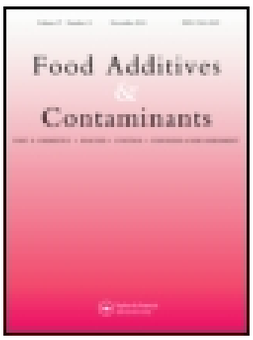

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Polyphenylsulfone (PPSU) for baby bottles: a comprehensive assessment on polymer-related non-intentionally added substances (NIAS)

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ABSTRACT

Polyphenylsulfone (PPSU) is a new material for the production of baby bottles. PPSU is a polyether plastic formally composed of bisphenol S (BPS) and 4,4′-dihydroxybiphenyl (DHBP), which both have slight endocrine activities in *in vitro* tests. So far, little is known about the presence and the release of potentially hazardous substances from PPSU baby bottles. In this study, we present a three-step approach for the analysis of PPSU starting with polymer characterisation in terms of chemical structure, total oligomer content and hydrolytic stability. Second is the determination of extractables focussing on monomers, monomer derivatives, linear and cyclic oligomers below 1000 Da and residual solvent. Third is a risk assessment on migration-related substances in accordance to European Union plastics regulation no. 10/2011 based on triplicate consecutive migration experiments using official milk simulant 50% ethanol. We analysed five types of PPSU baby bottles from different brands as well as corresponding raw materials from different manufacturers by various analytical techniques (high-performance liquid chromatography (HPLC)-diode array detector /fluorescence detector/Corona/electrospray ionisation-MS, HPLC-size exclusion chromatography, gas chromatography-mass spectrometry (GC-MS), ^{1}H-NMR). We found significant variations of PPSU materials from different producers with regard to polymer and oligomer chain end groups (methoxylation, chlorination), while total oligomer content below 1000 Da was similar (mean about 0.48%). BPS was not detected above 0.3 mg/kg polymer in any PPSU sample. Residual DHBP content ranged between 1.7 and 15.5 mg/kg polymer. The most common oligomer in all PPSU samples was the cyclic tetramer (about 1200 mg/kg polymer), which is the only cyclic compound below 1000 Da. Residual solvent, sulfolane, was determined to a maximum of 1300 mg/kg polymer. In migration tests, we detected exceedances of neither specific migration limits for listed substances nor of thresholds of toxicological concern for non-listed substances (monomer derivatives, oligomers). Based on our analytical results, no concerns exist regarding migration of polymer-related substances from PPSU baby bottles.

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Polyphenylsulfone; PPSU; baby bottles; NIAS assessment; bisphenol S (BPS); oligomers

Introduction

Since polycarbonate (PC) was restricted for the production of plastic baby bottles by the European Union (2011a), a variety of alternative materials has been established on the baby bottle market. Based on its low price and suitable properties, polypropylene (PP) became the most common plastic material for infant feeding bottles. Besides the catalytically polymerised isotactic PP material, several polycondensate plastics like polyamide, Eastman Tritan™ (Eastman) copolyester and polyethersulfone (PES) have a smaller market share (Onghena et al. 2014), while nothing was reported about baby bottles made from polyphenylsulfone (PPSU), to date.

A major problem of baby bottles made from PC is the low stability of the material against hydrolysis under slight alkaline pH conditions (Biedermann-Brem and Grob 2009). Hydrolysis can cause a release of the PC monomer bisphenol A (BPA), which is a known endocrine disruptor (Vandenberg et al. 2009; Rochester 2013; Yang et al. 2013; Kabir et al. 2015). In general, hydrolysis is also conceivable for other polycondensate plastics. Out of the mentioned variety of PC alternative materials for baby bottles, PES and PPSU are also made from bisphenols similar to BPA. PES is a polyether exclusively built from bisphenol S (BPS) units, while in PPSU polymer, BPS alternates with 4,4′-dihydroxybiphenyl (DHBP). For both substances, BPS (Héliès-Toussaint et al. 2014; Kang et al.

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2014; Rochester and Bolden 2015; Simon et al. 2016) and DHBP (Nishihara et al. 2000; Olsen et al. 2003), weak endocrine, especially estrogenic activities similar to BPA, were detected in *in vitro* test assays. However, for PES material or extracts, results were negative in estrogenic *in vitro* assays (Kang et al. 2014; Bittner et al. 2014; results for non-UV/microwave-stressed PES bottles).

The analysis of substances released from plastic infant feeding bottles is mostly based on migration experiments in accordance to the European Union (EU) plastics regulation no. 10/2011 (European Union 2011b) using a mixture of water and ethanol (50 vol.%) as official milk simulant applying three consecutive migrations at 70°C for 2 h for repeated use articles and hot-fill conditions (Simoneau et al. 2012; Onghena et al. 2014). Samples are often collected from the market, which might affect analysis results in terms of possible cross-contamination with substances released from components other than the baby bottle material. Main cross-contamination sources are bottle packaging (e.g. based on recycled paper or cardboard), printing inks used for the bottles, bottle leaflets or just gas phase transfer from the environment. Examples for these effects are positive detection of benzophenone as contamination from printing inks and the identification of recycled paper indicator contaminants like diisobutyl phthalate or 2,6-diisopropyl naphthalene in bottles made from Tritan™, silicone or PP presented by Simoneau et al. (2012) and Onghena et al. (2014).

In our study, we present an approach of a systematic analysis of a new material, PPSU, used for the production of infant feeding bottles. Besides PPSU baby bottles collected from the market, we also analysed bottles directly provided by the manufacturers as well as the corresponding PPSU raw material pellets. We divided our study into three major parts. First is the general characterisation of PPSU materials from different manufacturers dealing with questions of hydrolytic stability, polymer size, polymer composition and total content of substances below 1000 Da as potential migration-related substances. Second is the identification and quantification of polymer-related substances, especially monomers, monomer derivatives, oligomers below 1000 Da and residual solvents, which are extractable from the PPSU materials. Third is a risk assessment based on migration experiments in accordance to EU plastics regulation no. 10/2011 (European Union 2011b).

Materials and methods

Samples

All PPSU samples analysed in this study are listed in Table 1. Three different types of PPSU raw material pellets were directly provided by the baby bottle producers. One non-food-grade material was marketed. Five types of baby bottles made from PPSU were provided either by the baby bottle producers (n = 3) or were sampled from the market (n = 2). Baby bottles from the producers were packed in aluminium foil and to avoid cross-contamination were not equipped with final caps, teats, leaflets or packaging. Bottles PPSU-F1 and PPSU-F3, made from the corresponding raw material pellets PPSU-G1 and PPSU-G3, respectively, were unprinted. Bottles PPSU-F4 and PPSU-F5, collected from the market, were packed in PET/board cartons, equipped with PP caps and silicone teats.

In addition, we used PES, PC and Eastman Tritan™ (EX401) polymer pellets, purchased from the manufacturers, to compare hydrolytic stability of PPSU materials. PES was also used as reference

Table 1. PPSU sample materials analysed in this study.

Sample category	Sample code	Raw material manufacturer	Baby bottle brand	Additional information
PPSU raw material	PPSU-G1	A	1	Amber ('natural') pellets
	PPSU-G2	Unknown	2	Amber ('natural') pellets
	PPSU-G3	B	1	White ('natural') flakes
	PPSU-G4	Unknown	–	Black coloured pellets, no food grade
PPSU baby bottle	PPSU-F1	A	1	300 mL, from the producer, produced from PPSU-G1
	PPSU-F2	Unknown	2	150 mL, from the producer
	PPSU-F3	B	1	300 mL, from the producer, produced from PPSU-G3
	PPSU-F4	A	3	320 mL, from the US market
	PPSU-F5	Unknown	4	260 mL, from the European market

material for size exclusion chromatography (SEC) and ^{1}H-NMR experiments.

Chemicals

Commercially available

Reference substances. DHBP (99%) and BPS (99%) were from Alfa Aesar (Karlsruhe, Germany). 4,4′-Cyclohexylidenebisphenol (BPZ, 98%), 4,4′-dimethoxybiphenyl (DMBP, 99%), biphenyl (BP, 99%), 2-aminobenzamide (ABA, 98%), sulfolane (99%) and dicyclohexylmethanol (DCHM, 98%) were purchased from Sigma-Aldrich (Steinheim, Germany). 4-Hydroxy-4′-methoxybiphenyl (HMBP, 95%) was from TCI Europe (Zwijndrecht, Belgium). 4,4′-Dichlorodiphenyl sulfone (BPS-CC, 97%) was from Acros Organics (Geel, Belgium). Irganox® 245 (98%), Tinuvin® 234 (99%) and Uvinul® 3030 (97%) were donated by BASF SE (Ludwigshafen, Germany).

Reagents. Iodomethane (99%) was from Acros Organics. Lithium chloride (LiCl, 99%), sodium sulphate (puriss. pa 99%), ammonium formate (for mass spectrometry 99%), sodium (in kerosene, 99.8%) and tetramethylsilane (TMS, analytical standard 99.5%) were from Sigma-Aldrich. Citric acid (99.5%) and potassium carbonate (99%) were purchased from Grüssing (Filsum, Germany).

Solvents. Methanol (MeOH, gradient grade 99.9%) was from Merck Chemicals (Darmstadt, Germany). Ethanol (EtOH, absolute 99.95%), acetonitrile (ACN, HPLC super gradient 99.95%), dimethyl sulfoxide (DMSO, analytical reagent 100%), isohexane (HPLC grade 98%) and 2-propanol (HPLC grade 100%) were purchased from VWR Chemicals (Fontenay-ous-Bois, France). Deuterated dimethyl sulfoxide (DMSO-d_6, 99.8%) was from Deutero. Deuterated chloroform (99.8%) was from Armar AG. Dichloromethane (DCM, HPLC grade 99.9%), acetone (Rotisolv HPLC 99.9%) and chloroform (99.9%) were from Carl Roth (Karlsruhe, Germany). Ethyl acetate (EA, puriss. p.a. 99.5%), diethyl ether (puriss. analytical 99.5%) and 1,4-dioxane (reagent plus 99%) were purchased from Sigma-Aldrich. Formic acid (FA, LC-MS grade) was from J&K chemicals. Dimethylformamide (DMF, 99.94%) was from Fisher Scientific. Tetrahydrofuran (THF, reagent grade 99%) was from Honeywell Research Chemicals and tert-butyl methyl ether (chem solute. reinst 99%) was from TH Geyer (Renningen, Germany). Double-distilled water was prepared in-house (Destamat® Bi 18E).

Self-synthesised

1,1′-Sulfonylbis[4-methoxy-benzene (BPS-MM). Methoxylation of BPS was performed according to Chang et al. (2013). In a round-bottomed flask, BPS (1 g) and potassium carbonate (2.7 g) were diluted in acetone (50 mL) and heated and stirred for 30 min at 50°C. Subsequently, iodomethane (2.5 mL) was slowly added dropwise. After 15 h reaction time at 50°C, the reaction was stopped. At this point, the conversion of BPS to BPS-MM was 64% (percentage of BPS-MM peak area compared to peak areas of BPS and by-products, HPLC UV-255 nm determined using chromatography method M1). For purification of BPS-MM, the reaction mixture was filtered, evaporated with a rotary evaporator (Heidolph VV 2000), dissolved in DCM and washed with water. After evaporation, the residue was purified using a self-packed silica gel 60 (Merck) column (filling height 20 cm, diameter 4.5 cm) with isohexane/EA (3:1, v/v) as eluent. The eluent of the BPS-MM fraction was evaporated and the purity of the dried BPS-MM product was 99.0% (HPLC UV-255 nm peak area percentage).

1-Chloro-4-[(4-methoxyphenyl)sulfonyl]-benzene (BPS-CM). Methoxylation of BPS-CC was performed according to Langler et al. (2003). In a three-necked flask, (MeOH, 10 mL) was added dropwise to sodium (0.45 g). Subsequently, BPS-CC (4.9 g) was added and the reaction was performed for 5 days at 65°C. At this point, the conversion of BPS-CC to BPS-CM was 49% (percentage of BPS-CM peak area compared to peak areas of BPS-CC and by-products, HPLC UV-255 nm, determined using chromatography method M1). Water (80 mL) was added to the reaction mixture for precipitation of BPS derivatives. After evaporation, the mixture was fractionated using a self-packed silica gel 60 column (filling height 20 cm, diameter 4.5 cm) using isohexane/EA (3:1, v/v) as eluent. The eluent of the BPS-CM fraction was evaporated and the purity of the dried BPS-CM product was 99.3% (HPLC UV-255 nm, peak area percentage).

Instrumentation

^{1}H-NMR spectrometer

A Bruker Avance III 600 MHz NMR spectrometer was used for polymer characterisation in free induction decay mode with zg30 pulse program and 20 s relaxation delay time. Spectra were recorded at room temperature and normalised with TMS as chemical shift reference (0.0 ppm).

Size exclusion chromatography

Analysis was performed using a Merck-Hitachi D-7000 HPLC system composed of L-7200 autosampler, L-7100 quaternary pump, L-7614 degasser, L-7350 column oven and L-7455 diode array detector (DAD). Two SDV SEC columns (1000 Å 300 × 8 mm 5 µm and 100 Å 300 × 8 mm 5 µm) from Polymer Standards Service were connected in series. Isocratic eluent was DMF with lithium chloride (5 g/L) to prevent adduct formation. Flow was 1 mL/min, column oven temperature was 50°C and injection volume was 10 µL. Chromatograms were recorded at a wavelength of 275 nm because of the specific UV absorption of the eluent.

Reversed phase (RP)-HPLC

Three RP-HPLC systems with different detectors were used for the determination of monomers and oligomers. For oligomer identification, an Agilent 1200 HPLC-DAD/ESI(+)-MS system equipped with G1329 autosampler, G1312 binary pump, G1375B degasser, G1316A column oven, G1315 DAD and G6410A Triple Quadrupole MS was used. Detection mode was positive electrospray ionisation (ESI+) with a fragmentation voltage of 100 V and a total ion current (TIC) mass range from 80 to 1.500 amu. For monomer and oligomer quantification in extract and migrate solutions, a Thermo Fisher Scientific Ultimate 3000 HPLC-DAD/Corona system equipped with WPS-3000SL autosampler, DGP-3600SD dual tertiary pump, SRD-3600 degasser, TTC-3000SD column oven, DAD-3000 DAD detector and Corona Veo charged aerosol detector (CAD) without inverse gradient compensation was used. For CAD measurement, a power function value of 1.0 and an evaporator temperature of 35°C were adjusted. Migrate solutions were analysed with an Agilent 1100 series HPLC-DAD/fluorescence detector (FLD) system equipped with G1313A autosampler, G1312A binary pump, G1322A degasser, G1316A column oven, G1315B DAD and G1321A FLD. FLD settings (extinction/emission wavelengths) were 272/356 nm optimised for selective and sensitive detection of DHBP derivatives. All DAD chromatograms were recorded at a wavelength of 255 nm.

Two different chromatographic methods were used for HPLC monomer and oligomer separation. Method 1 (M1): 250 × 3 mm stainless steel column with Multospher 120 RP18 HP 5 µm material (CS Chromatography Service). Mobile phase was FA in water (eluent A; 0.015%; v/v) and ACN/2-propanol (eluent B; 80/20; v/v). Percentage of B increases in the first 40 min from 27% to 90% continuing to 100% at 52 min, holding this for 18 min followed by an equilibration step for additional 10 min. Flow was 0.5 mL/min, oven temperature was 35°C and injection volume was 10 µL. Method 2 (M2): 125 × 2 mm stainless steel column with Nucleodur C18 HTec 3 µm material (Macherey-Nagel). Mobile phase was A: FA in water (0.015 vol.-%) and B: ACN/2-propanol (2/1; v/v). Percentages of B were 36% (start conditions), 66% (8 min), 72% (12 min), 90% (from 19 to 21 min) followed by an equilibration plateau (36%) until 28 min. Flow was 0.35 mL/min, oven temperature 45°C and the injection volumes were 2 µL for extract solutions and 100 µL for migrant solutions.

GC-MS

Determination of volatiles was performed on an Agilent 7890A gas chromatograph equipped with 7683 autosampler, 7683B injector and 5975C mass detector with electron impact ionisation. An HP-5 capillary column (length 30 m, diameter 0.25 mm, 0.25 µm film) from Hewlett-Packard was used for separation. The screening temperature programme started at 50°C (4 min holding) followed by a linear heating rate of 15°C/min until 22 min. Helium flow was 1.0 mL/min, and the splitless injection volume was 1 µL. TIC chromatograms were recorded with a mass scan range between 40 and 800 amu.

Methods

Polymer characterisation

Average molecular mass and polymer chain end groups. To achieve a homogenous polymer powder, pellets or bottle materials were ground in a ball mill

(Retsch MM 400, Haan, Germany) after liquid nitrogen treatment. About 10 mg powder was completely dissolved in deuterated chloroform (PPSU) or deuterated DMSO (PES), respectively, and analysed by ^{1}H-NMR. For average molecular mass calculation, signals were normalised by the number of representing protons. The signals of the aromatic protons from BPS and DHBP in the polymer chain were put into relation to the signals of the aromatic protons from chlorinated BPS moieties as well as the protons from the methoxylated end groups.

Relative oligomer content below 1000 Da. Ground polymer powder of PES or PPSU was completely dissolved in DMF with a concentration of 1 g/L and analysed by SEC. The 1000 Da cut was calculated by using PES reference chromatograms with the characteristic peak pattern of the cyclic BPS oligomers (n = 3 to n = 7). The percentage of oligomers below 1000 Da was calculated relative to the total peak area in the SEC chromatograms at an UV wavelength of 275 nm.

Stability against hydrolysis. About 50 mg ground polymer powder was treated by 2 mL of aqueous solutions of citric acid (0.1 M, pH 2.0) or sodium carbonate (0.1 M, pH 11.1), respectively. Simulated hydrolysis was performed in a sealed 4 mL glass vial for 1 and 2 h at 100°C (Pierce Reacti Heating/Stirring Module 18971). The reaction solutions were cooled, admixed with 500 µL ACN, neutralised and centrifuged (5 min, 4000 rpm). The monomers were determined by HPLC-DAD/Corona using HPLC chromatography method M1.

Extractables

Identification of oligomers. About 100 mg ground polymer powder was extracted with 2 mL ACN for 1 h at 120°C in a sealed 4 mL glass vial. The extract solutions were analysed by HPLC-DAD/ESI(+)-MS using M1. To promote specific adduct formation, about 10 mg/L ammonium formate was added to the eluents A and B prior to analysis. Oligomers were tentatively identified by the combination of the predicted molecular masses M of their $[M + H]^+$ (proton), $[M + 18]^+$ (ammonium, main masses) and $[M + 39]^+$ (potassium) adducts and the retention behaviour.

Quantification of monomer derivatives and oligomers. To determine an UV wavelength of almost equal absorbance, UV spectra of available BPS and DHBP monomer derivatives were recorded. For this, stock solutions of each substance with equal concentrations of 0.05 mmol/L diluted in ACN were analysed using a Carl Zeiss Specord® S600 spectrophotometer with 10-mm-quartz cuvettes. UV spectra were recorded at room temperature with blank subtraction of ACN solvent. For verification of photometric results, standard substance calibration curves for the available BPS and DHBP monomer derivatives were recorded and compared between 252 and 260 nm using HPLC-DAD and chromatography method M1.

Total extraction of monomers and oligomers below 1000 Da from PPSU polymer powder was achieved by a 10 times consecutive extraction with ACN (100 mg powder, 10 times 2 mL ACN, 120°C, 1 h). For oligomer quantification based on the UV chromophore properties of the oligomers, the linear calibration curve of BPS was used (UV λ = 255 nm). Oligomer UV quantification results were verified by HPLC-CAD measurements using second-degree polynomial calibration curves of the plastic additives Irganox® 245, Uvinul® 3030 and Tinuvin® 234 as unspecific non-volatile reference substances.

Determination of volatiles. BP and sulfolane were determined from ACN extract solutions of ground polymer (100 mg powder, 2 mL ACN, 1 h, 120°C) by GC-MS. DCHM (concentration 1 mg/L) was used as internal standard (IS) for compensation of MS detector variations. Quantification was done by external linear calibration with reference substances of BP and sulfolane.

Migration-related substances

Migration experiments into food simulants. Prior to first use, baby bottles were rinsed two times with hot water (70°C). In accordance to EU plastics regulation (European Union 2011b), bottles were filled to the maximum filling mark with preheated (70°C) food simulant for milk (50 vol.% EtOH in double distilled water). The open bottles were covered by a watch glass. BPZ (0.1 mg/L) in the simulant solution was used as IS for the compensation of slight volume losses. Triplicate consecutive migration experiments were performed in a preheated water bath

(Gesellschaft für Labortechnik, Typ 1012) for 2 h at 70°C. Between two migration experiments, the baby bottles were rinsed with hot water again.

The migration experiments with new bottles were repeated with double distilled water (no official food simulant) and, for a worst-case consideration, with a minimum bottle filling of 20 mL (50 vol.% EtOH), respectively. For all tests, blanks were performed using glass beakers.

Determination of non-volatiles. After the migration step, EtOH from the milk simulant 50% EtOH was mainly removed by a gentle nitrogen stream (reduction of the volume from 2 to about 0.8 mL). An aliquot of 20 µL of a second volume standard solution containing ABA (10 mg/L in ACN) was added before analysis with HPLC-DAD/FLD using chromatography method M2 and a large injection volume of 100 µL.

Determination of volatiles sulfolane and BP. After migration step, a liquid–liquid extraction of 50% EtOH migrant solution (10 mL aliquot) with chloroform (2 mL) was done by vortexing (IKA MS1 Minishaker) the mixture for 1 min. The resulting volume of the separated organic phase (mixture of EtOH and chloroform) was determined in preliminary experiments to be 4.4 mL (triple determination, RSD: 1.1%) using a measuring cylinder. For determination of volatiles, 1 mL aliquot of the organic phase was admixed with 100 µL DCHM IS solution (concentration 1 mg/L in chloroform), dried over sodium sulfate and analysed by GC-MS. Quantification was done with external linear standard calibration curves of BP and sulfolane.

Results and discussion

PPSU polymer is usually produced by etherification of the hydroxy component (DHBP) with the chlorinated BPS derivative BPS-CC in an aprotic polar solvent with high boiling point like *N*-methyl-2-pyrrolidinone or sulfolane under alkaline conditions (Blinne and Cordes 1978; Liedloff et al. 2014; Weber et al. 2014). After the polymerisation step, a modification of the residual reactive end groups is achieved by a methoxylation reaction of polymer chains using chloromethane. This information about the PPSU production processes was meaningful regarding the prediction of the polymer structure and of possible polymer-related non-intentionally added substances like oligomers ('predictable NIAS').

PPSU polymer characterisation

Average molecular mass and polymer chain end groups

Figure 1(A) shows the ^{1}H-NMR spectra of two PPSU materials from two different manufacturers. For ^{1}H-NMR calculations, all signal areas were determined in relation to signal number 9 of the methoxy end group, which is always represented by three protons (see Figure 1(A)).

$$Q_{\mathrm{OMe/Cl}} = \frac{\left(A_9/3\right)}{\left(A_1/2\right)} \tag{1}$$

$$Q_{\mathrm{BPS/DHBP}} = \frac{A_3 + A_2}{A_6 + A_7} \tag{2}$$

$$\mathrm{AM_W} = \frac{2}{\left(A_9/3\right) + \left(A_1/2\right)} \cdot N \tag{3}$$

$$N = \sum_x \frac{A_x}{n_x} \cdot M_x \tag{4}$$

$$N = \frac{(A_2 + A_3) \cdot 232.2\ \mathrm{Da}}{4} + \frac{(A_6 + A_7) \cdot 168.2\ \mathrm{Da}}{4} + \frac{A_1 \cdot 27.5\ \mathrm{Da}}{2} + \frac{A_9 \cdot 24.0\ \mathrm{Da}}{3} \tag{5}$$

The ratio of methoxy and chlorine end groups ($Q_{\mathrm{OMe/Cl}}$) in the polymer was determined using Eq. (1), where A_9 represents the signal area of the three methoxy protons (A_9) and A_1 represents the signal area of the two aromatic BPS protons next to the Cl position as shown in Figure 1(A). The molar ratio of BPS and DHBP units in the polymer chain ($Q_{\mathrm{BPS/DHBP}}$) was calculated following Eq. (2), where A_3 and A_2 represent the signal areas of the aromatic BPS protons next to the sulfonyl group and A_6 and A_7 represent the signal areas of the aromatic DHBP protons next to the CC-bridge between the phenyl groups.

As presented in Figure 1(B), significant differences exist between PPSU materials from different manufacturers. While chlorinated end groups

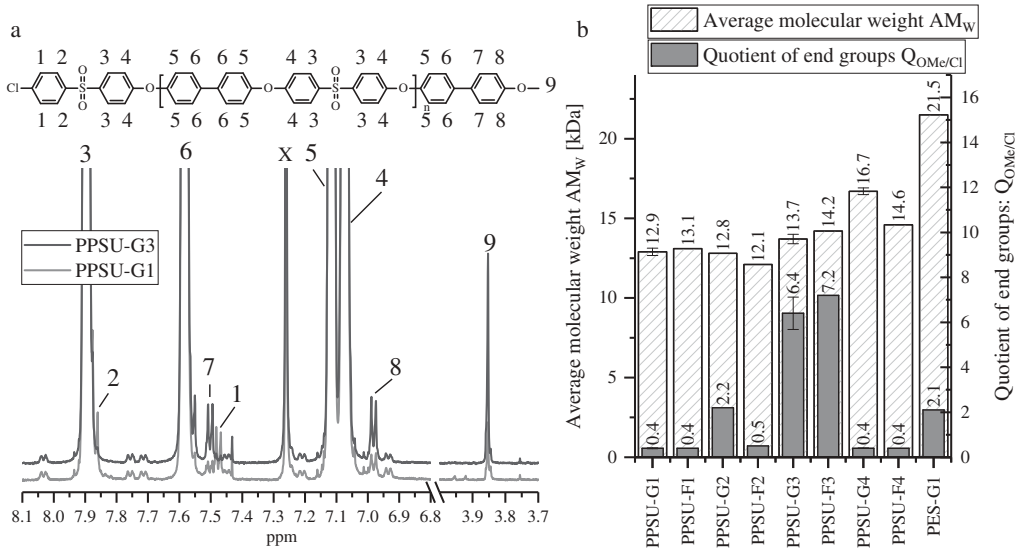

Figure 1. (a) ^{1}H-NMR spectra and signal declaration of two PPSU materials diluted in deuterated chloroform. Signal X is caused by residues of chloroform in the solvent. (b) Calculated polymer average molecular mass AM_W and quotient $Q_{OMe/Cl}$ of molar polymer chain end group relation of methoxy (OMe) and chlorinated (Cl) groups. When displayed, error bars represent the standard deviation of double determination.

dominate in PPSU-G1 (manufacturer A), polymer chain ends are mainly methoxylated in PPSU-G3 (manufacturer B). Furthermore, the ratio of BPS units compared to DHBP is 1.01 for PPSU-G1 and 0.98 for PPSU-G3. This calculation indicates that mainly BPS units are chlorinated while DHBP units are methoxylated. This is a plausible consequence of the monomers BPS-CC and DHBP that are supposed to be used in the polymerisation process of PPSU. A third material PPSU-G2 ($Q_{BPS/DHBP}$ 0.99), from an undisclosed manufacturer, has an intermediate end group characteristic compared to PPSU-G1 und PPSU-G3. The baby bottle PPSU-F1 ($Q_{BPS/DHBP}$ 1.01) is produced from the PPSU-G1 material as well as PPSU-F3 ($Q_{BPS/DHBP}$ 0.98) from PPSU-G3, which could be confirmed by the ^{1}H-NMR experiments. In contrast, we determined differences between PPSU-G2 and PPSU-F2 ($Q_{BPS/DHBP}$ 1.01) provided by the same baby bottle manufacturer. This indicates that at least this PPSU-G2 lot was not used to produce PPSU-F2.

We calculated the average molecular weight (AM_W) of PPSU polymers using Eqs. (3)–(5), where A_x is the signal area, M_x is the molecular weight of the represented molecule structure, n_x is the number of protons causing the signal and N is a sum as defined and presented by Eqs. (4) and (5). Index x represents signals 2 and 3 for BPS as well as 6 and 7 for DHBP units in the polymer chain, and signal 1 for chlorinated as well as signal 9 for methoxylated end groups. To calculate M_x values of the molecular structures as presented in Eq. (5), half of the mass of oxygen (8 Da) was assigned at all binding positions between all four different structure units (BPS, DHBP, OMe, Cl). Example 1: signal 1 represents Cl in end group position. This signal is caused by two (n_1 = 2) aromatic protons of a BPS unit next to the Cl end group (see signal 1 in Figure 1(A)). For calculation, the mass of this structural unit is 27.5 Da (M_1) as the molar weight of Cl (35.5 Da) is reduced by 8 Da (half of the oxygen molar mass). The remaining 8 Da have already been taken into account in the mass calculation by signal 2 (M_2). Example 2: signals 2 and 3 represent the four (n_2 = 4, n_3 = 4) aromatic protons of the BPS structure next to the sulphonyl group. Signal 2 as defined in Figure 1 only differs from signal 3 when BPS is in the end group position of the polymer chain. The masses (M_2 as well as M_3) of all BPS-based units in the polymer chain are 232.2 Da.

As presented in Figure 1(B), AM_W of PPSU samples ranges between 12.1 and 16.7 kDa. AM_W of the PPSU polymer samples was determined under the assumption that all polymer chain ends are either chlorinated or methoxylated. This simplified estimation has two probably negligible shortcomings: small amounts of existing hydroxylated end groups as well as the presence of cyclic oligomers were not taken into account (see

identification and quantification of oligomers). In ^{1}H-NMR spectra analysis, no evidence of significant amounts of residual hydroxylated end groups for any PPSU sample was detected. In contrast, no differentiation between signals from cyclic and linear PPSU oligomer or polymer structures could be made by ^{1}H-NMR.

Relative oligomer content below 1000 Da

The results of SEC experiments are presented in Figure 2. There are only minor differences between PPSU and PES materials in the total oligomer content below 1000 Da. For PPSU materials the peak pattern slightly differs caused by the variations in oligomer-type concentrations as presented in Table 4. The mean total oligomer content of all PPSU samples estimated by SEC calculation is 0.48% (RSD: 10.7%), which is very similar to the only PES sample.

Stability against hydrolysis

Results of hydrolysis experiments are presented in Table 2. A high release of monomer substances was detected only for PC under alkaline (pH 11.1) conditions. Even for Tritan™ copolymer, which is also a polyester similar to PC, no release of the acidic monomer terephthalic acid (TPA) was detected under the chosen conditions. Also, no monomer release was detectable for polyether materials PES and PPSU in alkaline or acidic milieus.

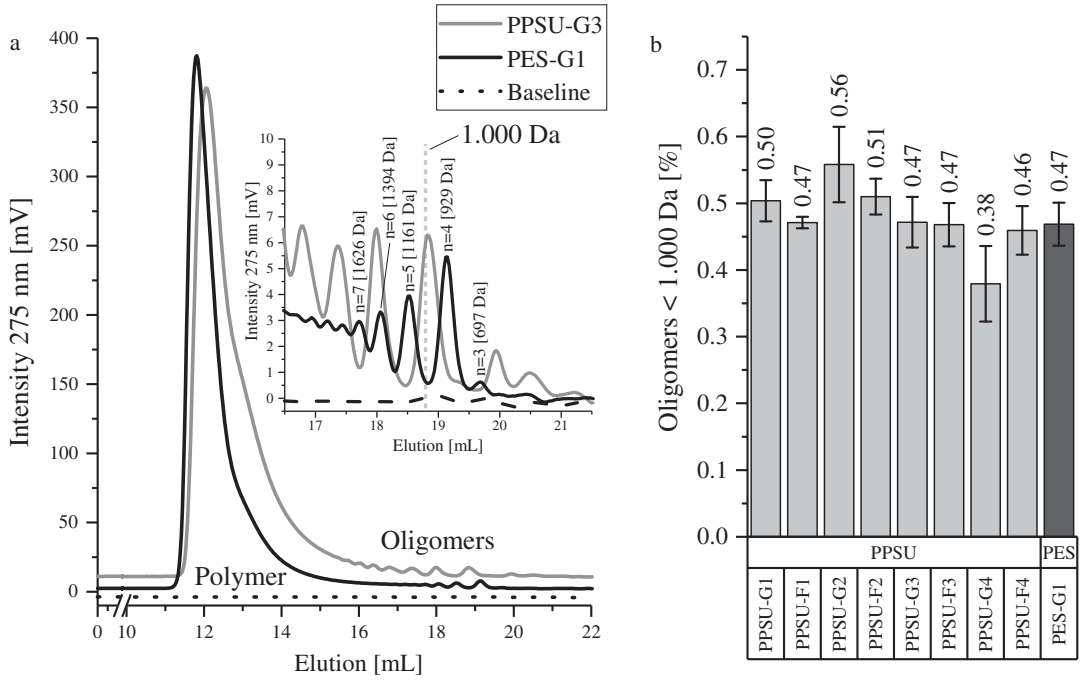

Figure 2. (a) HPLC-SEC (λ = 275 nm) chromatograms of dissolved PES and PPSU polymers. Molecular weight calibration (log(M) in dependence of elution volume) by cyclic PES oligomers (number of BPS units: n = 3 … 7). (b) Results of determination for oligomers below 1000 Da. Bars represent mean and standard deviations of double determination.

Table 2. Release of monomer substances from ground polymer under hydrolysis conditions. Limit of detection (LOD): 1 mg/kg polymer.

		BPA	TPA	BPS	DHBP
Material	Conditions	(mg/kg polymer)			
Polycarbonate	pH 2, 2 h, 100°C	4.9	x	x	x
	pH 11, 1 h, 100°C	886	x	x	x
	pH 11, 2 h, 100°C	1859	x	x	x
Tritan™	pH 2, 2 h, 100°C	x	< LOD	x	x
	pH 11, 2 h, 100°C	x	< LOD	x	x
PES-G1	pH 2, 2 h, 100°C	x	x	< LOD	x
	pH 11, 2 h, 100°C	x	x	< LOD	x
PPSU-G2	pH 2, 2 h, 100°C	x	x	< LOD	< LOD
	pH 11, 2 h, 100°C	x	x	< LOD	< LOD

"x" is not determined.

Table 3. Extractable substances from PPSU tentatively identified by LC-ESI(+)-MS.

Type	Short name	Structure	*M* (Da)
M	BPS	BPS	250.3
M	DHBP	DHBP	186.2
M	BPS-MM	MeO-BPS-OMe	278.3
M	HMBP	HMBP	200.2
M	BPS-CM	Cl-BPS-OMe	282.7
M	BPS-CC	Cl-BPS-Cl	287.2
M	DMBP	DMBP	214.3
M	BP	Biphenyl	154.2
O	L2-CO	Cl-[BPS-DHBP]-OH	436.9
O	L2-MM	MeO-[BPS-DHBP]-OMe	446.5
O	L2-CM	Cl-[BPS-DHBP]-OMe	450.9
O	L3*-MM	MeO-[BPS-DHBP-BPS]-OMe	678.8
O	L3-MO	MeO-[DHBP-BPS-DHBP]-OH	600.7
O	L3-CM	Cl-[BPS-DHBP-BPS]-OMe	683.2
O	L3-CC	Cl-[BPS-DHBP-BPS]-Cl	687.6
O	L3-MM	MeO-[DHBP-BPS-DHBP]-OMe	614.7
O	C4	$[BPS\text{-}DHBP]_2$	801.0
O	L4-MM	MeO-$[DHBP\text{-}BPS]_2$-OMe	847.0
O	L4-CM	Cl-$[BPS\text{-}DHBP]_2$-OMe	851.4
O	L5*-MM	MeO-[BPS-DHBP-BPS-DHBP-BPS]-OMe	1079.2
O	L5-CC	Cl-[BPS-DHBP-BPS-DHBP-BPS]-Cl	1088.1
O	L5-MM	MeO-[DHBP-BPS-DHBP-BPS-DHBP]-OMe	1015.2
O	C6	$[BPS\text{-}DHBP]_3$	1201.5
O	L6-MM	MeO-$[DHBP\text{-}BPS]_3$-OMe	1247.4
O	L6-CM	Cl-$[DHBP\text{-}BPS]_3$-OMe	1251.9
U	U1	Unknown, probably BPS containing and chlorinated	491
U	U2	Unknown	Unknown
U	U3	Unknown	655
U	U4	Unknown	1041

Sorting by retention and molecule type. Explanations: type: monomer derivatives (M), oligomers (O) and unknown (U). Short names: linear oligomers (LX) and cyclic oligomers (CX) with X = number of monomer units. End groups: chlorinated (C), methoxylated (M) and hydroxylated (O).

Hydrolysis caused by boiling hard water was reported as the most relevant factor for BPA release from PC baby bottles (Biedermann-Brem and Grob 2009). In our hydrolysis experiments, the chosen conditions were considerably harsher than expected even in worst-case everyday use scenarios for baby bottles. We confirmed a high release of BPA from PC materials, especially in alkaline milieu. For Tritan™, total alkaline hydrolysis was reported by Brenz et al. (2016) using 0.53 M KOH (30 min, 100°C), which is significantly more alkaline than in our experiment. For the polyether materials PES and PPSU, hydrolysis under everyday use conditions should not be an issue, which is in line with literature (Yin et al. 2017).

Extractables

Identification of oligomers

Figure 3 shows a representative RP-HPLC-UV chromatogram of extracted polymer PPSU-G2 with the main oligomer peaks below and around 1000 Da tentatively identified by HPLC-ESI(+)-MS. The short names, the structures and the oligomer masses are presented in Table 3.

Only one cyclic oligomer below 1000 Da could be identified, the cyclic tetramer (C4), consisting of two BPS and two DHBP units. The next higher cyclic oligomer is the hexamer (C6, 1201 Da). These findings support the plausible presumption that BPS and DHBP units always alternate in the PPSU polymer chain. Almost all the other identified oligomers are linear molecules with mainly chlorinated and/or methoxylated end groups. No oligomers with chlorinated DHBP were identified, which is a plausible finding in accordance to the assumed monomers, DHBP and BPS-CC, usually used for the production of PPSU. In contrast, oligomers with methoxylated BPS end groups were tentatively identified, which is an unexpected finding with regard to the polymer production process. Hydroxyl terminations are always associated with DHBP molecules.

Some chromatographic characteristics for the identified linear oligomers can be described: for oligomers with equal numbers of BPS and DHBP units, the retention time of the chlorinated oligomer species is always higher than that of the methoxylated ones. For oligomers with an odd number of monomer units in the chain, species with more BPS than DHBP units always eluate earlier (e.g. see linear trimers L3-XX in Figure 3).

Quantification of monomer derivatives and oligomers

For quantification of oligomers without specific reference substances, the concept of chromophore concentration presented by Schaefer et al. (2004) for determination of polyester oligomers was adapted for PPSU oligomers. For this, besides identification of oligomers, the determination of an UV wavelength of equal molar absorption for PPSU oligomers is mandatory. We evaluated a wavelength of 255 nm to be suitable and specific for all BPS and DHBP monomer derivatives regardless of their end groups by comparison of substance UV spectra (Figure 4). For verification of photometric results, we recorded and compared linear calibration curves ranging between 252 and 260 nm (in 1 nm steps) for all monomer derivatives available (commercial and self-synthesised) using HPLC-DAD method M1. For

Table 4. Concentrations of PPSU monomers, oligomers and its derivatives in PPSU polymer determined subsequent to total extraction (10 times ACN, 120°C, 1 h).

		PPSU-G1	PPSU-F1	PPSU-G2	PPSU-F2	PPSU-G3	PPSU-F3	PPSU-G4	PPSU-F4
Type	Substance	mg/kg polymer							
M	DHBP	2.1	2.5	1.7	10.3	3.5	4.6	15.5	3.1
M	HMBP	2.1	2.4	4.6	3.2	8.2	10.5	3.8	4.8
M	DMBP	1.4	1.7	5.2	2.5	195.0	182.9	3.1	2.2
M	BPS	–	–	–	–	–	–	–	–
M	BPS-MM	3.1	3.5	2.2	3.4	5.7	11.8	17.1	3.5
M	BPS-CM	9.8	9.2	13.1	10.6	67.5	65.5	97.7	12.9
M	BPS-CC	6.8	8.5	5.5	6.1	36.0	28.7	111.8	9.2
M	BP	13.0	18.2	1.2	6.1	–	–	18.0	11.1
O	L2-CO	12.9	15.6	4.3	11.5	0.6	0.8	38.5	20.9
O	L2-MM	15.5	9.2	93.8	15.1	42.4	46.7	6.5	7.8
O	L2-CM	283.7	281.2	216.0	326.2	150.8	149.0	210.3	274.1
O	L3*-MM	11.6	13.6	17.7	9.1	13.5	14.2	15.9	11.2
O	L3-MO	4.8	6.5	10.7	5.8	2.9	2.7	18.7	8.2
O	L3-CM	57.0	58.4	33.7	44.6	7.3	7.1	42.9	50.0
O	L3-CC	710.3	702.3	244.1	683.9	11.1	10.4	451.5	605.7
O	L3-MM	61.4	63.0	483.9	158.0	638.3	633.1	72.4	58.2
O	C4	1239.1	1231.4	1403.3	1183.5	1099.5	1122.2	1385.2	1326.9
O	L4-MM	31.0	32.5	203.5	45.7	69.8	68.6	24.9	27.2
O	L4-CM	395.8	388.1	280.0	457.8	186.9	188.0	196.7	346.0
O	L5*-MM	29.0	33.4	16.8	35.1	0.2	0.2	19.4	27.2
O	L5-CC	820.3	809.5	280.9	725.1	13.8	14.0	595.4	781.0
O	L5-MM	89.6	87.8	635.3	210.8	807.3	784.6	86.2	40.8
M	Total	38.3	46.0	33.5	42.2	315.9	304.0	267.0	46.8
O	Total	3762.0	3732.4	3924.0	3912.3	3044.5	3041.6	3164.6	3585.2

Quantification of monomers and derivatives (M) with identical reference substances and of oligomers (O) based on chromophore concentration and external calibration with BPS (UV, 255 nm). Oligomer nomenclature in accordance to Table 3. Symbols: '–' means below LOD (~ 0.3 mg/kg polymer).

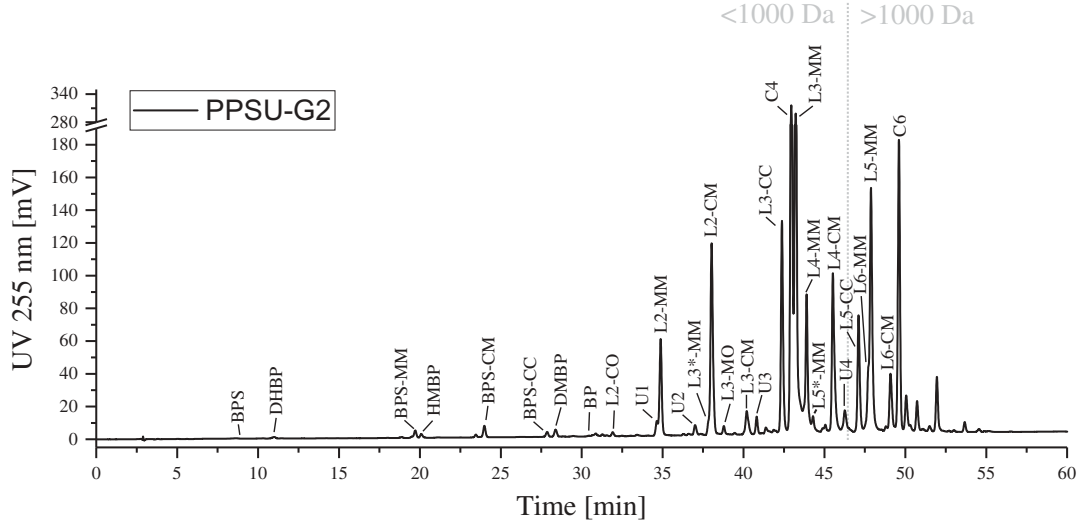

Figure 3. Representative RP-HPLC-UV chromatogram of extracted PPSU-G2 pellet powder using chromatography method M1. Extraction conditions (100 mg powder, 2 mL ACN, 1 h, 120°C). Identified monomer derivatives and oligomers of PPSU material. Substance labels according to Table 3.

chromophore concentration in accordance to Schaefer et al. (2004), Eq. (6) was used, where c_C is the chromophore concentration (mmol/L), c_S is the substance concentration (mg/L), n is the sum of BPS and DHBP units in the molecule (e.g. n = 1 for monomer derivatives, n = 4 for cyclic tetramer) and M_W is the molar weight of the substance (g/mol). Linear calibration curves were calculated following Eq. (7), where A is the UV 255 nm peak area (mV * min) and a is the slope of the calibration curve (mV * min * L/mmol). To ease the handling for calculation, we chose the equivalent Eq. (8) for substance calibration (Figure 5, calibration of monomer derivatives).

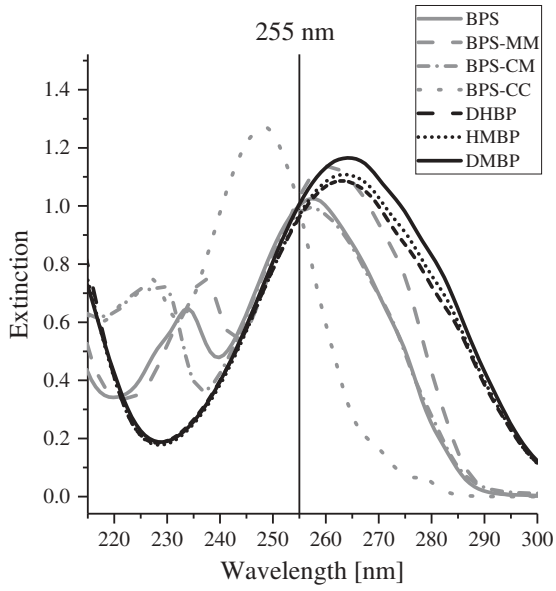

Figure 4. UV spectra of BPS and DHBP monomer derivatives using Specord® S600 spectrophotometer. Equal substance concentrations of 0.05 mmol/L in ACN. Blank subtraction of ACN solvent.

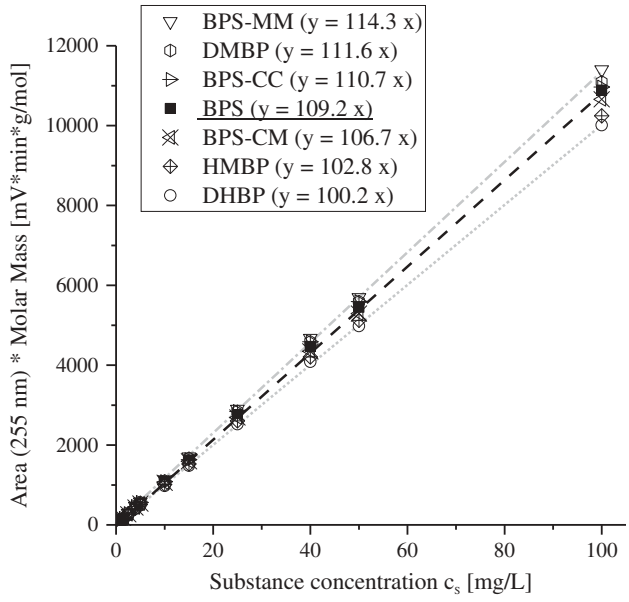

Figure 5. Linear calibration curves (λ = 255 nm) of seven BPS and DHBP monomer derivatives dissolved in DMF and analysed by HPLC-DAD using chromatography method M1. Chromophore calibration of substances in accordance to Eq. (8). Median slope of BPS calibration, minimal slope of DHBP calibration (–8.2%) and maximum slope of BPS-MM calibration (+4.7%).

$$c_C = c_S \cdot \frac{n}{M_W} \tag{6}$$

$$A = a \cdot c_C \tag{7}$$

$$A \,.\, M_W = a \cdot c_S \cdot n \tag{8}$$

$$c_{S;O} = \frac{A_O \cdot M_{W;O}}{a_{BPS} \cdot n_O} \tag{9}$$

We confirmed that 255 nm is the best compromise UV wavelength with the smallest range of calibration curve slopes for all seven monomer derivatives (relative slope range of 12.9%; see Figure 5). Out of seven calibration curves of all monomer derivatives, we chose the BPS calibration curve for the application of the chromophore concentration concept to determine PPSU oligomers following Eq. (9), where $c_{S;O}$ is the oligomer concentration (mg/L), A_O is the oligomer peak area determined by HPLC-UV-255-nm (mV * min), a_{BPS} is the slope of the BPS calibration curve (109.2 mV * min * L/mmol), $M_{W;O}$ is the molar mass of the oligomer (g/mol) and n_O is the sum of BPS and DHBP units in the oligomer.

We compared the oligomer quantification results of UV-255-nm determination by chromophore concentration with unspecific CAD detection for non-volatile substances (Figure 6). No significant differences in results of oligomer determination were detected. We concluded that the specific and more sensitive UV-255-nm approach with BPS calibration is a suitable method for the determination of PPSU oligomers based on their chromophore properties.

Monomer derivatives and oligomers in PPSU materials

Several extraction experiments of PPSU materials with different organic solvents like DMSO, EtOH, THF, 1,4-dioxane, DMF, DCM, chloroform and ACN were performed. While PPSU polymer is completely soluble in DMF and chloroform, almost completely soluble (high concentrations of oligomers but also polymeric compounds) in DMSO, DCM, THF and 1,4-dioxane and hardly soluble in EtOH, we chose ACN as suitable solvent for monomer and oligomer extraction. To achieve a total extraction of oligomers below 1000 Da, we repeated ACN extraction (120°C, 1 h) 10 times. The relative increase of oligomer concentration was less than 1% already after the fifth extraction step. Total extraction of monomer derivatives was already achieved after the first extraction step.

The results of the extraction experiments are presented in Table 4. Remarkable differences in the specific monomer and oligomer concentrations between the

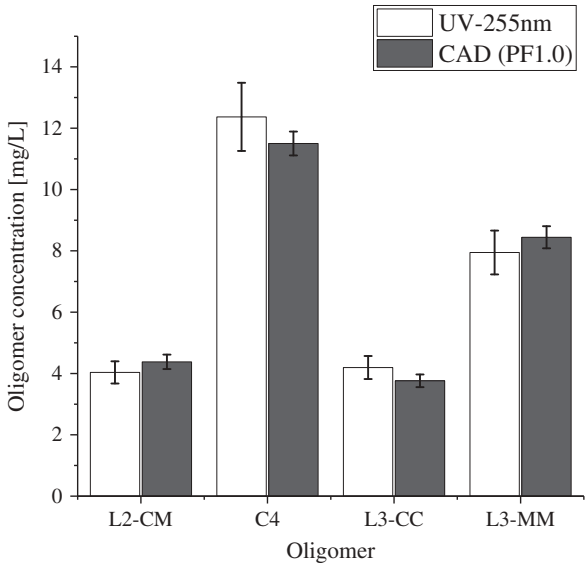

Figure 6. Comparison of PPSU oligomer quantification extracted from PPSU-G2. Determination via specific chromophore concentration (UV λ = 255 nm) using BPS linear calibration (white) and via unspecific CAD detection for non-volatile substances and polynomic calibration curves (grey). Error bars: standard deviation of triple determination.

PPSU materials from different manufacturers were noticed. With regard to the corresponding materials, the total content of monomer derivatives was determined to be below 50 mg/kg polymer for four out of six processed (bottles) and unprocessed (pellets) PPSU samples. However, two PPSU types had a higher total content of monomer derivatives of about 300 mg/kg polymer. For PPSU-G3 material from manufacturer B, DMBP was the dominating monomer derivative with almost 200 mg/kg polymer. For food grade materials, residual polymerisation monomers were determined at a maximum of about 10 mg/kg polymer for DHBP and 36 mg/kg polymer for BPS-CC, respectively. BPS was not detectable in any PPSU sample (LOD: 0.3 mg/kg polymer). This is a plausible finding because only the chlorinated BPS derivative (BPS-CC) is used for the polymer production (Blinne and Cordes 1978; Liedloff et al. 2014; Weber et al. 2014). In five out of six PPSU materials, BP was determined up to a concentration of 18 mg/kg polymer.

Extractable oligomers from PPSU are mainly linear with chlorinated or methoxylated end groups as a result of the polymer production process by different manufacturers (see Table 4). Only very low quantities of hydroxylated oligomers like L2-CO and LC3-MO in Table 4 could be determined, which confirms the ^{1}H-NMR results. In addition, the molar ratio of chlorinated and methoxylated chain ends of the extracted oligomers is equivalent to the results of the whole polymer determined by ^{1}H-NMR (Figure 1(B)). The concentration of the only cyclic oligomer below 1000 Da (C4) is comparable for all PPSU materials (about 1.2 g/kg polymer). The sum of all identified and quantified oligomers below 1000 Da is up to 0.4% of the whole polymer for the investigated PPSU samples. This is slightly less than the relative oligomer content below 1000 Da estimated by SEC calculation (SEC mean 0.48%, see Figure 1).

Determination of volatiles

Besides semi-volatile monomer derivatives like DMBP or BPS-CC, two volatile substances (sulfolane as a residual solvent of the polymer production process, and BP) were detectable in GC-MS screening analysis of extracted PPSU materials above a general LOD of roughly 10 mg/kg polymer for volatile substances (for results, see Table 5).

The content of residual sulfolane differs for the analysed PPSU samples ranging from 'below LOD' to about 1.3 g/kg polymer. When sulfolane was detected, also pentamethylene sulfone (PMS) was identified as a probable contamination of sulfolane. Concentrations of PMS are about 1.0–1.5% of sulfolane concentrations (estimated by GC-MS peak area comparison). Sulfolane can be used as a solvent in the polymer production process for PPSU (Blinne and Cordes 1978; Liedloff et al. 2014; Weber et al. 2014). Because of its high boiling point (285°C), it is not completely removed even during drying and hot processing of the polymer (e.g. extrusion). The results of the

Table 5. Determination of volatile substances sulfolane and biphenyl in PPSU material extract solutions via GC-MS.

Sample code	Sulfolane (mg/kg polymer)	Biphenyl (mg/kg polymer)
PPSU-G1	565.0 ± 41.2	14.5 ± 1.6
PPSU-F1	552.8 ± 22.0	19.3 ± 1.8
PPSU-G2	1266.3 ± 76.8	0.9 ± 0.3
PPSU-F2	1184.3 ± 91.5	5.9 ± 0.3
PPSU-G3	< LOD	< LOD
PPSU-F3	< LOD	< LOD
PPSU-G4	433.7 ± 27.2	20.1 ± 2.3
PPSU-F4	934.2 ± 58.5	11.8 ± 0.8

Results are mean ± standard deviation of double determination. LOD sulfolane: 10 mg/kg polymer; LOD biphenyl: 0.5 mg/kg polymer.

corresponding pellet and bottle samples PPSU-G1/F1 also indicate that no significant decrease of sulfolane occurs during the bottle production step. GC-MS results of BP are in line with the results determined by HPLC-UV analysis as presented in Table 4.

Formation of NIAS in thermal processing

Extraction results of volatile and non-volatile NIAS for the analysed baby bottles are very similar compared to the results of the corresponding pellet materials (PPSU-G1/F1 and PPSU-G3/F3). These results confirm that NIAS like oligomers are already present in the raw material and are neither reduced nor increased via bottle production, which is normally a blow moulding process.

Migration-related substances

Migration results for oligomers and monomers

We established a method for determination of non-volatile polymer-related substances released from PPSU materials. We checked accuracy by recovery experiments with standard stock solutions of monomers and their derivatives DHBP, HMBP, DMBP, BPS, BPS-MM, BPS-CM, BPS-CC and BP in two concentrations (1 and 0.1 mg/L, respectively, in simulant 50% EtOH) as well as with an PPSU-G2 ACN oligomer extract solution diluted 1:20 in 50% EtOH. Recovery rates were between 95 and 101% for all substances except for BP (less than 10% recovery rate because of the high volatility of this substance).

Results of three consecutive migration experiments in accordance to EU plastics regulation no. 10/2011 (European Union 2011b) with full bottle filling are presented in Table 6. In general, migration is low for polymer-related substances from PPSU baby bottles into the official food simulant for milk (50% EtOH, 2 h, 70°C). For all five types of PPSU baby bottles that were analysed, no release of oligomers above LOD (0.1 µg/kg) was determined in the second or third migration step, respectively. Instead, a slight migration of monomer derivatives was determined for all bottles. Only one substance, DMBP, was detected above 1 µg/kg food simulant in the third migration experiment with baby bottles PPSU-F3 and PPSU-F5. No release for the potentially endocrine active substance DHBP was detected in the third migration step (LOD 0.02 µg/kg).

Replacing the food simulant 50% EtOH with double distilled water for migration experiments leads to an even lower release of polymer-related substances. For PPSU-F3, only HMBP (0.07 µg/kg) and DMBP

Table 6. Results of migration experiments in accordance to EU regulation no. 10/2011 for PPSU baby bottles (three times consecutive migration, full bottle filling with milk simulant 50% EtOH, 2 h, 70°C).

		PPSU-F1 (300 mL)			PPSU-F2 (150 mL)			PPSU-F3 (300 mL)			PPSU-F4 (320 mL)			PPSU-F5 (260 mL)		
		µg/kg food simulant														
#	Substance	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
M	DHBP	–	–	–	0.08	0.04	–	–	–	–	0.07	–	–	0.04	0.02	–
M	HMBP	0.15	0.05	0.04	0.19	0.06	0.05	0.60	0.22	0.17	0.31	0.07	0.04	0.35	0.18	0.12
M	DMBP	0.05	0.03	0.02	0.08	0.04	0.03	7.42	2.33	1.85	0.12	0.06	0.03	5.13	2.86	1.79
M	BPS	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
M	BPS-MM	0.26	–	–	0.17	–	–	2.28	0.17	0.16	2.30	0.21	0.16	0.07	0.02	–
M	BPS-CM	1.01	–	–	0.52	0.16	–	1.87	0.82	0.25	–	–	–	0.83	0.38	0.31
M	BPS-CC	0.22	–	–	0.11	–	–	0.63	0.21	–	0.26	–	–	0.13	0.12	0.10
O	L2-CO	–	–	–	–	–	–	–	–	–	0.11	–	–	–	–	–
O	L2-MM	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
O	L2-CM	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
O	L3*-MM	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
O	L3-MO	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
O	L3-CM	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
O	L3-CC	0.35	–	–	0.43	–	–	–	–	–	0.29	–	–	–	–	–
O	L3-MM	–	–	–	–	–	–	0.28	–	–	–	–	–	0.23	–	–
O	C4	0.27	–	–	0.27	–	–	0.21	–	–	0.24	–	–	0.34	–	–
O	L4-MM	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
O	L4-CM	0.13	–	–	0.23	–	–	0.10	–	–	0.16	–	–	–	–	–
O	L5*-MM	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
O	L5-CC	0.17	–	–	0.12	–	–	–	–	–	0.12	–	–	–	–	–
O	L5-MM	–	–	–	–	–	–	0.17	–	–	–	–	–	0.14	–	–
M	Total	1.69	0.08	0.06	1.15	0.30	0.08	12.80	3.75	2.43	3.06	0.34	0.23	6.55	3.58	2.32
O	Total	0.92	–	–	1.05	–	–	0.76	–	–	0.92	–	–	0.71	–	–

Symbols: '–' means below LOD (in general 0.1 µg/kg food simulant, exceptions 0.02 µg/kg for DHBP, HMBP and DMBP).

(0.72 µg/kg) were above LOD in the first migration step. As a rule of thumb for PPSU bottles, migration into water can be estimated to be about 10 times lower compared to migration into 50% EtOH under the same time and temperature conditions.

Migration rates can be increased significantly by reducing the bottle filling. We performed migration experiments with 20 mL of milk simulant (50% EtOH) instead of full bottle fillings (results see Table 7). The release of substances from PPSU baby bottles increases about one to two orders of magnitude compared to the fully filled bottles. The highest release was again determined for the bottle PPSU-F3, especially for the substance DMBP. We suggest that, on the one hand, the increased migration rate for less-filled bottles is influenced by the higher surface-to-volume ratio. On the other hand, we suppose that under migration conditions (70°C, 2 h) a thin film of liquid (EtOH/water azeotrope) is formed on the inner wall of the baby bottle, accelerating the extraction. This effect with milk simulant 50% EtOH may not sufficiently reflect real food conditions.

To the best of our knowledge, no investigations about migration from PPSU baby bottles have been published to date. For comparable PES material Simoneau et al. (2011) detected no migration of BPS (LOD 0.1 µg/kg) or BPS-CC (LOD 0.3 µg/kg) in the first migration steps of 30 PES bottles. Only one substance, diphenylsulfone, was detected above LOD in two PES baby bottles (about 1.5 µg/kg, first migration). Furthermore, no release of polymer-related substances from PES baby bottles into 50% EtOH (2 h, 70°C) was described by Onghena et al. (2014). Because of the different monomer composition, the variety of potentially migrating substances from PPSU is higher. But in general the tendency of very low migration of these polymer-related analytes is similar to PES baby bottles.

Migration results for sulfolane and BP

We performed recovery experiments with standard stock solutions of BP and sulfolane in 50% EtOH with three different substance concentrations (1, 10 and 33 mg/L, respectively). Liquid–liquid extraction was tested with several solvents: diethyl ether, EA, DCM, chloroform and tert-butyl methyl ether. Best phase separation and recovery rates were determined with chloroform. Mean recovery rates for BP were 98.7% (RSD 5.2%) and for sulfolane 45.5% (RSD 3.4%). LOD for BP was 5 µg/kg food simulant and for sulfolane 10 µg/kg food simulant.

Table 7. Results of migration experiments for PPSU baby bottles with reduced bottle filling (three times consecutive migration, 20 mL milk simulant 50% EtOH, 2 h, 70°C).

		PPSU-F1 (20 mL)			PPSU-F2 (20 mL)			PPSU-F3 (20 mL)		
		µg/kg food simulant								
#	Substance	1	2	3	1	2	3	1	2	3
M	DHBP	1.79	0.44	0.29	2.18	0.54	0.30	0.87	0.46	0.24
M	HMBP	4.92	1.31	1.02	3.05	0.64	0.55	13.4	9.01	5.23
M	DMBP	2.99	0.56	0.28	1.26	0.27	0.17	222.8	96.1	59.0
M	BPS	–	–	–	–	–	–	–	–	–
M	BPS-MM	6.61	1.36	0.68	6.83	1.70	0.52	6.03	0.56	0.19
M	BPS-CM	7.29	1.55	0.45	9.27	1.19	0.37	22.9	4.07	1.73
M	BPS-CC	2.22	0.59	0.37	0.50	0.14	–	8.23	5.50	0.83
O	L2-CO	0.37	0.13	–	0.24	–	–	–	–	–
O	L2-MM	0.39	–	–	0.55	0.10	–	0.44	–	–
O	L2-CM	4.25	0.67	0.14	5.45	0.81	0.19	3.29	0.35	–
O	L3*-MM	0.18	–	–	0.10	–	–	–	–	–
O	L3-MO	–	–	–	–	–	–	–	–	–
O	L3-CM	0.37	–	–	0.29	–	–	–	–	–
O	L3-CC	5.24	0.88	0.48	3.68	0.76	0.21	–	–	–
O	L3-MM	2.90	0.64	0.30	2.14	0.55	0.19	2.79	0.54	0.16
O	C4	0.51	0.15	0.10	1.01	0.26	0.11	4.88	1.06	0.33
O	L4-MM	–	–	–	–	–	–	0.26	0.11	–
O	L4-CM	0.99	0.46	0.25	0.78	0.51	0.18	0.46	0.20	0.13
O	L5*-MM	–	–	–	–	–	–	–	–	–
O	L5-CC	0.24	0.11	–	0.17	–	–	–	–	–
O	L5-MM	–	–	–	–	–	–	0.24	0.16	–
M	Total	25.82	5.81	3.09	23.09	4.48	1.91	274.23	115.7	67.22
O	Total	15.44	3.04	1.27	14.41	2.99	0.88	12.36	2.42	0.62

Symbols: '–' means below LOD (in general 0.1 µg/kg, exceptions 0.02 µg/kg for DHBP, HMBP and DMBP).

No migration of BP above LOD was determined for first migrates using 50% EtOH and full baby bottles. BP was only detected in the first migrate of the 'worst-case' simulation (20 mL bottle filling, 50% EtOH) using bottle PPSU-F1 (17.5 ± 4.2 µg/kg food simulant, mean ± standard deviation of double determination).

Determination of sulfolane in the first migrate solutions was below LOD for all bottles (50% EtOH, full bottle fillings). Results were above LOD for PPSU-F1 (52.4 ± 4.3 µg/kg food simulant) and PPSU-F2 (46.4 ± 2.4 µg/kg food simulant) with reduced baby bottle filling in the first migration step (20 mL, 50% EtOH, results without consideration of recovery rate).

Risk considerations

BPS (0.05 mg/kg food), BPS-CC (0.05 mg/kg food) as well as DHBP (6 mg/kg food) are listed with specific migration limits by European plastics regulation no. 10/2011 (European Union 2011b). As presented in our analytical results, no concern of exceeding the legal limits for these substances exists for the analysed PPSU baby bottles. Furthermore, the potentially endocrine substance BPS was not detectable (below 0.3 mg/kg polymer) in the PPSU material. In contrast, DHBP could be detected in small amounts in PPSU material (up to 15 mg/kg polymer), but migration was below LOD (0.02 µg/kg simulant, full bottles) and about 0.3 µg/kg simulant (reduced bottle fillings) in the third migrates of PPSU baby bottles, respectively. Compared to PC, no hydrolysis for PPSU baby bottles is expected under everyday use conditions. Therefore, it can be assumed that the endocrine activity based on the possible release of PPSU monomers is negligible.

Evaluation of not-listed monomer derivatives and PPSU oligomers can be done by the threshold of toxicological concern (TTC) concept (Cramer et al. 1978; Kroes et al. 2004; Munro et al. 2008; EFSA 2012). All identified monomer derivatives, the linear and cyclic oligomers of PPSU (see Table 3) as well as sulfolane and biphenyl are assessed as Cramer class III substances without structural alerts of genotoxicity by using Toxtree (v2.6.13) toxic hazard estimation software (Patlewicz et al. 2008). The exposure-based threshold for these substances is 1.5 µg/kg bodyweight (bw) per day. The European Food Safety Authority (EFSA) evaluated the daily consumption for infants' baby bottle contents to be considered in exposure calculations to 150 g/kg bw per day (EFSA 2016). For infants of 3 kg bw, Cramer III exposure threshold results in an analytical threshold of 10 µg/kg food (simulant). No identified polymer-related substance released from PPSU baby bottles exceeds this threshold even in the first migrate (50% EtOH, 2 h, 70°C, full bottle fillings). Only one substance released from two PPSU baby bottles, DMBP, almost reaches the threshold in the first migrate. With reduced baby bottle fillings (20 mL instead of 300 mL), the threshold of 10 µg/kg food (simulant) was exceeded by six times with substance DMBP for one out of three PPSU baby bottles in the third migration step. Since this exceedance might be significantly affected by the official milk simulant 50% EtOH forming a thin film of EtOH/water azeotrope at the wall of the baby bottle, this should not be a relevant issue under real conditions.

For sulfolane, we cannot ensure that the Cramer III threshold will not be exceeded because of the poor recovery (about 45%) and the analytical LOD of 10 µg/kg food simulant (without consideration of recovery rate). Health Canada (2014) established a tolerable daily intake (TDI) value for sulfolane of 4.12 µg/kg bw per day based on a sub-chronic study in rats (HLS 2001). The TDI was calculated using the benchmark dose limit modelling approach and an uncertainty factor of 1000. Considering the EFSA (2016) data for exposure calculation for infants (3 kg bw; 150 g/kg bw daily food consumption), the analytical equivalent to TDI value for sulfolane is 27.5 µg/kg food (simulant). This value is above our LOD for sulfolane in migrate solutions even under consideration of the specific recovery rate. We can conclude that none of the analysed PPSU baby bottles caused an exceedance of the TDI for sulfolane even in the first migration step (2 h, 70°C, 50% EtOH).

Based on our analytical results, no concerns regarding migration of polymer-related substances from PPSU baby bottles exist.

Conclusion

We present a comprehensive three-step approach for the analysis and risk assessment of a new polymer, PPSU, used for the production of infant feeding

bottles based on a predictable NIAS assessment. In general, PPSU material exhibits low tendency to release substances of potential toxicological concern to food simulants based on the low initial content of these substances in the raw material as well as the chemical stability of the polymer against hydrolysis. Although the PPSU polymer formally consists of two potentially estrogenic substances, BPS and DHBP, we also do not expect significant endocrine activity since migration of these two substances and similar oligomer derivatives with hydroxyl end groups was determined to be negligible. Two substances, DMBP as a NIAS derived from DHBP monomer, and sulfolane as residual water-soluble solvent from PPSU polymerisation, might be relevant for migration processes for some PPSU bottle samples, even though we could not detect exceedances of thresholds for the baby bottle samples that were analysed in this study.

Based on our analytical results, PPSU seems to be a promising material for the production of infant feeding bottles.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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