Modern Environmental Science and Engineering (ISSN 2333-2581)
December 2016, Volume 2, No. 12, pp. 792-799
Doi: 10.15341/mese(2333-2581)/12.02.2016/005
Academic Star Publishing Company, 2016
www.academicstar.us

Determination of Organophosphate Esters in Cigarettes and Cigarette Smoke

Haruki Shimazu

School of Science and Engineering, Kindai University, Osaka, Japan

Abstract: The present study examines the concentration levels of organophosphate esters (OPEs) in cigarettes and cigarette smoke and to know the emission characteristics of OPEs. Seven OPEs were determined in cigarette smokes for five types of Japanese cigarettes. The median total OPE concentrations were 95.5 ng/m^3 before smoking and 282 ng/m^3 after smoking. The median concentrations of tris(2-butoxyethyl) phosphate (TBEP), which was the most abundant OPE, were 68.3 ng/m^3 before smoking and 253 ng/m^3 after smoking. Tris(2-chloroethyl) phosphate (TCEP) and triphenyl phosphate (TPP) were also detected frequently. The relationship between suspended particulate matter (SPM), TBEP, TCEP, and TPP after smoking is significantly proportional. This may indicate that the SPM formation is associated with those OPE formation during smoking. Furthermore, five OPEs were determined in the cigarettes. Median TBEP contents in the cigarettes ranged from N.D. to 9210 ng per cigarette, and the median TBEP emissions from cigarettes while smoking ranged from 3630 to 6730 ng per cigarette. The relationships between TBEP, TCEP and TPP after smoking were significantly positive. The results probably show that parts of TBEP in the cigarettes were transformed to TCEP and TPP, and those OPEs were emitted into the air.

Key words: cigarette, polycyclic aromatic hydrocarbons, sidestream cigarette smoke, suspended particulate matter

1. Introduction

Organophosphate esters (OPEs) are a group of man-made chemicals widely used worldwide as organic plasticizers, flame retardants, hydraulic fluids, antifoaming agents, and for other industrial applications. Global consumption of OPEs has increased from 186,000 to 292,000 tons between 2001 and 2011 [1, 2]. OPEs have been found in various environments, including air [3, 4], indoor air [5, 6], sediments [7, 8], soils [9, 10], and surface water [11, 12].

Some OPEs exhibit carcinogenic or neurotoxic properties. The World Health Organization (WHO) reported that tris(2-chloroethyl) phosphate (TCEP) and tris(1,3-dichloro-2-propyl) phosphate (TDCPP) were carcinogenic [13]. Tris(2-butoxyethyl) phosphate (TBEP) and tris(2-chloroisopropylethyl) phosphate are suspected carcinogens [13, 14]. TBEP, tributyl phosphate (TBP), TCEP, and triphenyl phosphate (TPP) are all considered neurotoxic [13-16]. Triethyl phosphate (TEP) is thought to be a weak enzyme inhibitor [17]. Therefore, OPEs are drawing attention in many countries. TCEP is on the Candidate List of substances of very high concern issued by the European Union [18]. The use of TCEP, TDCPP, and tris(1-chloro-2-propyl) phosphate (TCPP) as flame retardants in children's products is prohibited or about to be prohibited by the USA and Canada [19, 20].

Many studies have provided evidence that smoking is a major cause of lung cancer [21, 22] and heart disease [23, 24]. Cigarette smoke contains numerous toxic chemicals and carcinogens [25, 26]. This study examined the occurrence of OPEs in Japanese cigarettes and smoke. The primary objective of this work was to determine the concentrations of OPEs in

Corresponding author: Haruki Shimazu, Dr., research areas/interests: environmental engineering. E-mail: hshimazu@civileng.kindai.ac.jp.

cigarette smoke, and identify the emission characteristics of the OPEs.

2. Materials and Methods

2.1 Samples

Five brands of cigarettes were investigated in this study. Tar and nicotine contents per cigarette ranged from 1 to 21 mg and from 0.1 to 1.9 mg, respectively. Table 1 lists the OPE levels in air and cigarette samples before and after smoking.

The numbers of air samples collected for Brands A-D and Brand E were 5 and 4, respectively. The air sampling room was 2.5 m high, 5.3 m in length, and 5.0 m in width (approximately 66 m^3). The air samples were collected at a rate of 400 L/min for 2.0 h (48 m^3) using a high-volume air sampler (HV-500R; Sibata Scientific Technology Ltd., Souka, Japan) before the cigarettes were smoked. A quartz fiber filter (QR-100; Advantec, Tokyo, Japan) was used in the sampler. The filter had a minimum particle collection efficiency of 99.99% for particles 0.3 μm in diameter when air passed through the sampler at a speed of 5 cm/s. After the initial air sampling, two cigarettes were smoked in the sampling room. The sidestream smoke samples were collected at a rate of 400 L/min for 2.75 h (66 m^3). Particulate OPEs collected on the quartz fiber filters were analyzed as described below.

OPEs levels were analyzed in 4 cigarettes per brand. Cigarette filters and leaves were cut into three and six segments, respectively (Fig. 1). A segment of the filters and two segments of the leaves were analyzed as described below.

Table 1 Numbers of air and cigarette samples in this study.

	Air sample		Cigarette sample	
	Before smoking	After smoking	(before smoking)	
			Filter	Leaf
Brand A	5	5	4	8(4×2)
Brand B	5	5	4	8(4×2)
Brand C	5	5	4	8(4×2)
Brand D	5	5	4	8(4×2)
Brand E	4	4	4	8(4×2)
Total	24	24	20	40(20×2)

Note: Two segments of cigarette leaves for cigarette sample were analyzed.

2.2 OPEs

Table 2 lists the targeted seven OPEs in this study; we selected these OPEs because of their known toxic effects.

Seven standard material-grade OPEs were purchased from Tokyo Chemical Industry Co, Ltd, (Japan) and diluted with acetone and hexane, to produce calibration standards.

2.3 Analytical Methods and Instruments

The quartz fiber filters were weighed using an electronic scale before and after smoking. The filterswere cut into 16 segments after smoking. All

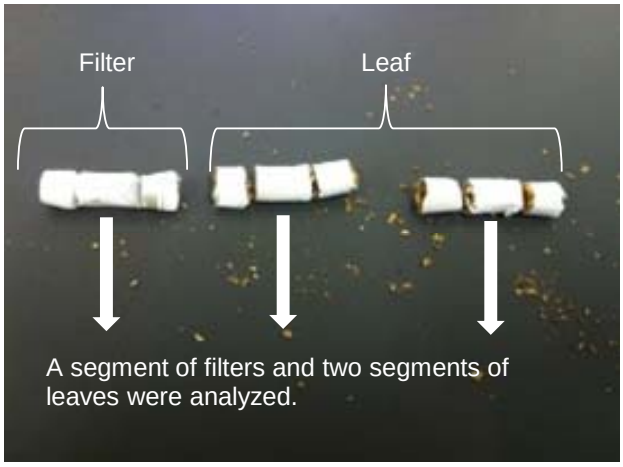

Fig. 1 Analyzed segments of cigarette sample.

Table 2 OPEsmeasured in this study.

OPEs	Abbr	DL
Tris(2-butoxyethyl) phosphate	TBEP	140
Tributyl phosphate	TBP	3.2
Tris(2-chloroethyl) phosphate	TCEP	14
Tris(1,3-dichloro-2-propyl) phosphate	TDCPP	170
Tris(2-ethylhexyl) phosphate	TEHP	42
Triethyl phosphate	TEP	6.0
Triphenyl phosphate	TPP	40

Note: The abbreviations are used in this study. The detection limits (DL) were calculated as three times the signal-to-noise ratio at the baseline of the chromatogram. DL units are pg per 2μL-extract.

segments were placed into 260-mL bottles and extracted with 40 mL of dichloromethane for pesticide residue and polychlorinated biphenyl analysis by Wako Pure Chemical Industries, Ltd. (Tokyo, Japan) for 15 min by ultrasonic cleaner. The extract was concentrated to 2 mL using a rotary evaporator, and filtered using a disposable filter device (PURADISCTM 25TF; Whatman, Maidstone, UK). The extract was then concentrated to 0.1 mL under N_2 flow. Next, hexane was added to the extract to produce a final volume of 2 mL.

Cigarette filters and leaves were weighed, placed into cellulose extraction thimbles, and extracted with 40 mL of dichloromethane for 15 min by ultrasonic cleaner. The extract was concentrated to 2 mL using a rotary evaporator, then filtered using a disposable filter and concentrated to 0.1 mL under N_2 flow. Hexane was then added to the extract to produce a final volume of 2 mL.

OPE concentrations in the extracts were determined using a gas chromatography-mass spectrometer (5975B inert XL E/CI MSD; Agilent Technologies, Santa Clara, CA, USA) equipped with an HP-5MS capillary column (30 m × 0.25 mm i.d., 0.25 μm film thickness; Agilent Technologies). The GC conditions were as follows: Splitless injection, 2 μL; injection port temperature, 250°C; GC temperature program: 70°C (hold 1.5 min) to 180°C at 20°C/min, and to 280°C at 5°C/min (hold 1 min); the carrier gas was helium. The mass spectrometer was operated in the electron impact mode with an electron energy of 70 eV. After each OPE was identified using three representative fragment ions, it was quantified using the largest one. Quantification was performed using an external calibration method. The detection limits shown in Table 2 were calculated as three times the signal-to-noise ratio at the baseline of the chromatogram. The recoveries and the variation coefficients of the measured OPEs ranged from 70 to 110% and from 5 to 20%, respectively.

Suspended particulate matter (SPM) concentrations were calculated as the difference between the weight of the quartz fiber filters before and after air sampling divided by 48 m^3 (before smoking) or 66 m^3 (after smoking).

3. Results and Discussion

3.1 OPEs in Air Samples

Seven OPEs were detected in the air samples before smoking the cigarettes (Table 3). TBEP, TBP, TCEP, and TEP were detected in all 24 samples. TPP was detected in 15 of the 24 samples. TDCPP and tris(2-ethylhexyl) phosphate (TEHP) were detected in one sample. The median concentration of TBEP, which was the most abundant OPE, was 68.3 ng/m^3, and its concentrations ranged from 28.1 to 246 ng/m^3. The median total OPE concentration was 95.5 ng/m^3, and the total OPE concentrations ranged from 44.2 to 307 ng/m^3.

All seven OPEs were also detected after smoking the cigarettes (Table 4). TBEP, TBP, TCEP, and TPP were detected in all 24 samples. Other OPEs were detected in 19 samples (TEP), three samples (TDCPP), and one sample (TEHP). The median concentration of TBEP, which was the most abundant OPE, was 253 ng/m^3, and its concentrations ranged from 169 to 333 ng/m^3. The median total OPE concentration was 282 ng/m^3, and the total OPE concentrations ranged from 184 to 376 ng/m^3. The concentrations of TBEP, TCEP, and TPP in the air samples were higher after smoking than before. The medians of those concentration differences between before and after smoking were 177 ng/m^3 for TBEP, 3.07 ng/m^3 for TCEP, and 2.18 ng/m^3 for TPP.

The concentrations of TBP, TDCPP, and TEHP before and after smoking were almost identical. However, the concentrations of TEP were higher before smoking than after.

The median concentration of SPM before smoking was 17 μg/m^3, and SPM concentrations ranged from 8 to 30 μg/m^3. After smoking, the median SPM concentration was 117 μg/m^3, and concentrations ranged from 96 to 146 μg/m^3. The relationships between

Table 3 OPEs in air samples before smoking.

	Brand A	Brand B	Brand C	Brand D	Brand E
TBEP	58.0 (5/5) [52.8-108]	55.0 (5/5) [28.1-123]	117 (5/5) [69.5-246]	66.7 (5/5) [48.2-117]	65.7 (4/4) [62.7-115]
TBP	23.7 (5/5) [6.88-27.0]	5.44 (5/5) [3.83-9.60]	13.2 (5/5) [5.84-47.3]	8.28 (5/5) [6.60-11.8]	10.3 (4/4) [9.82-11.3]
TCEP	9.13 (5/5) [7.84-10.1]	6.44 (5/5) [5.13-6.85]	7.35 (5/5) [4.12-7.96]	4.37 (5/5) [2.74-5.91]	13.2 (4/4) [11.6-14.5]
TDCPP	N.D. (0/5) [N.D.]	N.D. (1/5) [N.D.-4.47]	N.D. (0/5) [N.D.]	N.D. (0/5) [N.D.]	N.D. (0/4) [N.D.]
TEHP	N.D. (0/5) [N.D.]	N.D. (0/5) [N.D.]	N.D. (0/5) [N.D.]	N.D. (1/5) [N.D.-0.694]	N.D. (0/4) [N.D.]
TEP	3.77 (5/5) [2.51-5.56]	2.64 (5/5) [1.02-4.29]	5.33 (5/5) [2.58-6.85]	1.05 (5/5) [0.640-2.36]	4.72 (4/4) [3.89-7.41]
TPP	N.D. (0/5) [N.D.]	0.940 (5/5) [0.865-1.13]	0.848 (3/5) [N.D.-1.19]	0.970 (5/5) [0.654-1.26]	1.37 (2/4) [N.D.-3.40]
Σ7OPEs	92.9 (5/5) [73.7-147]	68.0 (5/5) [44.2-149]	141 (5/5) [82.0-307]	87.3 (5/5) [60.6-136]	99.8 (4/4) [88.4-142]

Table 4 OPEs in air samples aftersmoking.

	Brand A	Brand B	Brand C	Brand D	Brand E
TBEP	253 (5/5) [205-265]	259 (5/5) [252-285]	253 (5/5) [221-313]	187 (5/5) [169-240]	294 (4/4) [245-333]
TBP	13.3 (5/5) [7.90-14.3]	10.7 (5/5) [8.03-13.4]	11.5 (5/5) [9.85-38.3]	8.71 (5/5) [6.76-10.9]	14.2 (4/4) [11.8-16.3]
TCEP	14.8 (5/5) [12.2-15.6]	10.3 (5/5) [9.08-11.6]	7.25 (5/5) [6.57-8.89]	4.62 (5/5) [3.01-5.90]	17.3 (4/4) [15.7-18.0]
TDCPP	N.D. (0/5) [N.D.]	N.D. (0/5) [N.D.]	3.22 (3/5) [N.D.-3.33]	N.D. (0/5) [N.D.]	N.D. (0/4) [N.D.]
TEHP	N.D. (0/5) [N.D.]	N.D. (1/5) [N.D.-2.95]	4.45 (5/5) [1.51-6.76]	N.D. (0/5) [N.D.]	N.D. (0/4) [N.D.]
TEP	1.18 (5/5) [0.659-1.90]	N.D. (0/5) [N.D.]	1.33 (5/5) [0.735-1.78]	0.526 (5/5) [0.389-0.579]	1.27 (4/4) [1.02-1.78]
TPP	6.42 (5/5) [5.17-6.96]	3.09 (5/5) [2.96-3.32]	2.32 (5/5) [2.16-3.08]	2.49 (5/5) [1.94-3.06]	8.37 (4/4) [7.40-9.71]
Σ7OPEs	290 (5/5) [231-300]	282 (5/5) [278-313]	306 (5/5) [249-340]	203 (5/5) [184-258]	335 (4/4) [282-376]

Note: The upper values show median concentration (detection rate) and the lower values show [concentration range]. All units are ng/m^3. N.D. means not detected. Σ7OPEs means total OPE concentrations.

SPM concentrations and the concentrations of TBEP, TCEP, and TPP, which were detected frequently, were not proportional before smoking. However, the correlation coefficients between SPM and those OPEs after smoking were 0.597 ($p < 0.01$) for TBEP, 0.404 ($p = 0.05$) for TCEP, and 0.438 ($p < 0.05$) for TPP. This may indicate that SPM is associated with the formation of these OPEs during smoking.

3.2 OPEs in Cigarettes

The arithmetic means of the filter weights from the five cigarette brands (n = 4) were 0.24 g for Brand A, 0.25 g for Brand B, 0.25 g for Brand C, 0.24 g for Brand D, and 0.19 g for Brand E. The means for leaf weights were 0.54 g for Brand A, 0.58 g for Brand B, 0.58 g for Brand C, 0.67 g for Brand D, and 0.72 g for Brand E.

Table 5 displays OPE levels in cigarette filters. TCEP and TPP were not detected at all in the 20 samples. Other OPEs were detected in 19 samples (TBP), 12 samples (TEP), seven samples (TDCPP), and five samples (TBEP and TEHP). The median concentration of TBP, which was the most abundant OPE, was 676 ng/g, and TBP concentrations ranged from not detectable (ND) to 14,000 ng/g. The median

total OPE concentration was 3,430 ng/g, and total OPE concentrations ranged from ND to 22,200 ng/g.

Table 6 displays OPE levels in cigarette leaves. TBP was detected in 39 out of 40 samples. TBEP, TEHP, and TPP were detected in multiple samples. The median concentration of TBEP, the most abundant OPE, was 7,100 ng/g, and its concentrations ranged from ND to 24,900 ng/g. The median total OPE concentration was 9,780 ng/g, and concentrations ranged from 250 to 25,700 ng/g. The total concentrations of OPEs in cigarettes were higher in leaves than in filters.

3.3 OPE Emission Characteristics during Smoking

TBEP emission characteristics are described here because TBEP was the most abundant OPE found in our samples. Fig. 2 presents median TBEP contents in cigarettes and median TBEP emissions per cigarette during smoking. TBEP emissions per cigarette were calculated as the difference between concentrations before and after smoking multiplied by 66 m^3 and then divided by two, because two cigarettes were smoked during the experiments. Median TBEP contents ranged from ND (less than about 370) to 927 ng per cigarette for filters and from ND (less than about 700) to 8,410 ng per cigarette for leaves. Median TBEP emissions during smoking ranged from 3,630 to 6,730 ng per cigarette. For Brands A and D, the median of the sum of TBEP contents in cigarette filters and leaves was higher than the median TBEP emissions. For Brand E, the median of the sum of TBEP contents in cigarette filters and leaves was almost identical to the median TBEP emissions. Fig. 3 presents the relationships between TBEP, TCEP, and TPP after smoking for Brands A, D, and E. The correlation coefficients were 0.773 between TBEP and TCEP, and 0.867 between TBEP and TPP. TBEP was detected in cigarettes, but TCEP and TPP were not detected. This may imply that some TBEP in cigarettes was transformed to TCEP and TPP, and these OPEs were emitted into the air during smoking. Although TBEP concentrations in cigarettes were ND for Brand B and very low for Brand C, median TBEP emissions were high. The relationships between TBEP, TCEP, and TPP after smoking were not significant. Therefore, the TBEP production mechanism during smoking for Brands B and C cannot be elucidated from the results of this study.

Further experiments are needed to measure other OPEs in cigarettes and investigate other cigarette brands.

Table 5 OPEs in cigarette filters.

	Brand A	Brand B	Brand C	Brand D	Brand E
TBEP	3620 (3/4) [N.D.-5430]	N.D. (1/4) [N.D.-4320]	1520 (3/4) [N.D.-3190]	1360 (2/4) [N.D.-3910]	N.D. (0/4) [N.D.]
TBP	1160 (4/4) [710-1760]	475 (4/4) [143-642]	206 (4/4) [93.1-818]	1140 (3/4) [N.D.-1390]	3020 (4/4) [331-14000]
TCEP	N.D. (0/4) [N.D.]	N.D. (0/4) [N.D.]	N.D. (0/4) [N.D.]	N.D. (0/4) [N.D.]	N.D. (0/4) [N.D.]
TDCPP	6410 (4/4) [3740-9240]	N.D. (0/4) [N.D.]	N.D. (0/4) [N.D.]	N.D. (1/4) [N.D.-493]	1560 (2/4) [N.D.-7590]
TEHP	298 (2/4) [N.D.-1280]	N.D. (0/4) [N.D.]	159 (2/4) [N.D.-1580]	N.D. (0/4) [N.D.]	N.D. (1/4) [N.D.-620]
TEP	57.8 (2/4) [N.D.-159]	118 (4/4) [85.7-146]	113 (3/4) [N.D.-130]	81.9 (3/4) [N.D.-179]	N.D. (0/4) [N.D.]
TPP	N.D. (0/4) [N.D.]	N.D. (0/4) [N.D.]	N.D. (0/4) [N.D.]	N.D. (0/4) [N.D.]	N.D. (0/4) [N.D.]
Σ 7OPEs	12000 (4/4) [5610-15800]	698 (4/4) [229-4900]	2230 (4/4) [1950-3410]	2610 (3/4) [N.D.-5900]	4430 (4/4) [635-22200]

Table 6 OPEs in cigarette leaves.

	Brand A	Brand B	Brand C	Brand D	Brand E
TBEP	14700 (8/8) [6800-21400]	N.D. (2/8) [N.D.-1110]	1530 (8/8) [511-23400]	12600 (7/8) [N.D.-15400]	8410 (5/8) [N.D.-24900]
TBP	429 (8/8) [173-955]	310 (8/8) [201-916]	247 (8/8) [175-292]	79.6 (7/8) [N.D.-283]	410 (8/8) [250-10700]
TCEP	N.D. (0/8) [N.D.]	N.D. (0/8) [N.D.]	N.D. (0/8) [N.D.]	N.D. (0/8) [N.D.]	N.D. (0/8) [N.D.]
TDCPP	N.D. (2/8) [N.D.-1750]	N.D. (0/8) [N.D.]	N.D. (0/8) [N.D.]	N.D. (0/8) [N.D.]	N.D. (1/8) [N.D.-1190]
TEHP	715 (7/8) [N.D.-1770]	141 (5/8) [N.D.-263]	146 (5/8) [N.D.-1250]	409 (7/8) [N.D.-906]	392 (5/8) [N.D.-738]
TEP	129 (5/8) [N.D.-309]	68.5 (6/8) [N.D.-97.3]	35.4 (5/8) [N.D.-80.4]	78.7 (5/8) [N.D.-155]	N.D. (0/8) [N.D.]
TPP	N.D. (0/8) [N.D.]	N.D. (0/8) [N.D.]	N.D. (0/8) [N.D.]	N.D. (0/8) [N.D.]	N.D. (0/8) [N.D.]
Σ7OPEs	17200 (8/8) [7210-22800]	732 (8/8) [270-1610]	1830 (8/8) [987-24900]	12900 (8/8) [491-16300]	13400 (8/8) [250-25700]

Note: The upper values show median concentration (detection rate) and the lower values show [concentration range]. All units are ng/m^3. N.D. means Not detected. Σ7OPEs means total OPE concentrations.

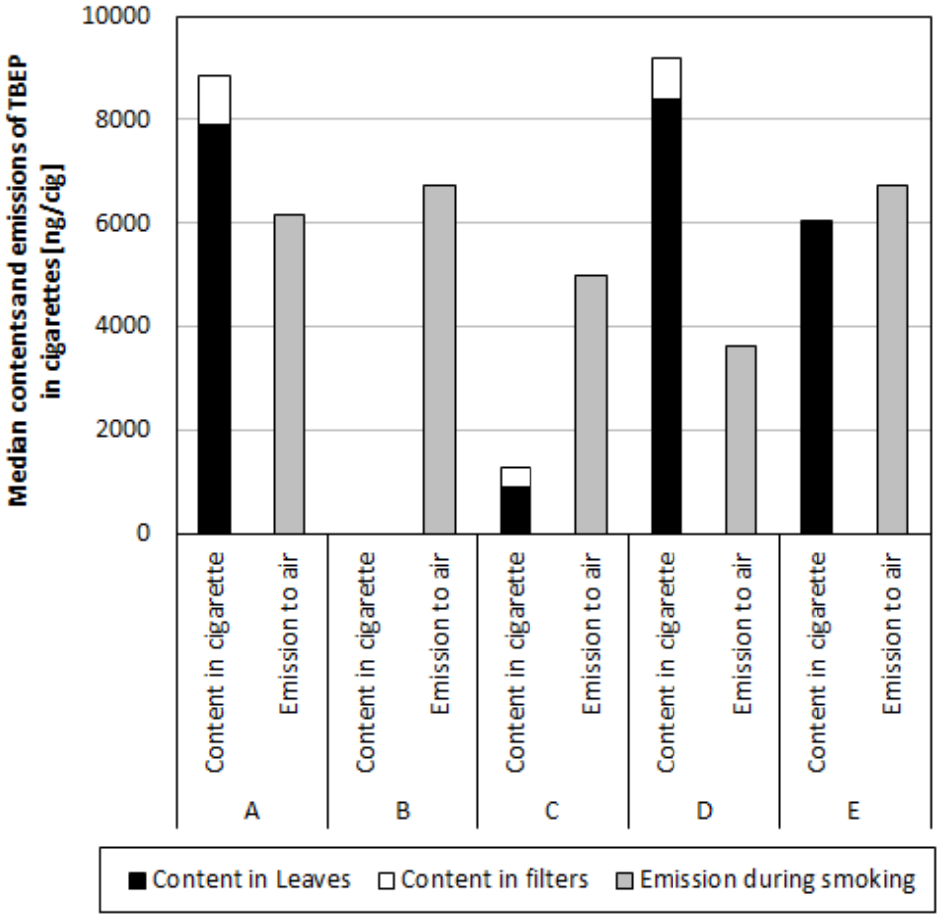

Fig. 2 Comparison of median TBEP contents in cigarettes and median TBEP emissions from cigarettes during smoking for Brands A–E. Solid bars and open bars show contents for leaves and filters

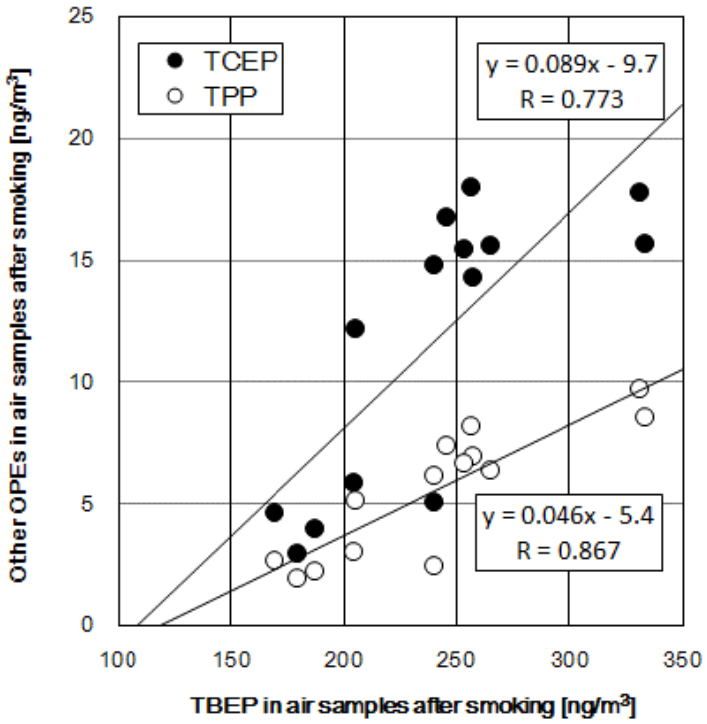

Fig. 3 Relationship between TBEP, TCEP, and TEP in air samples after smoking.

4. Conclusions

Seven OPEs in five cigarette brands and their formation and emissions during smoking were investigated. OPEs were measured in air samples before and after smoking. TBEP was the most abundant OPE detected. Significant proportional relationships were observed between SPM concentrations and the concentrations of TBEP, TCEP, and TPP after smoking. This may indicate an association between OPE formation during smoking and SPM.

Five of the OPEs were also detected in the cigarettes. The concentrations and contents of total OPEs were higher in cigarette leaves than in cigarette filters.

In several brands of cigarettes, the relationships between TBEP, TCEP, and TPP after smoking were significantly positive. TBEP was detected in cigarettes, but TCEP and TPP were not detected; this may imply that some TBEP is transformed to TCEP and TPP during smoking.

References

[1] A. Marklund, B. Andersson and P. Haglund, Organophosphorus flame retardants and plasticizers in Swedish sewage treatment plants, *Environ. Sci. Technol.* 39 (2005) 7423-7429.

[2] Townsend Solutions, *Plastic Additives 8 Global Market Study*, 2012.

[3] A. Salamova, M. H. Hermanson and R. A. Hites, Organophosphate and halogenated flame retardants in atmospheric particles from a European arctic sites, *Environ. Sci. Technol*. 48 (2014) 6133-6140.

[4] S. Lai, Z. Xie, T. Song, J. Tang, Y. Zhang, W. Mi, J. Peng, Y. Zhao, S. Zou and R. Ebinghaus, Occurrence and dry deposition of organophosphate esters in atmospheric particles over the northern South China Sea, *Chemosphere* 127 (2015) 195-200.

[5] M. A. Abdallah and A. Covaci, Organophosphate flame retardants in indoor dust from Egypt: Implications for human exposure, *Environ. Sci. Technol.* 48 (2014) 4782-4789.

[6] F. Yang, J. Ding, W. Huang, W. Xie and W. Lei, Particle size-specific distributions and preliminary exposure assessments of organophosphate flame retardants in office air particulate matter, *Environ. Sci. Technol.* 48 (2014) 63-70.

[7] Y. Kawagoshi, I. Fukunaga and H. Itoh, Distribution of organophosphoric acid triesters between water and sediment at a sea-based solid waste disposal site, *J. Mater. Cycles. Waste Manag.* 1 (1999) 53-61.

[8] H. W. Chung and W. H. Ding, Determination of organophosphate flame retardants in sediments by microwave-assisted extraction and gas chromatography–mass spectrometry with electron impact and chemical ionization, *Anal. Bioanal. Chem.* 395 (2009) 2325-2334.

[9] E. Fries and I. Mihajlovic, Pollution of soils with organophosphorus flame retardants and plasticizers, *J. Environ. Monit.* 13 (2011) 2692-2694.

[10] H. Shimazu, T. Shibata, T. Horie, Bioaccumulation characteristics of organophosphoric acid triesters and polycyclic aromatic hydrocarbons in *Phragmites*, *J. Water Environ. Technol.* 11 (2013) 287-297.

[11] J. A. Andresen, A. Grundmann and K. Bester, Organophosphorus flame retardants and plasticisersin surface waters, *Sci. Total Environ.* 332 (2004) 155-166.

[12] E. Martínez-Carballo, C. González-Barreiro, A. Sitka, S. Scharf and O. Gans, Determination of selected organophosphate esters in the aquatic environment of Austria, *Sci. Total Environ.* 388 (2007) 290-299.

[13] WHO, Flame Retardants: Tris(chloropropyl) phosphate and tris(2-chloroethyl) phosphate, *Environmental Health Criteria 209*, 1998.

[14] WHO, Flame Retardants: Tris(2-butoxyethyl) phosphate, tris(2-ethylhexyl) Phosphate and tetrakis (hydroxymethyl) phosphonium salts, *Environmental Health Criteria 218*, 2000.

[15] WHO, Tributylphosphate, *Environmental Health Criteria 112*, 1991.

[16] WHO, Triphenylphosphate, *Environmental Health Criteria 111*, 1991.

[17] R. E. Gosselin, R. P. Smith, and H. C. Hodge, *Clinical Toxicology of Commercial Products* (5th ed.), Baltimore, 1984, p. II-302.

[18] European Chemicals Agency, *Inclusion of Substances of Very Concern in the Candidate List*, 2009.

[19] TÜV Rheinland Group, *US Tightens Requirements on Flame Retardants for Children Products*, 2013.

[20] Health Canada, *Regulations Amending Schedule 2 to the Canada Consumer Product Safety Act (TCEP)*, 2014.

[21] C. H. Lee, Y. C. Ko, L. S. Cheng, Y. C. Lin, H. J. Lin, M. S. Huang, J. J. Huang, E. L. Kao, H. Z. Wang, The heterogeneity in risk factors of lung cancer and the difference of histologic distribution between genders in Taiwan, *Cancer Causes Control.* 12 (2001) 289-300.

[22] IARC, Tobacco smoke and involuntary smoking, *IARC Monographs on the Evaluation of the Carcinogenic Risks to Humans*, 2004, p. 83.

[23] A. C. Villablanca, J. M. McDonald and J. C. Rutledge, Smoking and cardiovascular disease, *Clin. Chest. Med.* 21 (2000) 159-172.

[24] B. Messner and D. Bernhard, Smoking and cardiovascular disease — Mechanisms of endothelial dysfunction and early atherogenesis, *Arterioscler. Thromb. Vasc. Biol.* 34 (2014) 509-515.

[25] IARC, Overall evaluations of carcinogenicity: an updating of IARC monographys, Vols. 1-42, Suppl. 7. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, 1987.

[26] IARC, Some non-heterocyclic polycyclic aromatic hydrocarbons and some related exposures. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, 2010, p. 92.