6–374.6)	105.2 (63.5–258.1)	276.2 (125.7–746.3)
	GC-HRMS								
Kamangar $(2008)^{10}$	GC-MS	8 CS	21	1983 (536–2906)	282	37.1 (8.03–53.3)	72.8 (24.5–99.9)	51 (21.4–76.3)	121.4 (42.3–169)
Schlemitz (1997) ¹⁹	SFE; GC-MS	2 CS	16	7006 (6476–7536)	2230	496 (225–542)	154 (1.7–307)	1065 (387–1742)	515 (451–579)
Ruschenburg (1985) ¹⁵	GC-MS	5 CS	1	N/A	N/A	80^{a} (24–461)	N/A	N/A	N/A

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Table 2.

Transfer rates of polycyclic aromatic hydrocarbons to mate infusions.

Author (year)	Dry mate, amount of water, infusion time	Repeats	Findings
Tfouni ¹⁷ (2018)	1.5 g mate infused with 200 mL boiling water for 3 min	Once	B[a]P and other members of PAH4 were below the level of quantification, therefore no percentage was reported. The authors report that their findings are consistent with those of Duedahl-Olesen, showing a 2.3% transfer rate of PAHs into the infusions.
Thea ²⁰ (2016)	50 g mate infused with 30 mL of 70 (hot) or 4 C (cold) H_2O for 20s, repeat to collect 500 mL H_2O	16–17 times	Between 0.4 and 4.1 ng/g of B[a]P in dry mass was transferred into the hot infusions. B[a]P mass fraction in dry samples was not given. However, assuming a mass fraction of 40 ng/g (obtained from other studies), an estimated 1 to 10% of B[a]P in the samples were transferred in to hot infusions. Transfer to cold infusions was 3–4 fold lower.
Schulz ¹⁶ (2014)	20 g mate, infused in 2 L boiling H_2O for 10 min (and alternatively for 30 min)	Once	When brewing for 10 min, all PAHs in the infusion were below the limit of detection. When brewing for 30 min, a maximum of 0.50% of PAHs were transferred into the infusion.
Kamangar ¹⁰ (2008)	5 g mate, infused with 30 mL H_2O at 80 C (hot), or 5 C (cold) for 5 min; total 12 times	12 times	Approximately 9% of $B[a]P$ was transferred into the infusion after adding water the first time. Over 12 infusions, nearly 50% was transferred. There was no major difference between transfers to hot and cold infusions.
Zuin ²⁷ (2005)	1 g mate infused with 100 mL boiling H_2O for 5 min	Once	Approximately $1-2$ ng of B[<i>a</i>]P per gram of dry material was transferred into the infusion. Assuming that the dry samples had 40 ng/g of B[<i>a</i>]P, we can estimate a transfer rate of 2.5–5%.
Camargo ²⁶ (2002)	25 g mate infused with 500 mL boiling H_2O for 5 min	Once	Negligible amounts of PAHs were transferred into the infusions.
Ruschenburg ¹⁵ (1985)	15 g of mate infused with 1000 mL of water	Once	Approximately 2–10% of B[a]P was transferred into the infusion.

PAH: polycyclic aromatic hydrocarbon; B[a]P: Benzo[a]pyrene.