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Modified ion source triple quadrupole mass spectrometer gas chromatograph for polycyclic aromatic hydrocarbon analyses

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ABSTRACT

We describe modified gas chromatography electron-impact/triple-quadrupole mass spectrometry (GC–EI/MS/MS) utilizing a newly developed hydrogen-injected self-cleaning ion source and modified 9 mm extractor lens. This instrument, with optimized parameters, achieves quantitative separation of 62 polycyclic aromatic hydrocarbons (PAHs). Existing methods historically limited rigorous identification and quantification to a small subset, such as the 16 PAHs the US EPA has defined as priority pollutants. Without the critical source and extractor lens modifications, the off-the-shelf GC–EI/MS/MS system was unsuitable for complex PAH analysis. Separations were enhanced by increased gas flow, a complex GC temperature profile incorporating multiple isothermal periods, specific ramp rates, and a PAH-optimized column. Typical determinations with our refined GC–EI/MS/MS have a large linear range of 1–10,000 pg μl^{-1} and detection limits of <2 pg μl^{-1}. Included in the 62 PAHs, multiple-reaction-monitoring (MRM) mode enabled GC-EI/MS/MS identification and quantitation of several constituents of the MW 302 PAH isomers. Using calibration standards, values determined were within 5% of true values over many months. Standard curve r^2 values were typically >0.998, exceptional for compounds which are archetypally difficult. With this method benzo[a]fluorene, benzo[b]fluorene, benzo[c]fluorene were fully separated as was benzo[b]fluoranthene, benzo[k]fluoranthene, and benzo[j]fluoranthene. Chrysene and triphenylene, were sufficiently separated to allow accurate quantitation. Mean limits of detection (LODs) across all PAHs were 1.02 ± 0.84 pg μl^{-1} with indeno[1,2,3-c,d] pyrene having the lowest LOD at 0.26 pg μl^{-1} and only two analytes above 2.0 pg μl^{-1}; acenaphthalene (2.33 pg μl^{-1}) and dibenzo[a,e]pyrene (6.44 pg μl^{-1}).

1. Introduction

Polycyclic aromatic hydrocarbons (PAHs) are a widely distributed, highly-monitored class of contaminants, commonly defined as having two or more single or fused aromatic rings with shared carbon atoms and are typically found in complex mixtures. They originate from a number of sources; namely natural biological processes (biogenic), incomplete combustion (pyrogenic) and collection and utilization of fossil fuels (petrogenic). PAHs are semi-volatile with low vapor pressure and are resistant to chemical reaction, thus tending to accumulate rather than degrade [1,2]. Their lipophilic (hydrophobic) nature results in low aqueous solubility and leads PAHs to bioaccumulate across biological membranes. Atmospheric PAHs exist as either free gas-phase molecules, or associated with airborne particulate matter, with higher MW PAHs more likely to be particulate-bound [3–5].

There are three modes of human exposure to PAHs: (1) direct dermal contact, (2) inhalation and (3) ingestion, with inhalation and ingestion typically the primary pathways. Respiratory PAH burden includes both free and particulate-bound fractions. Hassan et al., demonstrated free gas-phase PAHs to comprise 67% of respiratory PAHs at a study site in Giza, Egypt [6]. Upon inhalation, non-particulate bound PAHs are immediately available to partition across biological membranes. Significant effort has been applied to clarify the association of inhaled PAHs with increased incidence of respiratory syndromes, especially asthma and lung cancer [7,8]. Food preparation, particularly smoking or high-temperature grilling of high-fat content meats, provides an immediate pathway to gastro-intestinal exposure to pyrogenic PAHs including

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benz[a]pyrene (BAP), a long-established carcinogen thought to play a role in cancers of the digestive tract [9–12]. To evaluate PAH exposures in humans, methods monitoring metabolites in urine have been established [13,14].

PAHs, including chemically modified oxy- and nitro-polycyclic aromatic hydrocarbons (OPAHs and NPAHs, respectively) as well as alkylated-PAHs (RPAHs), have been shown to undergo wide geographic dispersal far from originating sources [15] and subsets of PAHs have been demonstrated to be mutagenic and/or carcinogenic [16]. RPAH ratios are signature characteristics used to establish PAH sourcing [17]. In typical petrogenic mixtures, RPAHs are more abundant than their unsubstituted parental counterpart. Accurate source identification requires the ability to identify and quantitate both parental and alkylated products. Toxicological fates of PAHs are areas of active research and monitoring programs are widespread [18,19].

In 2010, the US Environmental Protection Agency (EPA) established a relative potency factor (RPF) approach for assessing both individual PAHs and complex PAH mixtures as part of their integrated risk information system (IRIS) [20]. For RPF determinations, potency was assessed relative to BAP using studies which included both BAP and additional PAHs. RPFs for individual PAHs were calculated relative to a BAP value assigned as 1.0. The EPA determined RPFs for 26 PAHs, including many not in the canonical suite of 16 PAHs the EPA has defined as priority pollutants. Several of these PAHs have RPFs significantly greater than BAP, including benz[l]aceanthrylene (RPF 5), dibenz[a,h]anthracene (RPF 10), benzo[c]fluorene (RPF 20), dibenzo[a,l]pyrene (RPF 30), and benz[j]aceanthrylene (RPF 60). Differential RPFs of these magnitudes accentuate the difficulty in accurate risk assessment when evaluating multipart mixtures, especially when limited in the number and type of identifiable PAHs. That PAHs typically occur in mixtures further emphasizes the need for improved methodology to identify and rigorously quantitate individual PAHs within these complex combinations.

The characteristics of PAHs – persistence, bioaccumulation, and pervasive human exposure with associated health risks – make the ability to monitor a wide range of PAHs of interest to a number of regulatory agencies, including the EPA, the National Oceanic and Atmospheric Administration (NOAA), the World Health Organization (WHO), European Committee for Standardization (CEN), European Food Safety Authority (EFSA), the Food and Drug Administration (FDA) and the United States Department of Agriculture (USDA), all of whom maintain active monitoring programs. The intellectual effort expended in developing resources for environmental sampling [21,22], extraction [23] and analysis of PAHs [9] from a variety of foodstuffs and environmental matrices are indications of the breadth of interest in PAH detection and quantification.

Historically, PAHs have been analyzed by high-performance liquid chromatography coupled to an ultraviolet (HPLC/UV), diode-array (HPLC/DAD) or fluorescence detector (HPLC/FLU); or gas chromatography with a flame ionization detector (GC/FID), GC/MS or GC/MS/MS [24–26]. Because PAH isomers have the same chemical formula and mass and share significant underlying structural similarities, MS products from isomers often share ion fragments with identical mass to charge ratios (m/z), thus accurate identification requires chromatographic separation of isomers prior to MS detection and final confirmation with appropriate standards.

High-throughput PAH determinations with "off the shelf" instrumentation, particularly single quadrupole systems, are problematic. Many labs encounter difficulties maintaining robust analysis conditions. After relatively few runs, internal standards (ISTD) will give inconsistent response across the calibration range and the range of external standard (ESTD) linearity diminishes. Marginally performing injectors and columns lead to poor resolution and greater peak broadening, limiting rigorous quantitation of detected analytes and preventing identification of additional PAHs of interest.

Additionally, high boiling points, particularly of large PAHs, lead to a marked tendency toward desublimation and deposition within the instrument, limiting sensitivity of detection, reproducibility of quantification and requiring high temperatures and iterative cycles of injector and instrument cleaning to restore performance. The propensity toward deposition also requires high inlet temperatures and the use of liners with glass wool. Efforts to increase separation, especially with high-molecular weight (HMW) PAHs, defined as having molecular weights greater than 300, include coupling liquid chromatographic (LC) separation with a 60 m GC column (LC–GC–MS), which increases separation but requires greater system gas pressures and extends run times [27–29]. Recently Sakuma et al., generated an application note describing an LC-MS/MS system utilizing a fluorescence detection (LC–FLD–MS/MS) method for PAH and RPAH analysis of a limited number of compounds, including 26 PAHs and 11 RPAH derivatives as well as 11 photo-oxidized PAH products [30]. While linearity with FLD detection was reported as four orders of magnitude, there were no r^2 values presented representing that range and the majority of PAHs analyzed were five-ring and smaller. Several additional published methods provide accurate PAH determinations, but are limited to relatively small subsets of analytes [31,32].

Initial efforts to perform rigorous analysis of PAHs using impact-ionization mass spectrometry (EI/MS) were unsuccessful. Using a standard EI source lacking H_2 injection, instrument performance would rapidly degrade. Attempts at rudimentary 3-point calibrations spanning 2 orders of magnitude were unsuccessful. Reinjection of the same standard gave highly variable results, with inter-day and intra-day variation of 25% or more. In its "off the shelf" configuration, the instrument was unsuitable for complex PAH analysis.

We developed a hydrogen-injected, self-cleaning ion source (SCIS) on the GC-EI/MS/MS system to address many of the difficulties encountered in PAH analysis mentioned above. The SCIS introduces hydrogen directly into the ion source through a specially engineered auxiliary pneumatic control module. We changed the extractor lens from the standard 3 mm to 9 mm. The modified instrument was coupled to a novel PAH-select column, and sensitivity and resolution were further refined through iterative adjustment of method parameters. The study presented here utilizes H_2 injection, a 9 mm extractor lens, a PAH-select column and the refined instrument parameters to demonstrate accurate quantitative identification of a suite of 62 PAHs ranging from the two-ring structure of naphthalene with a molecular weight (MW) of 128.17 and a boiling point (BP) of 218 °C, to PAHs in the 302 group with MWs of 302.17 and BPs up to 595 °C (dibenzo[a,l]pyrene). Also included in the suite of 62 are 20 accurately quantified RPAHs, providing the requisite analytical tools for precise PAH sourcing determinations. Additional PAHs within the 302 group were identifiable and application of the method enabled identification of several PAHs not previously identified or quantified from complex mixes, including high relative RPF compounds typically not quantifiable on standard 30 m columns. Only through these modifications were we able to quantify these 62 PAHs with excellent sensitivity and precision.

2. Materials and methods

2.1. GC/MS/MS

The GC/MS/MS instrument was an Agilent 7000B GC/MS/MS. Modifications were made to the instrument to improve the analytical performance in PAH analysis, see Fig. 1. The source was

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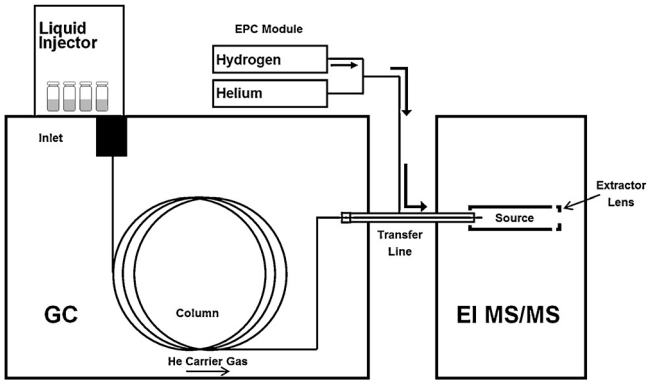

Fig. 1. Schematic of modified ion source triple quadrupole mass spectrometer GC. Hydrogen is injected directly in the EI MS/MS source during typical operation. Low pressure helium can be substituted when hydrogen is not required.

replaced with the extractor source from an Agilent 7000 C, which has increased thermal conduction to the draw-out lens from the source heater. The standard 3 mm extractor lens in the source was replaced with an optional 9 mm extractor. The transfer line was replaced with a CI transfer line, which has provision for sending a gas around the outside of the column and directly into the source. Hydrogen was supplied to the transfer line with an Electronic Pneumatic Control (EPC) module. The hydrogen channel of the EPC module contained a frit calibrated to inject 0.2 ml min^{-1} of hydrogen into the source with a pressure of 50 psi. When hydrogen injection is not required, the hydrogen pressure is set to off and a second channel of the EPC module is used to supply approximately 0.015 ml min^{-1} of helium to keep the path into the source purged. This configuration is referred to as the Self-Cleaning Ion Source (SCIS).

One microliter of sample was injected in pulsed splitless mode with an injector temperature of 320 °C, injection pulse pressure of 35 psi until 0.3 min, purge flow to split valve 25 ml min^{-1} at 0.7 min, thermal auxiliary 2 (MSD transfer line) heater at 320 °C and source temperature at 340 °C. Helium carrier gas was held at a constant flow of 2 ml min^{-1}. The injection liner was an Agilent Ultra Inert, single taper, repacked with a very small amount of deactivated glass wool (Restek, Bellefonte, PA). Sample was injected onto an Agilent J & W Select PAH column (part number CP7462), 30 m × 0.25 mm × 0.15 μm, with an oven program of 60 °C for 1 min, ramping 40 °C min^{-1} to 180 °C, 3 °C min^{-1} to 230 °C, 1.5 °C min^{-1} to 280 °C, hold for 10 min, ramp 6 °C min^{-1} to 298 °C then a final ramp of 16 °C min^{-1} to 350 °C with a 4 min hold at 350 °C. The QQQ collision cell helium quench gas was set to 2.25 ml min^{-1} with N_2 collision gas at 1.5 ml min^{-1}. Total run time was 47.25 min. Complete GC/MS/MS instrument conditions are appended in Supplemental Table S1.

2.2. Optimized PAH detection

Analyte separation was optimized through an iterative cycle of GC oven temperature profile adjustments derived from a method developed by Oostdijk and existing methodology in our laboratory [33,34]. Gas flow rates and temperature parameters were systematically evaluated by making minor changes in flow, temperature or ramp rate, and examining the effect on chromatographic separation for a population of reference compounds, including evaluating peak shape, and repeating the process. Final parameters include specifically defined ramp rates and ranges as well as the necessary inclusion of several isothermal holds which dramatically improve PAH separation.

2.3. Sample preparation

Solutions containing 62 native compounds were prepared by combining commercially available 16 EPA priority pollutant PAHs, custom PAH mixes and individual PAH standards made from neat stocks or solutions, then diluted to volume with isooctane. All standard commercial and custom mixtures were purchased from AccuStandard Inc. (New Haven, CT) and were guaranteed to be greater than 97% pure. Individual compound sources are listed in Table 1. Working standards were prepared by dilution of the stock standard with isooctane and stored in the dark at 4 °C. Perylene-D12 was purchased from Chemservice, Inc. (Westchester, PA) and used at 500 pg μl^{-1} as an internal standard for instrument quantitation. Perylene-D12 is a readily available standard reference material which gives robust and reproducible signal and was selected from the list of suitable internal standards recommended within EPA method 8270D. Because of its relatively large size (MW 264), it is emulative of larger PAHs, which are typically more analytically recalcitrant. Additional deuterated surrogates, naphthalene-D8, acenaphthylene-D8, phenanthrene-D10, fluoranthene-D10, chrysene-D12, benzo[a]pyrene-D12, and benzo[ghi]perylene-D12 were added at 500 pg μl^{-1} and used as internal-standard-corrected surrogates to quantify those compounds most similar in analytical behavior (complete list in Table 1). For analysis of samples requiring additional manipulations or extractions, these additional deuterated analytes also function as extraction and recovery surrogates [18,30]. All organic solvents were Optima grade from Fisher Scientific (Pittsburgh, PA).

2.4. Data analysis

GC/MS/MS data were analyzed using MassHunter Quantitative Analysis v.B.06.00 SP1 build 6.0.388.1 (Agilent Corp. Wilmington, DE) software. As indicated above, internal standard (ISTD) and surrogates were spiked at 500 pg μl^{-1} in the standard sets. Surrogate standards were quantified relative to the perylene-D12 internal standard. Native compounds were quantified relative to the most appropriate surrogate standard as defined by compound similarity and retention time as per EPA standard methodology. For example, naphthalene-D8, with a retention time (RT) of 4.12 min, is used to quantify eleven compounds ranging from naphthalene (RT = 4.13) to 2,6-diethylnaphthalene (RT = 6.22). In GC/MS/MS MRM each analyte was positively identified by retention time, target ion, and at least one unique confirmation ion. Confirmation ions must occur at the same retention time as target ions and had to be within ±30% of expected values to be considered confirmatory.

2.5. Method calibration and validation

PAHs were quantified using internal standard calibration with 7–9 point calibration curves with resulting coefficients of determination (r^2) typically >0.99. Extracted ion chromatograms (EICs) were used to calibrate each method. Typical calibration curves ranged from 1 to 10,000 pg μl^{-1}. The method was calibrated using EICs for each PAH. As per standard EPA methodology, the GC/MS/MS LODs for PAH compounds were determined by running the 1 pg μl^{-1} standard 7 times, calculating the standard deviation, and multiplying by the Student's t value for the 99% confidence interval. The LOQ was calculated as 5 times LOD.

3. Results and discussion

3.1. Effect of H_2 injection on system performance

Fig. 2 shows four separate metrics demonstrating the effect of H_2 addition on instrument performance. Panel A and B show

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Table 1
Complete list of the 62 PAH analytes examined in this study. PAHs quantified in this method are presented in order of elution, with retention times, quantifying and qualifying ions, limits of detection (LODs), and calibration fit (CF) r^2 values. r^2 values were determined from 7 to 9 point calibration curves as described in materials and methods and represent calibration ranges from 1 pg μl^{-1} to 10 ng μl^{-1}. CAS numbers and suppliers are also provided.

Peak #	Name	Molecular weight	Retention time	Quantifier precursor ion	Quantifier product ion	Collision energy (V)	Qualifier precursor ion	Qualifier product ion	Collision energy (V)	Detection limit LOD (pg/μl)	CF r^2	CAS #	Source
1	Naphthalene-D8 SS*	136.22	4.11	136	108	20	136	84	25	0.33	na	1146-65-2	CDN
2	Naphthalene†	128.17	4.12	128	102	20	128	78	20	1.04	0.9999	91-20-3	AS
3	2-Methylnaphthalene†	142.2	4.57	142	141	15	142	115.1	20	0.70	0.9998	91-57-6	AS
4	1-Methylnaphthalene†	142.2	4.69	142	141	15	142	115.1	20	0.28	0.9998	90-12-0	AS
5	2-Ethylnaphthalene†	156.22	5.00	141	115	15	156	141	15	0.97	0.9997	939-27-5	AS
6	2,6-Dimethylnaphthalene†	156.22	5.07	156	141	15	141	115	15	0.89	0.9999	28804-88-8	AS
7	1,6-Dimethylnaphthalene†	156.22	5.22	156	141	15	141	115	15	0.81	0.9998	575-43-9	AS
8	1,4-dimethylnaphthalene†	156.22	5.37	156	141	15	141	115	15	1.24	0.9994	571-58-4	AS
9	1,5 dimethylnaphthalene†	156.22	5.40	156	141	15	141	115	15	1.19	0.9999	571-61-9	AS
10	1,2-Dimethylnaphthalene†	156.22	5.49	156	141	15	141	115	15	0.94	0.9996	573-98-8	AS
11	Acenaphthylene-D8 SS*	160.24	5.66	160	158	30	158	156	30	0.33	na	93951-97-4	CIL
12	Acenaphthylene‡	152.19	5.69	152	126	30	152	102	30	2.33	0.9995	208-96-8	AS
13	1,8-Dimethylnaphthalene‡	156.22	5.72	156	141	15	141	115	15	0.83	0.9998	569-41-5	AS
14	Acenaphthene‡	154.08	5.86	153	127	30	153	77	45	1.07	0.9995	83-32-9	AS
15	2,6-Diethylnaphthalene‡	184.28	6.22	169	154	20	169	153	30	0.81	0.9999	59919-41-4	SA
16	Fluorene-D10 PRC	176.18	6.67	176	174	15	174	172	20	0.33	0.9992	81103-79-9	CIL
17	Fluorene‡	166.22	6.73	166	165	15	165	164	20	0.79	0.9970	86-73-7	AS
18	Dibenzothiophene‡	184.26	9.24	184	152	25	184	139	30	0.24	0.9965	132-65-0	AS
19	Phenanthrene-D10 SS*	188.29	9.60	188	160	20	188	186	15	1.67	na	1517-22-2	CIL
20	Phenanthrene§	178.23	9.71	178	152	25	176	150	25	0.46	0.9999	85-01-8	AS
21	Anthracene§	178.23	9.86	178	152	25	176	150	25	1.05	0.9998	120-12-7	AS
22	2-Methylphenanthrene§	192.25	11.61	192	191	20	192	189	40	0.39	0.9990	2531-84-2	AS
23	2-Methylanthracene§	192.25	11.75	192	191	20	192	189	40	0.47	0.9990	613-12-7	AS
24	1-Methylphenanthrene§	192.25	12.23	192	191	20	192	189	40	1.06	0.9995	832-69-9	AS
25	9-Methylanthracene§	192.25	13.24	192	191	20	192	189	40	0.87	0.9988	779-02-2	AS
26	3,6-Dimethylphenanthrene¶	206.28	13.24	206	191	16	206	205	16	0.42	0.9982	1576-67-6	AS
27	2,3-Dimethylanthracene¶	206.28	15.14	206	191	16	206	205	16	0.34	0.9979	613-06-9	AS
28	Fluoranthene-D10 SS*	212.32	15.53	212	208	35	210	208	15	1.67	na	93951-69-0	CIL
29	Fluoranthene¶	202.26	15.66	202	200	35	201	200	15	0.54	0.9984	206-44-0	AS
30	p,p′ DDE D8-PRC	326.07	16.26	254	184	30	326	254	15	1.67	0.9997	93952-19-3	CDN
31	9,10-Dimethylanthracene¶	206.28	17.20	206	191	16	206	205	16	0.85	0.9991	781-43-1	AS
32	Pyrene D10-PRC	212.31	17.20	212	208	35	210	208	15		0.9600	1718-52-1	CIL
33	Pyrene$	202.25	17.20	202	200	35	201	200	15	0.42	0.9983	129-00-0	AS
34	Retene$	234.34	17.38	219	204	20	219	203	20	0.84	0.9977	483-65-8	AS
35	Benzo[a]fluorene$	216.28	19.35	216	215	25	215	189	25	1.67	0.9999	238-84-6	SA
36	Benzo[b]flourene$	216.28	19.73	216	215	25	215	189	25	1.67	0.9999	243-17-4	SA
37	Benzo[c]fluorene$	216.28	19.83	216	215	25	215	189	25	0.30	0.9939	205-12-9	SA
38	1-Methylpyrene$	216.28	20.89	216	215	25	215	189	25	0.38	0.9987	2381-21-7	AS
39	Benz[a]anthracene$	228.29	25.75	228	226	30	113	112	10	0.75	0.9989	56-55-3	AS
40	Cyclopenta[c,d]pyrene$	226.27	25.95	226	225	30	226	224	40	0.53	0.9982	27208-37-3	AS

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Table 1 (*Continued*)

Peak #	Name	Molecular weight	Retention time	Quantifier precursor ion	Quantifier product ion	Collision energy (V)	Qualifier precursor ion	Qualifier product ion	Collision energy (V)	Detection limit LOD (pg/μl)	CF r^2	CAS #	Source
41	Chrysene-D12 SS*	240.38	25.95	240	236	35	240	212	30	1.67	na	1719-03-5	CDN
42	Triphenylene[$]	228.28	26.04	228	226	30	113	112	10	0.41	0.9988	217-59-4	AS
43	Chrysene[$]	228.28	26.10	228	226	30	113	112	10	0.50	0.9999	218-01-9	AS
44	6-Methylchrysene[$]	242.33	27.67	242	241	20	241	239	30	0.89	0.9978	1705-85-7	AS
45	5-Methylchrysene[$]	242.33	27.74	242	241	20	241	239	30	1.67	0.9998	3697-24-3	AS
46	Benzo[b]fluoranthene D12-PRC	264.38	30.25	264	260	35	264	236	30	1.67	0.9991	205-99-2	CDN
47	Benzo[b]fluoranthene[††]	252.31	30.35	252	250	30	126	113	10	0.37	0.9997	205-99-2	AS
48	7,12-Dimethylbenz[a]anthracene[††]	256.34	30.43	256	241	15	241	239	25	0.94	1.0000	57-97-6	AS
49	Benzo[k]fluoranthene[††]	252.31	30.48	252	250	30	126	113	10	0.53	0.9989	207-08-9	AS
50	Benzo[j]fluoranthene[††]	252.31	30.56	252	250	30	126	113	10	0.56	0.9997	205-82-3	CH
51	Benz[j]+[e]aceanthrylene[††]	252.31	31.25	252	250	30	250	248	30	1.67	0.9979	202-33-5 & 199-54-2	TRC
52	Benzo[e]pyrene[††]	252.31	32.25	252	250	30	126	113	10	0.71	0.9998	192-97-2	AS
53	Benzo[a]pyrene-D12 SS*	264.39	32.41	264	260	35	264	236	30	1.67	na	63466-71-7	CIL
54	Benzo[a]pyrene[††]	252.31	32.58	252	250	30	126	113	10	1.18	0.9997	50-32-8	AS
55	Perylene-D12	264.38	33.14	264	260	35	264	236	30		na	1520-96-3	CIL
56	Indeno[1,2,3-c,d] pyrene[‡‡]	276.33	40.34	276	274	45	138	137	15	0.26	0.9974	193-39-5	AS
57	Dibenz[a,h]anthracene[‡‡]	278.33	40.41	278	276	35	125	124	10	1.02	0.9981	53-70-3	AS
58	Picene[‡‡]	278.35	41.29	278	276	35	125	124	10	0.74	0.9984	213-46-7	SA
59	Benzo[ghi]perylene-D12 SS*	288.4	41.60	288	284	40	144	142	20	1.67	na	93951-66-7	CIL
60	Benzo[ghi]perylene[‡‡]	276.33	41.71	276	274	45	138	137	15	0.34	0.9988	191-24-2	AS
61	Anthanthrene[‡‡]	276.33	42.20	276	274	45	138	137	15	0.33	0.9969	191-26-4	CH
62	Naptho[1,2-b]fluoranthene[‡‡]	302.37	44.20	302	300	40	302	301	20	1.67	0.9992	5385-22-8	CH
63	Naptho[2,3-j]fluoranthene[‡‡]	302.37	44.28	302	300	40	302	301	20	1.67	0.9985	205-83-4	CH
64	Dibenzo[a,e]fluoroanthene[‡‡]	302.37	44.43	302	300	40	302	301	20	0.47	0.9984	5385-75-1	AS
65	Dibenzo[a,l]pyrene[‡‡]	302.37	44.59	302	300	40	302	301	20	0.48	0.9980	191-30-0	SA
66	Naptho[2,3-k]fluoranthene[‡‡]	302.37	44.84	302	300	40	302	301	20	1.67	0.9977	207-18-1	CH
67	Naptho[2,3-e]pyrene[‡‡]	302.37	45.18	302	300	40	302	301	20	1.67	0.9989	193-09-9	CH
68	Dibenzo[a,e]pyrene[‡‡]	302.37	45.50	302	300	40	302	301	20	6.44	0.9987	192-65-4	AS
69	Coronene[‡‡]	302.37	45.69	300	298	50	300	299	35	0.70	0.9984	191-07-1	CH
70	Dibenzo[e,l]pyrene[‡‡]	302.37	45.72	302	300	40	302	301	20	1.67	0.9987	192-51-8	CH
71	Naptho[2,3-a]pyrene[‡‡]	302.37	45.86	302	300	40	302	301	20	1.67	0.9676	196-42-9	PSCI
72	Benzo[b]perylene[‡‡]	302.37	45.93	302	300	40	302	301	20	1.67	0.9965	197-70-6	CH
73	Dibenzo[a,i]pyrene[‡‡]	302.37	46.03	302	300	40	302	301	20	1.42	0.9963	189-55-9	AS
74	Dibenzo[a,h]pyrene[‡‡]	302.37	46.83	302	300	40	302	301	20	0.52	0.9950	189-64-0	AS

Two or more qualifying ions were identified for each compound.
All compounds were quantified by absolute peak area.
*Surrogates and **internal standards were held at 0.5 ng/μl, target compounds were quantified by 1/X linear least-squares fit.
Source: AS = AccuStandard (New Haven, CT), CIL = Cambridge Isotope Laboratories, Inc. (Andover, MA), CDN = C/D/N Isotope Inc. (Quebec, Canada), FI = Fisher (Hampton, NH), CS = ChemService (West Chester, PA), SA = Sigma–Aldrich (St. Louis, MO), CH = Chiron AS (Trondheim, Norway), TRC = Toronto Research Chemical (Ontario, Canada), PSCI = Penn State Cancer Inst. (Hershey, PA), Surrogate used for quantitation: [†]Naphthalene-D8, [‡]Acenaphthylene-D8, [§]Phenanthrene-D10, [¶]Fluoranthene-D10, [$]Chrysene-D12, [††]Benzo(a)pyrene-D12, [‡‡]Benzo(ghi)perylene-D12.
PRC = Performance Reference Compound.

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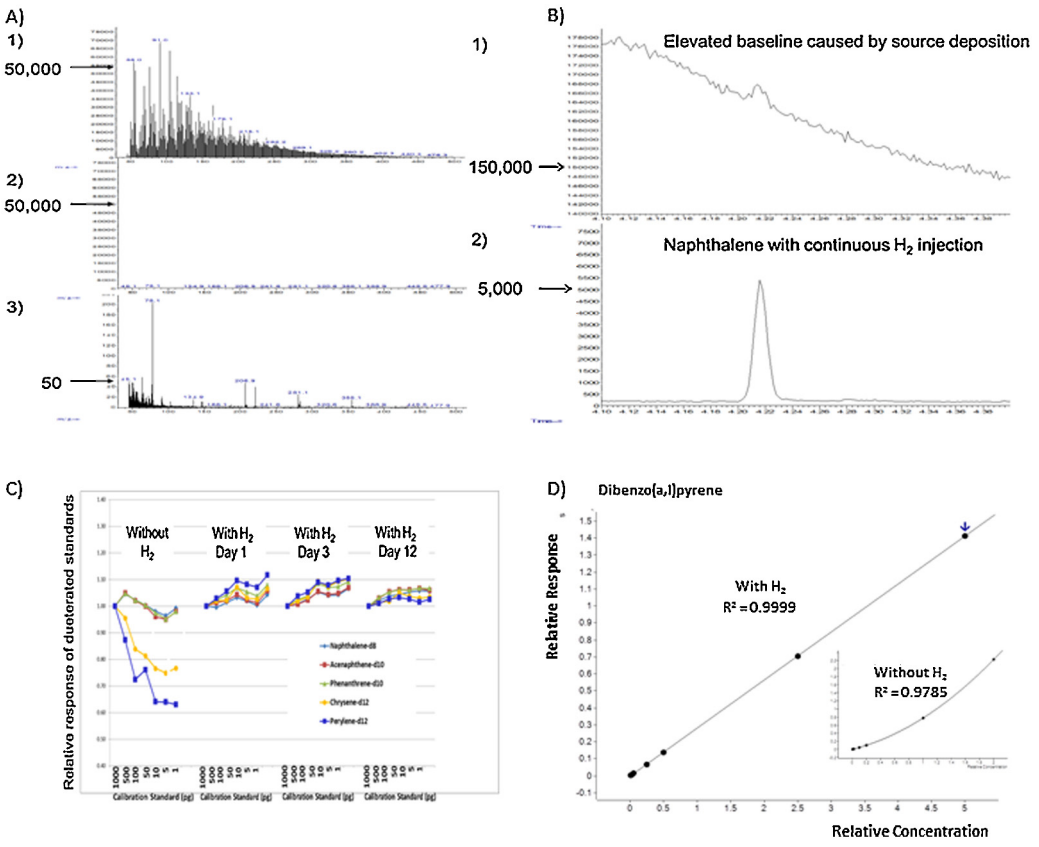

Fig. 2. Effect of hydrogen addition on GC/MS/MS instrument performance. Panel A, reduction in baseline with H2 addition. A-1, Hexane only was injected following 8 mixed PAH analytical runs without H_2 injection. Panel A-2, Hexane injected with H_2 continuous flow. Panel A-3, Expanded scale of hexane only injection with H_2 addition. Panel B, Restoration of analyte detection with H_2 addition. B1, 30 PAH standard mixture at 500 ng/analyte was injected after 8 previous runs of PAH analysis. B2, 30 PAH standard mixture at 500 pg/analyte was injected with H_2 augmentation, after 8 previous runs of PAH analysis without H_2. Panel C, stable and robust internal standard performance over time and concentration. Internal and surrogate standard signal was normalized to a 1000 pg sample over a 1–1000 pg calibration range. C1 IS/SS normalization without H_2 addition. C2 IS/SS normalization with H_2 addition on day 1. C3 IS/SS normalization with H_2 addition on day 3. C4 IS/SS normalization with H_2 addition on day 12. Panel D, Calibration curve of Dibenzo[a,l]pyrene run with continuous H2 from 1 to 1000 pg showing excellent linear fit ($r^2 = 0.99998$). Panel D inset attempted curve fit to dibenzo(a,l)pyrene calibration over the same range without H_2 ($r^2 = 0.9785$).

instrument baseline response to H_2, panel C shows standard response factor variability and robustness with time and concentration, and panel D shows calibration curves with r^2 values for an individual analyte, dibenzo[a,l]pyrene, injected with and without H_2 addition.

3.2. Accuracy

Table 2 shows representative accuracy determinations for naphthalene, benz[a]anthracene and dibenzo[a,l]pyrene over calibration range of four orders of magnitude. Determinations of absolute amounts of chrysene-D12 in the standard injections are also shown.

3.3. Identification and quantification of 62 PAHs

Results using the described method parameters on a model 7000B GC/MS/MS triple-quadrupole instrument retrofitted with a self-cleaning hydrogen injection system and 9 mm extraction lens are shown in Table 1, which lists the 62 analytes in elution

Table 2
Percent accuracy from a broad-range calibration curve. Calibration values for representative 2, 4 and 6-ring native compounds run as part of a complete calibration mixture are shown. Surrogate standard chrysene-D12 was included in each calibration mixture at 500 pg/μl.

Native compound Cal level (pg)	Naphthalene Accuracy (%)	Benz[a]anthracene Accuracy (%)	Dibenzo[a,l]pyrene Accuracy (%)	Deuterated compound Cal level (pg)	Chrysene-D12, SS Accuracy (%)
10000	101.4	102	105.2	500	103.8
5000	98	97.1	94.9	500	100.9
1000	98.5	98.2	86.1	500	97.9
500	96.4	94.8	81.6	500	97.6
100	95.2	93.6	76	500	99.1
50	96.3	92.4	74.3	500	99.3
10	96.5	89.9	80.1	500	99.5
5	95.4	95.2	100.7	500	101.5
1	122.2	136.7	201	500	100
Mean	99.99	99.99	99.99		99.96
SD	8.55	14.20	39.40		1.91

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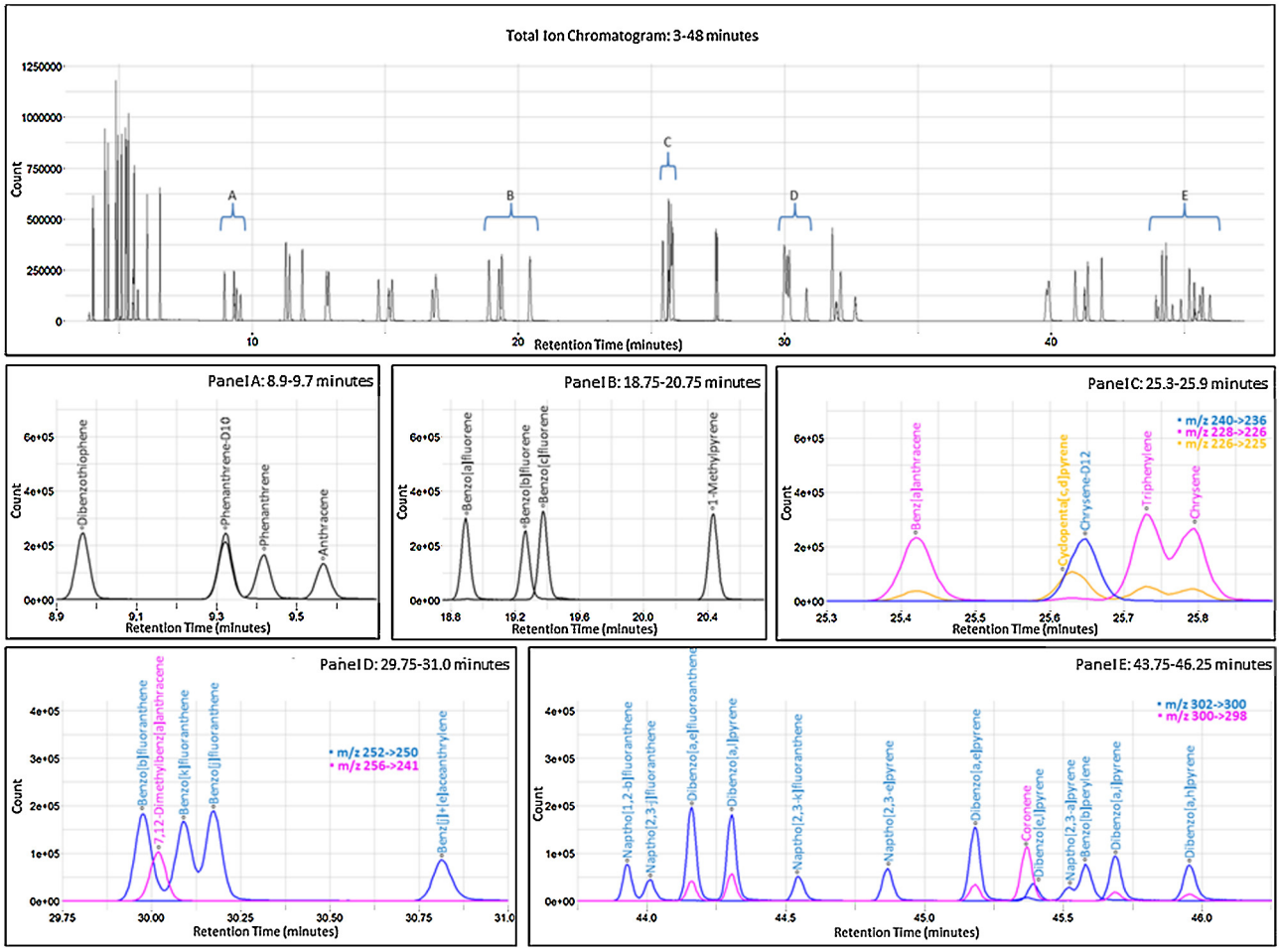

Fig. 3. Compiled total ion current (TIC) chromatographic trace representing 62 analytes, all at a concentration of 500 pg μl^{-1} analyzed on a triple-quadrupole GC/MS/MS retrofitted with a hydrogen injection, self-cleaning ion source (SCIS). Injections with 51 and 11 analytes respectively were used to generate one compiled trace. Panel A shows peaks for phenanthrene and anthracene. Panel B shows peaks corresponding to benzo[a]fluorene, benzo[b]fluorene, benzo[e]fluorene and 1-methylpyrene. Panel C shows the resolution of cyclopenta[c,d]pyrene and chrysene-D12, as well as triphenylene and chrysene. In Panel D, benzo[b]fluoranthene, benzo[k]fluoranthene, and benzo[j]fluoranthene are identified as well as 7,12-dimethylbenz[a]anthracene. Panel E shows the separation of multiple members of the PAH-302 group as well as coronene, a co-eluting compound mass-resolved from the 302 group by its *m/z* ratio.

order. Of particular interest are determinations of limits of detection (LOD) as well as the calibration fit r^2 (CF r^2) values for each analyte as calculated in Section 2. Mean CF r^2 value for the 62 PAH analytes is 0.9982 ± 0.004 from a seven point calibration curve spanning four orders of magnitude. Additional selectivity generated by the triple quadrupole instrument's capability to reduce instrument background by multiple-reaction-monitoring (MRM) analysis increased the linear range of response to span 1 pg μl^{-1} to 10,000 pg μl^{-1}. In our hands, systems without these modifications typically exhibit ≤ 0.98 r^2 values over a calibration range of only 10–1000 pg μl^{-1} (see Table S2).

Fig. 3 shows a compiled total ion current (TIC) chromatographic trace representing 62 analytes, all at a concentration of 500 pg μl^{-1} analyzed on a triple-quadrupole GC/MS/MS retrofitted with a hydrogen-injection, self-cleaning ion source (SCIS).

3.4. Discussion

Because of their broad distribution, environmental persistence and potential environmental and health influences, PAHs remain an ongoing interest of research groups and monitoring agencies. Regulatory concern is manifest by continuously evolving monitoring and risk assessment programs. As such, the ability to quickly and accurately identify and quantitate PAHs remains a priority. The method presented represents improvements in PAH detection and quantitation derived from both improvements in instrumentation, namely a self-cleaning ion source which provides H_2 injection into the MS source, a novel 9 mm extractor lens, a PAH-select column optimized for PAH separation and improvements in operation; specifically optimized gas flows and oven parameters. Utilization of the PAH-optimized column and the addition of hydrogen to the injection system allow robust and accurate determinations, decreasing instrument down-time. Additionally, the broad four order of magnitude range of linear instrument response greatly reduces the need for reanalysis of samples, increasing throughput for large-scale monitoring efforts.

Adding hydrogen to the mass spectrometer, with the filament current and electron filament on, is speculated to create active hydrogen species that clean the surfaces of the source and other components. Chromatograms generated using the hydrogen-injected source provided a consistently low baseline even after repeated injections, a significant improvement over the non-modified source. The low LOD supported by the consistent low baseline is especially important in analysis of environmental samples where relatively high LODs, as seen with previous instrumentation, might cause low-level contaminants to be undetected. Fig. 2 clearly demonstrates these phenomena. Panel A shows the improvement in baseline that occurs when a hexane blank is

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analyzed with a hydrogen-enabled SCIS on an instrument that has been fouled by previous PAH analytical runs. Consistently, baselines were reduced significantly (approximately three orders of magnitude in this instance). Panel B shows that the reduction in background is not driven by signal suppression, as native analyte signal remains consistent. The reduction in background now allows the detection of analyte signal that was previously masked by high non-specific signal. Panel C demonstrates both the dramatic improvement in standard signal consistency over a broad range of calibration concentrations and the robustness of day-to-day determinations over a 12 day test period. It is critical that signal from internal surrogates, present in all samples at constant concentration, is independent from overall analyte concentration. A typical result is seen in the "Without H_2" set of deuterated compounds in panel C. Perylene-D12 concentration is identical in all injections, but signal changes dramatically with the overall concentration of analytes in the complex mixture. Total PAH in these samples reflects the sum of all analytes, plus the deuterated standards. With the standard concentrations held at 500 pg, the range of ΣPAHs is from approximately 2500 pg for the 1 ppb calibration set with the majority of ΣPAHs coming from the deuterated standards, to 53,500 pg for the 1 ppm calibration set with the majority of ΣPAHs coming from the 51-PAH analyte mixture now present at a relatively high concentration. This consistent performance allows accurate quantitation of samples over a broad range of total concentrations, an important factor when analyzing environmental samples in which total concentration can vary widely. Panel D shows the improvement in linear response of benzo(a,l)pyrene, one of the 302 MW PAHs, shown with H_2 injection (main graph) and without (inset). r^2 values for the two linear fits are 0.9999 when run with H_2 injection, and 0.9788 without H_2. Supporting information Table S2 shows the effect on linear curve fit for several of the PAHs analyzed in this work. In no case, were r^2 values better without H_2 injection.

As demonstrated in Table 2, the results of the instrumentation changes led to exceptional accuracy over a broad calibration range relative to previously established GC/MS methodology. The mean value for absolute accuracy from nine determinations ranging from 1 pg μl^{-1} to 10,000 pg μl^{-1} for representative 2-ring (naphthalene), 4-ring (benz[a]anthracene), and 6-ring (dibenzo[a,l]pyrene) PAHs are all 99.99% with standard deviations of 8.5%, 14.2% and 39.4% respectively, with the majority of the deviation from the mean driven by the 1 pg μl^{-1} injection. Even with the relatively bulky 302 PAH dibenzo[a,l]pyrene, all values for injections from 5 pg μl^{-1} to 10,000 pg μl^{-1} were within 26% of their absolute values. Column 6 – entitled Chrysene-D12 SS – demonstrates the extraordinary repeatability shown by the chrysene-D12 surrogate standard (SS). Mean accuracy for the SS is 99.96% with an SD of 1.91%. As mentioned previously, the consistency of this determination indicates that internal standard response is not being affected by total PAH concentration, a common artifact in PAH analysis. This stands in marked contrast with our initial efforts with EI instruments where standard variability was so extreme that it precluded quantification calculations. The exceptional performance is not limited to only a few of the 62 analytes. Of particular note are the extraordinary sensitivity, accuracy and precision manifest by the low LODs and high r^2 values shown in the "detection limit" and "CF $r^{2''}$ columns of Table 1. Mean r^2 across the 62 analytes is 0.9982 ± 0.0041, with 29 analytes having r^2 values > 0.999. Mean LOD across all PAHs was 1.02 ± 0.84 pg μl^{-1} with indeno[1,2,3-c,d]pyrene lowest at 0.26 pg μl^{-1} and only two analytes with LODs above 2.0 pg μl^{-1}; acenaphthalene (2.33 pg μl^{-1}) and dibenzo[a,e]pyrene (6.44 pg μl^{-1}).

The robust nature of the described method is apparent in Fig. 3. The presented trace was generated by compiling TICs from separate injections of 51 and 11 PAHs (practical considerations of limited standard availability and expense prevented generation of a complete 62 analyte mix). The magnified regions of the chromatographic total ion current (TIC) each highlight a particular feature of the new method. Panel A shows clearly resolved peaks for phenanthrene and anthracene, two compounds indistinguishable by MS which require chromatographic separation. With the presented method, the two peaks are very well separated and easily identified and quantified. Panel B shows clearly defined peaks corresponding to benzo[a]fluorene, benzo[b]fluorene, benzo[c]fluorene and 1-methylpyrene, four compounds with identical transitions. Chromatographic separation allows individual identification and quantitation. The mass resolution capabilities of MRM mode using the GC/MS/MS is shown in Panel C by the resolution of cyclopenta[c,d]pyrene and chrysene-D12, two co-eluting compounds identifiable by their distinct m/z ratios and also shows full separation of benz[a]anthracene and partial chromatographic separation of triphenylene and chrysene. The ability to separate these commonly "lumped" analytes will allow for more accurate risk assessment. In Panel D, benzo[b]fluoranthene, benzo[k]fluoranthene, and benzo[j]fluoranthene show clear chromatographic separation, while co-eluting 7,12-dimethylbenz[a]anthracene is identified by its distinct transitions. Panel E shows the identification of multiple members of the PAH-302 group as well as coronene, a co-eluting compound mass-resolved from the 302 group by its distinct m/z ratio.

The ability to resolve alkylated PAHs from unsubstituted parental compound is critical in PAH sourcing. In cases where potential contaminant source is contested, the ability to differentiate petrogenic from pyrogenic or biogenic PAHs becomes even more critical. Recent studies by Jautzy et al., and Paulik et al., [35,36] as well as others have utilized PAH ratios to identify likely sources of detected PAHs. Amongst the 62 PAHs quantified by this method are 20 alkylated derivatives along with their parental counterparts. This broad spectrum of RPAH analytes provides another tool useful for determination of PAH contaminant origin.

PAHs identified within the MW 302 group include nine fully resolved analytes, two analytes which partially co-elute, and paired 300 and 302 PAHS which co-elute but are separable with appropriate mass selection. Included in this group is dibenzo[a,I]pyrene (RPF 30), one of the high RPF PAHs that are emerging as particular compounds of concern. As risk assessment evolves, accurate determinations of high RPF compounds are becoming a priority. Several studies have utilized a variety of methods for detection of some of these compounds [29,37–39]. Included in this method are three compounds with significantly higher RPF than BAP, dibenz[a,h]anthracene (RPF 10), dibenzo[a,I]pyrene (RPF 30) and benz[j]aceanthrylene (RPF 60). Benz[j]aceanthrylene with its exceptionally high RPF is quantified in neither the Oosdijk et al. nor Sakuma et al. methods [30,34]. The ability to accurately identify and quantify high-risk compounds such as these is critical to establishing accurate estimates of risk, particularly from complex mixtures.

In laboratory parlance, PAHs are considered "sticky", tending to foul instrumentation and requiring high levels of ongoing maintenance and instrument cleaning. While an existing method for quantifying 33 PAHs using GC/MS with a DB5MS column was used to generate data for a number of publications [40], attempts to expand the number of quantifiable analytes were unsuccessful due to difficulties maintaining rigorous quantification, even with known standard solutions. Substituting an EU-PAH column for the DB5MS column did little to alleviate the problems. Switching to a Select-PAH column on the same instrumentation allowed expansion of the number of quantifiable analytes, but only within a very limited dynamic range and with little intra-day robustness. Efforts to improve our ability to quantify additional PAHs on an "off-the-shelf" triple-quadrupole instrument were also unsuccessful, with

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day-to-day repetitions giving very erratic results. After extended effort, the conclusion drawn was that standard instrumentation was unsuitable to an expanded suite of PAH analytes, leading to considerations of the most appropriate instrument modifications that might improve PAH analysis.

Extractor lens dimension typically balances two performance parameters; sensitivity and dynamic range. Standard 3 mm lenses provide the greatest sensitivity but with limited dynamic range, while larger lenses provide extended dynamic range, but cost sensitivity. With the combination of the highly-selective MRM mode available on the triple-quadrupole instrument and the low baseline provided by the H_2-injected source, our rationale became to increase the extractor lens and attempt to increase the dynamic range, perhaps at the cost of some sensitivity of detection. Increasing the lens dimension from 3 mm to 6 mm did in fact increase the dynamic range, but with a surprisingly small reduction in sensitivity. The additional step from 6 mm to 9 mm again increased dynamic range, with only a minor difference in sensitivity. Importantly, the alteration of the 3 mm extraction lens to 9 mm also reduces the surface area available for PAH deposition, a consideration we hoped might solve our erratic ISTD problems. The final combination retains excellent sensitivity, broad dynamic range and provides extremely consistent ISTD values, as seen in Table 1.

With current methodologies, inadvertent misidentification of non-resolved peaks can lead to erroneous calculations of risk. In specific cases, such as chrysene and triphenylene, the inability to completely resolve co-eluting peaks has led to the practice of "lumping", such that the co-elution peak area is presumed to be equally descendent of both compounds. Risk assessment using such indiscriminately combined values is inherently inaccurate; an effect exacerbated by differences in RPF between co-eluting compounds [41].

Anticipating the application of the modified instrumentation to field-generated samples which might require extraction prior to analysis, seven additional deuterated standards ranging from two-ring (naphthalene-D8) to six-ring (benzo[g,h,i]perylene-D12) were utilized. While differences in analytical performance are always a consideration, pre-extraction addition of these surrogates provides a direct and rigorous method to correct for extraction and recovery efficiencies.

4. Conclusion

These improvements in the art allow rigorous and robust characterization of 62 individual PAHs from a complex mixture. H_2-injection into the source increased sensitivity and robustness by alleviating the need for iterative cleaning and recalibration. The incorporation of a 9 mm extractor lens in addition to the H_2-injection extended the dynamic range while retaining the sensitivity typical of a standard 3 mm lens. Meticulous optimization of method parameters and the utilization of a PAH-select column coupled with the novel instrumentation modifications expand the suite of PAHs subject to rigorous quantification. The ability to analyze a broader spectrum of PAHs on GC-EI/MS/MS instruments with these defined modifications increases opportunities for accurate monitoring and analysis which, in turn, leads to better opportunities for risk management and more effective regulation.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.chroma.2015.09.054.

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