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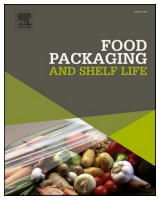

Food simulants and real food – What do we know about the migration of PFAS from paper based food contact materials?

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ABSTRACT

Per- and polyfluorinated alkyl substances (PFAS) can be found in food contact materials (FCMs). Therefore, migration into food occurs and contributes to human dietary exposure. Identification and minimization of possible exposure-pathways of these omnipresent and potentially toxic chemicals are important to mitigate health risks. Nonetheless, risk assessment procedures are mostly limited to considering the final PFAS concentrations in food without distinguishing the contribution of migration. Additionally, the use of food simulants during migration tests can potentially misrepresent migration results. Critically assessing reported migration behaviors of PFAS showed that the use of food simulants (especially Tenax®) in migration tests lead to an underestimation of PFAS exposure from FCMs. Reported PFAS concentrations migrated into food as well as consumption data from databases were used to estimate the dietary exposure. PFAS exclusively migrated from FCMs can considerably contribute to consumers' dietary exposure potentially impacting human health.

1. Introduction

Forever chemicals – this term describes a group of water, oil, and temperature resistant substances also called per- and polyfluorinated alkyl substances (PFAS). Over 5000 different compounds (United States Environmental Protection Agency, 2021) belong to this class, all containing a carbon backbone and at least three covalent bonds to fluorine atoms (Trier, 2017). The high stability of the chemicals results in very slow biological and/or environmental degradation (Wang et al., 2015); hence, the nickname "forever chemicals".

Since the discovery in 1938 of polytetrafluoroethylene, (Teflon™) (Teflon, 2021), the anthropogenic chemicals are used for a plethora of industrial applications e.g., firefighting foam (Dauchy et al., 2017), sports equipment (Nilsson et al., 2013), and carpets (Wu et al., 2020). Due to the persistence and widespread use of PFAS, the chemicals can be found all around the globe, even in the most remote environments like arctic ice caps (Young et al., 2007). With this in mind, it comes as little surprise that PFAS are also found in human serum (Toms et al., 2014; Gribble et al., 2015; Worley et al., 2017), plasma (Brantsæter et al., 2013; Morck et al., 2015), and breast milk (Awad et al., 2020). PFAS can pose a considerable risk for humanity and wildlife since multiple adverse health effects are connected to the omnipresent chemicals. Cancer (Barry et al., 2013; Girardi & Merler, 2019; Steenland & Winquist, 2021), altered thyroid function (Lopez-Espinosa et al., 2012; Preston et al., 2020), and developmental toxicity (Wolf et al., 2007; Gaballah et al., 2020) are just a small list of reported possible effects. Most recently, elevated concentrations of PFAS (especially perfluorobutanoic acid, PFBA) in human serum were also correlated with a more severe course of the COVID-19 infection (Catelan et al., 2021). Avoiding exposure to PFAS is nearly impossible due to their rampant occurrence in the environment. The intake of the chemicals can occur by inhalation of indoor air/dust (De la Torre et al., 2019; Zhang et al., 2020), direct contact with PFAS containing products (Trudel et al., 2008), or ingestion of contaminated water (Domingo & Nadal, 2019) and food (Sunderland et al., 2018; Susmann et al., 2019).

Comparison of different exposure pathways highlighted dietary exposure as a major source of PFAS intake (Trudel et al., 2008; Haug et al., 2011; Herzke et al., 2013). PFAS contaminations were reported for many different food products such as fish (Berger et al., 2009; Christensen et al., 2017), vegetables (Herzke et al., 2013; Eun et al., 2020), and meat (Death et al., 2021). Furthermore, a risk assessment performed by the European Food Safety Authority - Panel on Contaminants in the Food Chain (EFSA CONTAM Panel) underlined the potential danger for the health of consumers from PFAS contaminated food products

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(Schrenk et al., 2020). One of the most frequent applications of PFAS is the production of non-stick coating of paper and cardboard to generate water and grease-resistant material (Bokkers et al., 2019; Peters et al., 2019). Paper based food contact materials (FCMs) included in this category are fast-food packaging, microwavable popcorn bags, disposable paper plates, etc. Coatings used for the production of paper based FCMs typically contain mixtures of PFAS (Begley et al., 2005; Trier et al., 2011). Very little available information about the exact composition of the applied PFAS blends exists. However, 20–25 different types of PFAS coatings were reported (Trier, 2017). Components mostly found in these mixtures are fluorotelomer alcohols (FTOHs, see part A Fig. 1) and polyfluoro alkyl phosphate esters (PAPs, see part B Fig. 1). Whilst these substances are intentionally added (IAS) to the FCMs, only limited toxicological data is available. The data available indicated, among others, estrogenic activity (Rosenmai et al., 2016). More, importantly, degradation of FTOHs and PAPs due to atmospheric oxidation or biodegradation can lead to the formation of perfluoroalkyl carboxylic acids (PFCAs) and perfluorinated sulfonic acids (PFSAs) (Vestergren et al., 2008). These degradation products have lower molecular weights than their respective precursors and therefore higher mobility. More toxicological data is available regarding these compounds. The most prominent member of PFCAs is perfluorooctanoic acid (PFOA, see part C Fig. 1) and the best-known member of the PFSAs group is perfluorooctane sulfonate (PFOS, see part D Fig. 1). Both substances are confirmed to show strong persistence in the environment and bioaccumulation (Ludwicki et al., 2015). In human blood, the half-life of PFOS and PFOA are estimated to be up to 4.8 and 1.5 years, respectively (Olsen et al., 2007; Dourson & Gadagbui, 2021). The chemicals are among other adverse health effects associated with liver disease (Li et al., 2017) and reproductive toxicity (Wang et al., 2011). Indeed, Stockholm Convention has subjected PFOS (in 2009) and PFOA (in 2020) to its global treaty as Persistent Organic Pollutants (Downie et al., 2012). Direct contact between the FCMs and food could facilitate the migration of these PFAS into food products (Begley et al., 2008; Zabaleta et al., 2020) and therefore contribute to the dietary exposure of the consumer. Nonetheless, little data on risk assessments of the dietary exposure of PFAS migrated from paper based FCMs into real food was reported. A risk assessment requires the determination of several key factors such as migration behavior of the migrant, toxicological information, and exposure estimation based on dietary consumption (Mbabazi et al., 2011). However, migration itself is a complex process that depends on many factors such as contact time, temperature, and characteristics of food and migrants (Castle, 2006). Whilst these combined circumstances can highly influence the migration of PFAS into food (Begley et al., 2008), limited information on the topic can be found in literature. Additionally, migration tests from paper based FCMs often use food simulants (e.g., Tenax® or oil) instead of real food samples to simplify the analytical procedures (Begley et al., 2005; Chiang, 2012; Yuan et al., 2016). The use of food simulants to imitate real food was introduced for migration tests of all FCMs, in particular of plastic FCMs in the European Council Directive 85/572/ECC in 1985 (Council of the European Communities, 1985). This directive was replaced in 2011 by regulation EC 10/2011 issued by the European Commission (EC) (European Commission, 2011) it specifies further migration test conditions, again focusing on migration from plastic FCMs. To ensure the suitability of the presented food simulants, the link between real food, food simulants, and migration conditions was thoroughly established (Trier, 2017). Currently, equivalent regulations are not provided for paper based FCMs.

As a result, this review compiles available knowledge regarding the migration of PFAS from paper based FCMs. The observed migration behavior of PFAS into food will be summarized, discussed, and knowledge gaps identified. To explore the suitability of the application of food simulants, the migration performance into both food simulants and real food will be compared and an overview of the used analytical procedures provided. Consequently, the risk for consumers will be assessed by estimation of the dietary exposure exclusively caused by PFAS migrated from paper and board FCMs. Highlighting the importance of this form of exposure might point out a way to minimize human exposure to PFAS.

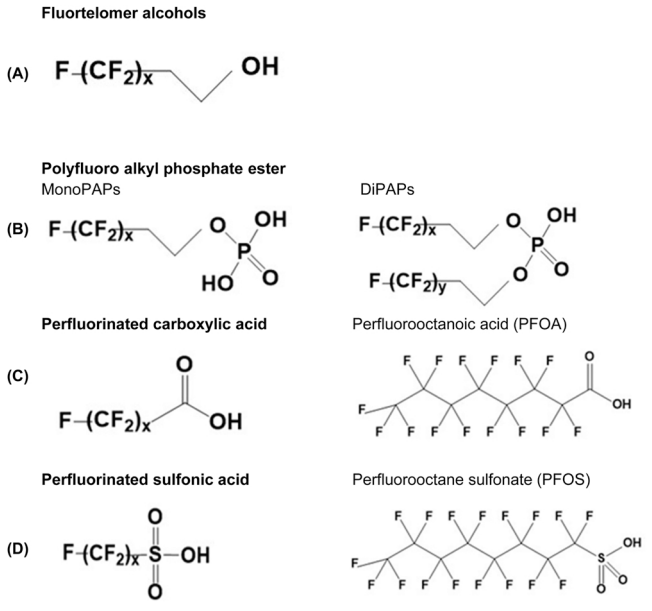

Fig. 1. Overview of molecular structures of different PFAS classes.

2. Analytical approaches

Assessment of consumer risks emanating from PFAS migration into food requires consideration of several aspects. First and foremost, the concentration in food products is essential.

The detected concentration of PFAS combined with the amount of consumed food product can be used to estimate the contribution to the dietary exposure. However, concentration in food after contact with FCMs is directly correlated to the presence of PFAS in FCMs itself and the transfer between the two components. To summarize, for a realistic investigation of the migration of PFAS from FCMs it is advantageous to assess the amount of PFAS in food, in FCMs, and to consider the migration conditions.

2.1. Analytical methods

Determination of PFAS in FCMs and food can be performed by application of different analytical methodologies. The most commonly used methods to investigate the migration from paper based FCMs into real food are summarized in the following paragraphs. A more detailed discussion regarding the analysis methodologies of PFAS in food can be found in other articles such as the work from Al Amin et al. (2020), Jahnke & Berger (2009), or Vorst et al. (2021) that focus on this topic.

2.1.1. Quantitation of targeted PFAS in FCMs, food, and food simulants

Migration studies regularly aim to compare the detailed PFAS composition of FCMs and the migration pattern into food. Therefore, these studies often apply targeted analytical techniques such as liquid chromatography or gas chromatography coupled with mass spectrometry to determine exact concentrations of PFAS in FCMs and foods/food simulants (Begley et al., 2005; Begley et al., 2008; Chiang, 2012; Choi et al., 2018). Overall, the predominant quantitative analytical method used was separation by liquid chromatography followed by tandem mass spectrometry (LC-MS/MS, Table 1). LC-MS/MS allowed reliable quantitation of different classes of PFAS including PFCAs/PFSAs, PAPs, and FTOHs. However, gas chromatography coupled to chemical ionization mass spectrometry (GC/CI-MS) could also be applied for the

Table 1
Overview of peer-reviewed articles addressing PFAS migration from paper based FCMs highlighting samples, analytical methods, and migration conditions.

		Quantitation in		Analytical Method			Migration
Studies	Analytes	Foods	Food Simulants	Sample prep.	Equipment/column	LC-Eluents	Conditions
Begley et al., 2005	PFOA, FTOHs	Microwave popcorn oil	Miglyol	Solvent extraction: EtOH: H_2O (FCMs) Hexane:H_2O (Miglyol) EtOH (popcorn oil)	LC-MS/MS (QqQ*)/ C_8	Solvent A: H_2O (PFOA) H_2O + 2 mM AA*, pH 4 (FTOHs) Solvent B: MeOH + 2 mM AA (PFOA) ACN:MeOH (FTOHs)	2 min, 702 W
Begley et al., 2008	PFOA, PAPs, S-PAPs	Microwave popcorn, chocolate spread, vinegar, butter	EtOH:H_2O*; H_2O; oil; emulsions, Miglyol	Solvent extraction: EtOH: H_2O (FCMs) Hexane:TFE*: H_2O (food)	LC-MS/MS (QqQ)/ C_8	Solvent A: H_2O + 2 mM AA Solvent B: MeOH	15 min at 100 °C 24 h at 40 °C 40 days at 4 °C
Chiang, 2012	PFOA	N.A*	Soy oil with seasoning	Solvent extraction: MeOH +KOH (1 M)* SPE*: Oasis WAX	LC-MS/MS (QqQ)/ C_{18}	Solvent A: H_2O + 2 mM AA Solvent B MeOH	15 min at 100 °C 24 h at room temp.
Choi et al., 2018	PFCAs/ PFSAs	N.A	EtOH:H_2O; H_2O; oil; acetic acid 3%; n-heptane	Solvent extraction: MTBE*	LC-MS/MS (QqQ)/ C_{18}	Solvent A: H_2O + 5 mM AA Solvent B: MeOH	30 min at 100 °C
Elizalde et al., 2018	PFCAs/ PFSAs	Milk powder	Tenax®	Solvent extraction: MeOH	LC-MS/MS (QqQ)/ C_{18}	Solvent A H_2O:MeOH (95:5) + 2 mM AA Solvent B MeOH	2 h at 80–160 °C 10 days at 40 °C
Fengler et al., 2011a & b	FTOHs	Muffin dough, muffin, butter	Tenax®	ASE*: Hexan SPE: StrataSi-1	GC/CI-MS/ Not specified	Not specified	Time: 5–60 min Temp.:120–220 °C
Fengler et al., 2012	PFCAs/ PFSAs FTOHs	Cheese, butter, bread, sugar, dough, fish fingers, fried grated potatoes	Tenax®	Not Specified	LC-MS/MS (PFCAs/ PFSAs) GC/CI-MS (FTOH)/ Not specified	Not specified	30 min at 100 °C 40 min at 180 °C 20 min at 220 °C 10 days at 20 °C 10 days at 40 °C
Gebbink et al., 2013	PFCAs/ PFSAs PAPs	Varying fast-food, pre-prepared meals, baked goods	N.A	Solvent extraction: MeOH (FCMs) ACN* (food) SPE: Oasis WAX	LC-MS/MS (QqQ)/ C_{18}	Solvent A: H_2O:MeOH (95:5)+ 2 mM AA + 5 mM 1-MP* Solvent B MeOH:ACN:H2O (75:20:5)+ 2 mM AA + 5 mM 1-MP	Food samples (before and after preparation)
Moreta & Tena, 2014	PFCAs/ PFSAs	Popcorn	N.A	Solvent extraction EtOH, MeOH (oil)	LC-MS/MS (QTof *)/ C_{18}	Solvent A H_2O + 0.8% formic acid Solvent B ACN + 0.8% formic acid	Food samples (before and after preparation)
Schlummer et al., 2012	PFCAs/ PFSAs FTOHs	N.A	Tenax®	Not specified	LC-MS/MS (PFCAs/ PFSAs) GC/CI-MS (FTOHs/ Not specified	Not specified	2 h at 200 °C 6 h at 120 °C 10 days at 60 °C
Still et al., 2013	PFCAs/ PFSAs FTOHs	Butter	N.A	Solvent extraction: ACN SPE: Oasis WAX+ ENVI-Carb	LC-MS/MS (QqQ)/ C_8 GC/CI-MS (FTOHs)/ RTX 200	Solvent A: H_2O + 5 mM AA, pH3.2 Solvent B:MeOH Solvent C: MTBE* (30% after 15 min)	45 days at 5 °C
Xu et al., 2013	PFCAs/ PFSAs PAPs	N.A	Miglyol, emulsions, EtOH:H_2O, acetic acid 3%;	Solvent extraction: EtOH: H_2O (FCMs) Hexane:EtOH: H_2O	LC-MS/MS (QqQ)/ C_8 (PAPs); C_{18} (PFCAs/PFSAs)	Solvent A: H_2O + 2 mM AA (PAPs) H_2O + 4 mM ammonium formate, pH 3.2 (PFCAs/ PFSAs) Solvent B: MeOH THF*:MeOH (PFCAs/ PFSAs)	15 min at 100 °C 2–240 h at 40 °C
Yuan et al., 2016	PFCAs FTOHs	N.A	EtOH:H_2O; water; oil	Solvent extraction MeOH (FCMs) SPE: WAX	LC-MS/MS (QTof)/ C_{18}	Solvent A H_2O + 0.1% formic acid (FTOHs); H_2O + 5 mM AA (PAPs) Solvent B MeOH	15 min at 100 °C

(*continued on next page*)

Table 1 (*continued*)

		Quantitation in		Analytical Method			Migration
Studies	Analytes	Foods	Food Simulants	Sample prep.	Equipment/column	LC-Eluents	Conditions
Zabaleta et al., 2020	PFCAs/ PFSAs PAPs	Rice, cereal, milk powder	Tenax®; EtOH: H_2O	Solvent extraction by FUSEL*: ACN: H_2O	LC-MS/MS (QqQ)/ C_{18}	Solvent A: H_2O:MeOH (95:5)+ 5 mM 1-MP + 2 mM AA Solvent B: MeOH:H_2O + 2 mM AA + 5 mM 1-MP	Short term: Time: 5–60 min Temp.: 80–160 °C Long-term 10 days at 60 °C

* Abbreviations: N.A (not analyzed), EtOH (ethanol), H_2O (water), TFE (trifluoroethanol), MeOH (methanol), KOH (potassium hydroxide), SPE (solid phase extraction), MTBE (methyl tert-butyl ether), ASE (accelerated solvent extraction), ACN (acetonitrile), FUSEL (focused ultrasonic solid-liquid extraction, QqQ (triple quadruple mass spectrometer), QTof (quadrupole-time of flight mass spectrometer), AA (ammonium acetate), 1-MP(1-Methylpyrene)

quantitation of FTOHs as shown by Fengler et al. (2011a), Schlummer et al. (2012), and Still et al. (2013). LC separation of PFAS was usually performed in reversed-phase C_{18} or C_8 columns. The aqueous solvent that was used varied between applications but always contained Milli-Q water with varying concentrations of additives e.g., ammonium acetate (AA). The organic solvent was mainly methanol based (MeOH) with the exception of an acetonitrile (ACN) usage by Moreta & Tena (2014).

The preferred instrumentation was a triple quadrupole (QqQ) operated in multiple reaction monitoring mode with negative electrospray ionization. These settings allowed the detection of the fluorinated compounds and simultaneously reduced background signals from interfering contaminations. A summary of the analytical methods is included in the overview presented in Table 1. For the targeted quantitation of PFAS in FCMs, a methanol based liquid/solid extraction was often performed. The preparation of real food samples varied due to differences in matrices and analytes considered. In a typical extraction protocol, the homogenized food sample was sonicated, centrifuged, and the supernatant cleaned by solid-phase extraction (SPE) or filtration. Quantitation of targeted PFAS provides detailed information about the analyzed PFAS in the samples. However, it also narrows down the analysis to a limited number of compounds within the PFAS classes PFCAs, PFSAs, PAPs or FTOHs.

2.1.2. *Detection of fluorine in FCMs, food, and food simulants*

Considering the great variety of the PFAS group, alternatives to targeted analysis of specific compounds can be advantageous to assess the presence of PFAS in FCMs and food. In many cases, it could be sufficient to confirm the presence of PFAS in FCMs without detailed information regarding the compounds. Since all PFAS contain a significant amount of fluorine atoms in their molecular structures, the detection of fluorine in FCMs can be used to indicate the potential presence of PFAS by evaluation of these fluorine values. Several analytical methods are available to qualitatively identify fluorine; examples are Raman spectroscopy (Trier, 2017) and sliding spark spectroscopy (Fengler et al., 2011a). More quantitative analytical methodologies use the total organic fluorine or the extractable organic fluorine. In the context of FCMs analysis, combustion ion chromatography (CIC) (Miyake et al., 2007; Schaider et al., 2017), particle-induced γ-ray emission spectroscopy (PIGE) (Ritter et al., 2017; Schaider et al., 2017), or instrumental neutron activation analysis (INAA) (Schaider et al., 2017) were successfully applied (Schultes et al., 2019).

2.2. *Migration test designs*

Migration tests are well-established tools for gathering information on FCMs to guarantee consumer safety. As previously mentioned, test procedures for plastic FCMs are regulated in the European Union (EU, European Commission, 2011), however, equivalent regulations are not provided for paper based FCMs. Often, the research community adapts the proposed EU guidelines for plastics to the migration tests for paper based materials. This is also the case for studies investigating the migration of PFAS from paper based FCMs into foods. The selection of simulants depends on the food matrix to be imitated. For instance, a mixture of ethanol:water (50:50, v:v) should be applied to imitate food with lipophilic properties, alcoholic food (alcohol content > 20%), and oil-in-water emulsions. Meanwhile, a mixture of ethanol:water (10:90, v:v) is recommended for the simulation of food with hydrophilic properties (European Commission, 2011). Real food typically consists of a complex composition of multiple components that interact and define the properties of the food. Therefore, the selection of suitable food simulants might require some compromise.

Table 1 represents some up-to-date migration studies of PFAS into real food and food simulants from paper based FCMs. Among those studies, five use food simulants (Chiang, 2012; Schlummer et al., 2012; Xu et al., 2013; Yuan et al., 2016; Choi et al., 2018), three use real food (Gebbink et al., 2013; Still et al., 2013; Moreta & Tena, 2014), and six use both (Begley et al., 2005; Begley et al., 2008; Fengler et al., 2011a; Fengler et al., 2012; Elizalde et al., 2018; Zabaleta et al., 2020) The most commonly used real food sample was popcorn (Begley et al., 2005; Begley et al., 2008; Gebbink et al., 2013; Moreta & Tena, 2014), followed by various fast-food samples e.g., muffins (Fengler et al., 2011a; Fengler et al., 2012; Gebbink et al., 2013). The selection of the investigated food samples is not surprising since fast-food wrappings are among the main applications of PFAS treated paper. Migration conditions cover the whole range of possible applications from high-temperature applications for shorter periods of time (Begley et al., 2008) to long-term storage at 5 °C (Still et al., 2013). An example of EU-Regulation conform migration conditions was performed by Zabaleta et al. (2020). The authors simulated long-term storage for 6 months at room temperature with an incubation of 10 days at 60 °C. Since PFOA and PFOS are among the most frequently found and toxic PFAS up-to-date, most migration studies focused on these compounds and their corresponding family of PFCAs/PFSAs. Additional focus was directed to the precursors: PAPs and FTOHs.

3. Migration behavior of PFAS from paper FCMs

The designs of the compiled studies can be divided into two main categories. The first category focuses on the detection of PFAS in food after “realistic” contact with FCMs e.g., Gebbink et al. (2013) and Moreta & Tena (2014). Typically, in these studies, the foods were bought from stores and were either directly analyzed or heated in the packaging as a regular consumer would. To determine the amount of PFAS that migrated from the FCMs, the samples were analyzed before and after heating. The second category also investigates migration behavior and possible influencing factors of the migration by varying migration conditions. These approaches mostly used more controllable (less realistic) migration conditions for instance the exposure of food/ food simulants to paper that was known to contain PFAS. The majority of the investigated articles can be assigned to the second category e.g., Elizalde et al. (2018) and Zabaleta et al. (2020). Different influencing factors on the degree of PFAS migration were reported and are discussed in the following paragraphs. Moreover, the migration of PFAS into food simulants and real food are compared.

An additional third category of studies assesses the amount of PFAS only in the final food product that was in contact with paper based FCMs (Tittlemier et al., 2006; Tittlemier et al., 2007; Ostertag et al., 2009). Whilst this approach provides important information for the assessment of consumer safety migration from FCMs cannot be assumed as the only source of the chemicals since PFAS can enter food products in many different ways. Therefore, studies from this category are not discussed in this work.

3.1. Influence of the experimental conditions

Following general rules of chemistry and physics, the migration of substances from FCMs into food can be influenced by experimental conditions such as temperature and contact time.

3.1.1. Migration temperature

Since the migration process is based on the principle of diffusion, temperature is consequently a key factor in migration studies. Temperature elevation typically results in increased migration due to increased molecular movement (Castle, 2006). Concordant results were observed for the migration of PFAS into food and/or food simulants (Begley et al., 2005; Begley et al., 2008; Fengler et al., 2011a; Gebbink et al., 2013; Elizalde et al., 2018; Zabaleta et al., 2020). Among other studies, Elizalde et al. (2018) observed a clear increase in migration of PFCAs at 120 °C compared to 80 °C after 2 h of exposing milk powders to paper packaging. For instance, the migration of PFHxA into low-fat milk increased from 17.32% at 80 °C to 36.32% at 120 °C (Elizalde et al., 2018). The same trend could be observed for the food simulant Tenax® when the temperature was raised from 80 °C to 160 °C. However, the migration percentages were noticeably lower than in the milk powder samples. The migration from PFHxA was increased from 3.10% (80 °C) to 4.18% (120 °C), and 4.85% (160 °C).

An increase in migration with elevated temperatures is particularly problematic for FCMs used for high-temperature applications e.g., baking or microwaving. Whilst the storage at lower temperatures may limit the migration of PFAS, the heating of the FCMs during processing can accelerate PFAS migration into foods. Results from Gebbink et al. (2013) could support this assumption. A comparison of the diPAPs patterns in popcorn before and after heating in contact with the paper based material showed a transfer of additional seven diPAPs that were not detected before the heating.

3.1.2. Contact time with FCMs

Another key factor for the degree of migration is contact time between the FCMs and food and/or food simulant. A well-established fact is that an increase in contact time increases the risk of migration (Castle, 2006). This was also observed for the migration of PFAS into food and/or food simulants (Begley et al., 2008; Fengler et al., 2011a; Xu et al., 2013; Zabaleta et al., 2020). A kinetic experiment performed by Begley et al. (2008) compared the migration of diPAPs from PFAS treated paper after 2 h and 24 h at 40 °C for food simulants (oil with emulsifier). The observed migration after 1 day was quadrupled compared to a contact time of 2 h. In the same study, a more than ten-fold increase from 0.03 to 0.39 μg/cm^2 was observed for the migration to chocolate spread, comparing a contact time of 1 day and 10 days at 40 °C, respectively.

Fengler et al. (2011a) performed another study investigating the time dependency of the migration into real food e.g., baking muffins in paper muffin cups. All the investigated FTOHs (6:2 FTOH, 8:2 FTOH, and 10:2 FTOH) showed an increase in migration as the baking time was prolonged from 10 min to 20 min. However, a further increase of the baking time to 30 min resulted in a noticeable decrease in the observed migration. For instance, the migration of 6:2 FTOH from muffin cups into muffin dough at 200 °C showed an increase from 134 ng/dm^2 to 3204 ng/dm^2 by extension of the contact time from 10 min to 20 min. Further extension of the baking time to 30 min, however, resulted in a decrease in the migration to 79 ng/dm^2. A possible reason for such decreased migration could be the FTOHs evaporation out of the muffins or their degradation into smaller PFCAs throughout extended baking time (Fengler et al., 2011a). More studies investigated the time dependency of the migration using food simulants. Xu et al. (2013) explored the time dependency of the migration profile of PFCAs from two commercial papers in five different food simulants. Over 22 h, the migration percentage of PFOA into ethanol:water (10:90, v:v, from here forward, ethanol based mixtures are addressed with their percentage on ethanol i.e., 10% ethanol) increased from about 60% to around 90%. The experiment was performed with a constant temperature of 40 °C. The migration percentage after 96 and 240 h did not increase further, suggesting that equilibrium was reached. Also, Zabaleta et al. (2020) presented an increase in migration from PFAS treated paper into ethanol based food simulants (50% and 95% ethanol in water) with increased contact time up to 30 min at room temperature and 60 °C. Approximately, 40% of PFHpA from PFAS treated paper migrated into 50% ethanol after 20 min of contact time at room temperature and increased close to 60% after additional 10 min of contact. Considering the results presented, it can be concluded that the migration of PFAS generally increases with an increase in the contact time over a certain time interval.

3.2. Influence of PFAS content and characteristics

Assuming mass transfer follows Fick's first law of diffusion, the occurring migration is proportional to the PFAS concentration in paper materials (Begley et al., 2005; Castle, 2006; Xu et al., 2013). Simplified, the principle states that a compound will move from an area of a higher concentration, along a concentration gradient, to an area of lower concentration (Castle, 2006). Therefore, assuming a constant diffusion coefficient, a higher concentration of PFAS present in FCMs could result in higher migration rates to food and/or food simulants. Nonetheless, no detailed experimental confirmation was presented in the studies discussing this matter. Besides the amount of PFAS in the FCMs, the characteristics of each individual compound can also influence their mass transfer. The common assumption is that longer carbon-chain length correlates with heavier and less volatile compounds, resulting in lower mobility. Larger compounds are thus assumed to migrate less easily (Castle, 2006; Trier, 2017). PFAS also seem to follow this trend (Still et al., 2013; Moreta & Tena, 2014; Yuan et al., 2016; Zabaleta et al., 2020). The collective data from Zabaleta et al. (2020) is illustrated in Fig. 2. The study investigated the migration from PFAS treated paper into real food (cereals, rice, and milk powder) and food simulant (Tenax®) after long-term exposure (at room temperature for 6 months). Migration percentages of a series of PFCAs (C_5 to C_{10}) showed a general increase with a decrease in the chain length. However, this was true only for a chain length between C_6 to C_{10} PFCAs. The migration percentage of PFPeA (C_5 chain length) into dried milk was 11%, which was about 5% lower than the migration percentage of PFHxA (C_6 chain length). Similar

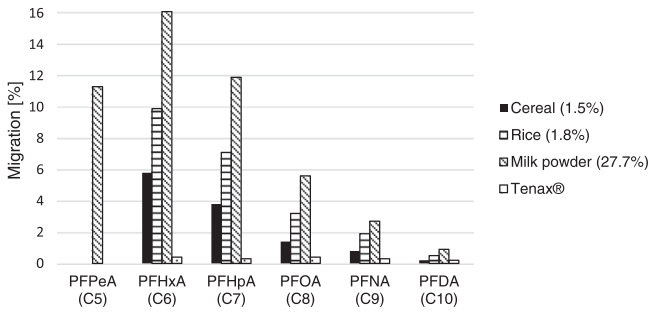

Fig. 2. Migration percentage of PFCAs to food or Tenax® after long-term storage. Compounds with increasing chain length are PFPeA (C5), PFHxA (C6), PFHpA (C7), PFOA (C8), PFNA (C9), PFDA (C10) (Zabaleta et al., 2020).

results were observed in the migration studies performed by Elizalde et al. (2018) and Still et al. (2013) that investigated the migration of PFCAs/PFSAs into milk powder and butter respectively. Additionally, it should be noted that no detectable PFPeA migration was reported into cereal, rice, or Tenax® by Zabaleta et al. (2020). No proven explanation was provided. It is possible that the migrated short-chain PFPeA could exit the food due to its high volatility, similarly as described by Fengler et al. (2011a) for FTOHs. In such a case, the air above the food could act as an additional phase in the migration system (FCM-food-air) and influence the preference of migration depending on the partitioning coefficients between different phases.

3.3. Influence of the food matrix

Besides the general experimental conditions and the migrant itself, the food matrix can also influence the degree of migration. The following factors were observed in previous studies.

3.4. Emulsifier and fat content

The presence of emulsifiers in foods intensely facilitates PFAS migration (Begley et al., 2008; Chiang, 2012; Xu et al., 2013). Begley et al. (2008) were the first to report enhanced migration of PFAS from paper to matrices that contain emulsifiers. Adding small amounts of soy lecithin and TWEEN 60 as ionic and non-ionic emulsifiers increased the migration of PFAS considerably (24 h incubation at 40 °C). The observed relative migration was increased from below 0.1 μg/cm^2 into miglyol to about 1.2 μg/cm^2 and about 0.5 μg/cm^2 by addition of soy lecithin or TWEEN 60 into emulsions of 80% miglyol and 20% water, respectively. Emulsifiers are very common additives in processed food and could make industrial food products a target for higher PFAS migration. The same could apply to takeaway dishes that usually contain emulsifiers in sauces or dressings and are packaged and possibly reheated in cardboard boxes and trays. Furthermore, many foods contain natural emulsifiers e.g., butter. The water-in-oil emulsion is made through phase inversion of cream and therefore contains a complex mixture of proteins (e.g., casein) and lipids (e.g., phospholipids) that stabilize food.

The presence of these naturally occurring emulsifiers could explain the results obtained by Begley et al. (2008). A comparison of water, miglyol, vinegar, butter, and various ethanol-water mixtures showed the highest relative migration of about 0.45 mg/kg food for the migration of diPAPs from a PFAS treated FCM into butter. The migration into other food simulants e.g., miglyol was considerably lower: below 0.05 mg/kg food and about 0.2 mg/kg food into 25% ethanol. Additionally, the migration performance of butter could be reproduced with an emulsion of 80% oil, 20% water, and a non-ionic modifier TWEEN 60. The similar diPAPs migration into butter and butter simulant (0.5 mg/kg food relative migration) further supports the assumption that emulsifiers play a key role in the migration of PFAS (Begley et al., 2008).

Besides the migration of PFAS into butter, the migration into milk powder also was investigated. Elizalde et al. (2018) compared migration into lyophilized low-fat milk (1.55% fat w/v) and whole milk (3.6% fat w/v). Both milk products had similar milk protein content of around 3.12% w/v that acts as a natural emulsifier. In addition to the milk protein, phospholipids that are included in the milk fat could also act as emulsifiers. The study indicated that most of the analyzed PFCAs migrated more toward milk powder with higher fat content: PFHxA (40% compared to 36%), PFHpA (36% compared to 29%), PFOA (22% compared to 16%), PFNA (12% compared to 7%), PFDA (48% compared to 29%), PFTrDA (63% compared to 44%), and PFTeDA (34% compared to 24%). However, no difference in migration of PFBA (9% in both milk powders) and PFPeA (30% in both milk powders) was reported. Furthermore, lower migration rates in high-fat milk powder were observed for PFUnDA (31% compared to 44%) and PFDoDA (48% compared to 63%).

Zabaleta et al. (2020) presented similar results in a recent study. Comparison of PFAS migration after 6 months of storage showed the highest migration rates into milk powder. Three different matrices were investigated: cereals (1.5% fat), rice (1.8% fat), and milk powder (27.7% fat) (Fig. 2). These observations indicated a trend of increased PFAS migration into fattier food matrices; however, the presence of possible phospholipids acting as emulsifier in the food makes a clear statement difficult. Begley et al. (2008) also compared migrations obtained after microwaving popcorns with different fat content and found popcorn labeled as “94% fat-free” contained at least 77% fewer fluorochemicals than standard popcorn of the same brand. Nevertheless, low-fat popcorn packaging itself could contain less PFAS as fat stains and leaks are less probable. Therefore, changes in fat content could not be indubitably identified as the determining factor for the reduced migration.

A migration study performed by Yuan et al. (2016) could confirm this assumption. The study investigated the migration of six different FTOHs (6:2 FTOH to 16:2 FTOH) and 15 PFCAs from paper bowls into various food simulants (10%, 30%, 50% ethanol, and oil). In order to imitate fatty foods or oil-in-water emulsions, food simulants containing 50% ethanol or vegetable oils are recommended (European Commission, 2011). Therefore, the increase of ethanol in the food simulant could simulate the increase of fat in food. The migration test was performed for 15 min at 100 °C (solutions were preheated in a sealed and closed tube, added to the FCMs, and cooled down over 15 min). Firstly, a decrease in PFCAs migration was observed with a decrease in ethanol in the food simulants. Of the 15 analyzed PFCAs (C_4-C_{18}), all were detected in 50% ethanol, twelve (C_4-C_{15}) were detected in 30% ethanol and only nine (C_4-C_{12}) were detected in 10% ethanol. Secondly, it was noticeable that the migration in pure oil was only observed for FTOHs and not for any of the analyzed PFCAs. Considering the surfactant properties of PFAS and the purpose of the coated paper based FCMs, this result is not surprising (Begley et al., 2008).

3.4.1. Water content

Another possible influencing factor for the migration of PFAS is the water content of food products. Fengler et al. (2011a) studied two different muffin recipes for possible differences in FTOHs migration. The muffin recipes were based on expert literature, containing the same basic ingredients but recipe 1 contained less egg, oil, and sugar than recipe 2. Therefore, the muffin doughs are further referred to as low-fat (recipe 1) and standard (recipe 2) dough (Fengler et al., 2011a & 2011b). What could be seen in the experiments was that the low-fat muffin showed significantly higher FTOHs values when baked at 180 °C for 40 min (about 100 times higher) than the standard dough. Contrary, when the temperature was increased to 200 °C (at 20 min baking time) the values of the standard muffin exceeded those of the low-fat one. The authors explained that in the beginning, the low-fat muffin dough contributed to faster FTOHs migration due to its lower water content, while water evaporation in the more moisture standard dough inhibited FTOHs uptake first. When the baking temperature was increased, nothing changed for the low-fat dough, whereas the moisture in the standard dough decreased faster. Combined with the higher fat content this contributed to increasing FTOHs migration.

No explicit experiments regarding the PFAS migration with varying water content have been reported. However, the application of pure water as a food simulant resulted in comparably low migration rates (Begley et al., 2008; Yuan et al., 2016). Only 0.004% for 16:2 FTOH (minimal migration) and 18% for PFBA (maximal migration rate) were reported by Yuan et al. (2016) for the migration into water.

To conclude, the migration of PFAS from paper based FCMs generally appeared to have increased with extension in contact time, increase in migration temperature, a decrease of the carbon chain length, increase in fat content, and presence of emulsifiers in the food matrix.

Overall, approximately the same influencing factors were recognized by Carnero et al. (2021), the review listed the general migration of PFAS from FCMs not focusing on paper based materials. Additionally, the pH

Table 2
Overview of studies, food items (sample size), and food consumption data used to estimate the dietary exposure.

Food	Studies	Exposure Hierarchy	Average consumption [g /kg bw per day]		High consumption [g /kg bw per day]	
			Child	Adult	Child	Adult
Popcorn (n = 9)	Begley et al. (2008), Gebbink et al. (2013),	L5–7: Popcorn (maize, popped)	0.20	0.20	0.68	0.44
Apple pie (n = 1)	Gebbink et al. (2013)	L4–7: Fruit pie-tarts	1.53	0.47	3.28	0.97
Pirogue (n = 1)	Gebbink et al. (2013)	L5–7: Pizza and similar with processed meat topping	1.72	0.50	3.42	1.01
Oatmeal (n = 1)	Gebbink et al. (2013)	L5–7: Oat porridge (NFA); L5–7:Oat grain	0.12	0.21	0.24	0.21
Potato chips (n = 1)	Gebbink et al. (2013)	L6–7: Potato crisps from potato slices	0.43	0.23	1.20	0.58
Fries (n = 1)	Gebbink et al. (2013)	L5–7: Fries (finger chips)	1.19	0.85	2.77	1.76
Sugar (n = 1)	Fengler et al. (2012)	L5–7: White sugar	0.14	0.10	0.43	0.32
Pizza (n = 4)	Fengler et al. (2012), Gebbink et al. (2013)	L5–7: Pizza and pizza-like dishes	1.70	1.17	3.82	2.64
Muffins (n = 6)	Fengler et al. (2012), Gebbink et al. (2013)	L5–7: Muffins	0.83	0.29	2.24	0.70
Burger (n = 4)	Fengler, (2011b), Gebbink et al. (2013),	L5–7: Hamburger with bread	1.26	0.83	2.57	1.64
Butter (n = 5)	Fengler et al. (2011b & 2012), Still et al. (2013)	L3–7: Butter	0.20	0.09	0.66	0.25
Cheese sliced (n = 3)	Fengler et al., 2012)	L4–7: Firm-ripened cheeses (NFA); L4–7:Processed cheese, sliceable	0.49	0.4	1.41	0.36
Fried potatoes (n = 2)	Fengler et al. (2012)	L5–7: Pan-fried potato	1.49	0.63	3.52	1.62
Bread (n = 3)	Fengler et al., 2012)	L5–7: Mixed wheat, rye bread, rolls (NFA) L5–7: Rye bread and rolls, whole meal	1.18	0.55	3.03	1.44
Fish finger (n = 2)	Fengler et al. (2012)	L5–7: Fish fingers, breaded	0.77	0.47	1.56	0.76

value and the salt content of the food matrix were reported to increase the chances of PFAS migration from PFAS treated cooking utensils (AbdulFadl et al., 2019). However, no studies investigated these factors for paper based FCMs.

3.5. Migration to food simulants compared to real food

Considering the plethora of factors influencing the occurrence of migration, it is not surprising that multiple studies reported the poor performance of food simulants to mimic the migration of PFAS into food (Begley et al., 2008; Elizalde et al., 2018; Zabaleta et al., 2020). Particularly, cautionary measures must be taken in the simulation of lipophilic foods containing natural emulsifiers e.g., infant whole milk powder (Still et al., 2013; Elizalde et al., 2018) or other dry food e.g., rice and cereal. The usage of the food simulants recommended in EC regulation 10/2011, Tenax® and oil, have been shown to underestimate the migration of PFAS from FCMs. This is illustrated in Fig. 2 containing the compiled results from Zabaleta et al. (2020). Already in 2008, Begley et al. stated that the low vapor pressure of some PFAS could be responsible for low or no migration into Tenax®.

The presented data indicates that the use of food simulants for the investigation of the migration from PFAS into food should be carefully considered. This is especially the case when EC recommendations for migration tests developed for plastic FCMs are applied to paper FCMs. Instead of the proposed food simulants oil and Tenax®, alternative simulants for instance emulsions, could be used. Nonetheless, to evaluate the migration of PFAS from FCMs realistically, real food should be used. Xu et al. (2013) proposed the use of model substances only to get a general idea about the migration of PFAS. Detailed migration tests should be performed with specific products (Xu et al., 2013).

Furthermore, it should be mentioned that the direct comparison of migration performance using real food, food simulants, and the same migration conditions is limited to the food simulants Tenax® (Elizalde et al., 2018; Zabaleta et al., 2020) and miglyol (Begley et al., 2005; Begley et al., 2008) of the studies presented in Table 1. This highlights the necessity for further studies investigating this topic.

While currently no regulations exist that were developed for the migration tests on paper based FCMs, the Council of Europe recommends the application of migration conditions developed for plastic FCMs to investigate the compliance of paper based FCMs (Trier, 2017). Nevertheless, it has been recognized that this approach can be problematic in the context of PFAS migration, and guidelines try to address this issue and improve testing procedures. For example, the Nordic Council of Ministers recommends the use of alcohol-based simulants to better take into account the specific physiochemical properties of PFAS e.g., a mixture of 95% ethanol may be used for initial screening experiments, and 50% ethanol to test migration into food that contains emulsifier or to investigate migration into dry food. Yet, the optimal food simulants to mimic dry food are still not identified (Trier, 2017). Another example for such efforts to improve migration tests on paper based FCMs are technical guidelines such as those published by the European Directorate for the Quality of Medicines and HealthCare (EdQm) (EdQm, 2021). This two-part document consists of the Council of Europe Resolution CM/Res (2020) that covers updates regarding the general safety and quality of FCMs on the one hand, and of a technical guide on paper and board FCMs on the other hand. Included in the technical guide are topics such as additional definitions, additional testing conditions and methods for analysis of particular compounds.

With regard to migration test conditions, the technical guide stresses the necessity to test the most extreme predicted contact conditions between the FCMs and food, as well as the prioritized use of real food to investigate migration. Nevertheless, no further specifications for food simulant selection in the context of PFAS migration are provided. Furthermore, specific migration limits for some constituents or contaminants in food simulants are specified. This, again, does not apply for PFAS, as migration limits of this substance class are listed as “still under discussion”.

4. Risk assessment of PFAS migrating from paper based FCMs

As stated earlier, the contribution of migration to dietary PFAS intake is often neglected in typical risk assessment procedures. Here, we estimate this contribution through exposure scenarios based on data found in literature. This estimate will be used to illustrate the risk that may be related to PFAS exposure from food contaminated by PFAS migration from paper based FCMs and to highlight some problematic factors in the risk assessment procedure itself. Only concentrations of PFAS detected in real food will be used for the exposure estimation.

4.1. PFAS exposure safety thresholds

Potential consumer health concerns can be predicted by comparison

of the estimated weekly PFAS exposure with the tolerable weekly intake (TWI) i.e. the safety threshold. In 2018, EFSA CONTAM Panel released a TWI value of 6 ng/kg body weight (bw) per week for PFOA and 13 ng/kg bw/week for PFOS (Knutsen et al., 2018). In view of new toxicological findings, bioaccumulation of some PFAS, detected PFAS concentrations in human serum, but mainly effects on the immune system EFSA issued an updated guideline in 2020. The updated TWI value is 4.4 ng/kg bw/week for the sum of PFNA, PFOA, PFOS, and PFHxS (Schrenk et al., 2020). Nevertheless, other PFAS that were reported to migrate from paper based FCMs are also associated with other possible adverse health effects such as liver toxicity (Bil et al., 2021) or reproductive toxicity (Rosenmai et al., 2013). Consequently, investigation of the suitability of the established EFSA recommended procedures in the context of PFAS migration may be advantageous for consumer safety.

4.2. Dietary PFAS exposure estimation due to migration from FCMs

4.2.1. PFAS content in food

For the determination of PFAS migrated from FCMs into food, suitable literature was selected. To ensure a realistic estimation of PFAS migration, only studies that performed migration tests into real food samples after contact with paper based FCMs were selected. An overview of the selected studies including their food items is provided in Table 2. Migration conditions are summarized in Table 1 and specified further in the supplementary materials ("Overview Data & Mig. Conditions"). The combined assessment of these studies allowed the consideration of 19 different PFAS that migrated into 15 different food matrices after intended contact with paper based FCMs. A summary of the found average amounts of each PFAS are summarized in Table 3 and a detailed overview is provided in the supplementary materials.

4.2.2. Food consumption data

All statistics on food consumption and food categories were extracted from the EFSA Comprehensive European Food Consumption Database (EFSA, 2021). Dietary habits of children (36 months to 9 years) and adults (18–64 years) in the Swedish population were chosen. For the research on food consumption of children the survey with the abbreviation "NFA" performed by Enghardt-Barbieri et al. (2006) was used. The study investigated food consumption of 1473 subjects 2003–2006. The study with the abbreviation "RIKSMATEN 2010" performed by Amcoff et al. (2012) was used for research on food consumption of 1210 adults. Each food item in Table 2 was assigned to an exposure hierarchy. For each hierarchy, the average consumption (mean) and high consumption (95th percentile) of each age group were determined from the surveys (Table 2).

4.2.3. Risk assessment procedures

To estimate exposure scenarios, PFAS concentrations in food migrated from PFAS containing FCMs were combined with food consumptions for children or adults according to Eq. (1).

$$\text{Weekly Dietary Exposure} = \sum\left(PFAS\left[\frac{ng}{g\ food}\right]\right) x\ \frac{food\ consumption\ per\ day\ x\ 7\ [g\ food]}{body\ weight\ [kg]} \quad (1)$$

The sum of PFAS *(Σ PFAS [ng/g food])* was calculated in three different ways: summarizing all available PFAS contents (total PFAS), conversion of PFAS contents to PFOA equivalents (relative potency factor (RPF) approach developed by Bil et al. (2021), and summarizing a group of four PFAS (PFOA, PFOS, PFNA, PFHxS) (short PFAS4). Conversion of PFAS to PFOA equivalents and the PFAS4 can be used for comparison with the available toxicological threshold guidelines (4.4 ng/kg bw per week Σ (PFAS4)). The used RPF are summarized in Table 3. In order to predict the worst-case scenario, higher-ranging RPF were used for the conversion of PFPeA (RPF = 0.05), PFHpA (RPF = 1), and PFDA (RPF = 10). DiPAPs, S-DiPAP, and 10:2 FTOH were not part of the original study of Bil et al. (2021) and only limited toxicological data is available, therefore, the used RPF values were based on molecular similarities. The 10:2 FTOH and the thioether analog S-DiPAP were considered with the same RPF value as 8:2 FTOH and 8:2 diPAP, respectively. Additionally, for the calculation of the sum of PFAS, the reported lower limit of quantitation (LOQ) was used when the compound concentrations were below the LOQ. In addition, only Σ (PFOA, PFOS, PFNA) (short Σ (PFAS3)) could be assessed since PFHxS was not included in the considered studies. Furthermore, the total weekly intake of "*total PFAS*" and the "*PFOA Equivalent*" was calculated without the contribution from popcorn. The considered studies were conducted in 2008 and 2013. Since then, research on the topic and improved guidelines resulted in a general decrease of PFAS use in popcorn bags. Therefore, the observed contents are not representative for state-of-the-art FCMs. Comparison of the calculated total weekly intake considering the "PFOA Equivalent", the "total PFAS", or the "Σ (PFAS4)" additionally provides information on the suitability of EFSA's recommended TWI value for to assess the possible risk of PFAS migration from paper FCMs.

4.3. Risk assessment: results & discussion

The estimated weekly intakes of PFAS for each food item and the corresponding total weekly intakes are provided in Table 4.

In conformity with the application of the EFSA recommended exposure estimation procedure, Σ (PFAS3) (PFHxS was not included or detected in the considered studies) resulted in total weekly intakes from 0.37 to 1.50 ng/kg bw/week. None of the estimated exposure scenarios exceeded the guideline value of 4.4 ng/kg bw/week. This may indicate that the migration of PFAS from paper based FCMs does not pose a risk to the consumer. However, this approach could only considers three out of 19 investigated compounds. The enormous difference between the weekly intakes of total PFAS (725–4241 ng/kg bw/week) and the EFSA-Sum approach highlights the substantial neglect of PFAS other than PFOA, PFNA, PFOS, and PFHxS. The majority of migrated PFAS belongs to the group of FTOHs (Table 3) but no guideline values for the TWI of FTOHs is currently available. Consequently, the risk to the consumer cannot be directly evaluated. An indirect approach to comprehensively assess consumer risk was proposed by Bil et al. (2021). The liver toxicity of several PFAS was assessed and compared to PFOA to establish RPF values (Table 3). Concentrations of individual PFAS were converted to PFOA equivalent using their corresponding RPF.

Total weekly intake of PFOA equivalents ranges from 28 to 152 ng/kg bw/week - all exceeding the TWI (4.4 ng/kg bw/week), and therefore, possibly posing a health risk to the consumer, especially for children with lower body weights. Nevertheless, further data on analytes without available toxicological reference values is needed to fully understand the health risks to consumers.

However, it should be noted that these calculations include variations in the detection of PFAS, the foods consumed, and the assumed RPF values that may affect exceedances of the toxicological threshold. Also,

Table 3
Overview of detected PFAS (with averaged PFAS amounts) in food items and relative potency factors (RPF) used for the conversion into PFOA equivalents (detailed composition of averaged PFAS amounts provided in supporting documents).

	Popcorn	Apple Pie	Pirogue	Oatmeal	Chips	Fries	Sugar	Pizza	Muffin	Burger	Butter	Cheese	Potato	Bread	Fish Finger	RPF
Detected PFAS	[ng/g food]															
6:2 DiPAP	0.003	0.002	N.D	0.0002	0.006	0.002	N.A	0.001	0.003	0.004	N.A	N.A	N.A	N.A	N.A	0.02
8:2 DiPAP	0.001	N.D	N.D	0.0001	0.004	0.0001	N.A	N.D	0.0001	0.002	N.A	N.A	N.A	N.A	N.A	0.04
10:2 DiPAP	0.011	N.D	N.D	0.002	0.035	0.002	N.A	N.D	0.002	0.002	N.A	N.A	N.A	N.A	N.A	0.04
S-DiPAP	1833	N.A	N.A	N.A	N.A	N.A	N.A	N.A.	N.A.	N.A.	N.A.	N.A	N.A	N.A	N.A	0.04
PFBA	* N.A	N.A	N.A	N.A	N.A	N.A	0.003	0.001	0.002	N.A.	0.005	0.006	0.002	0.001	0.0003	0.05
PFPeA	**N.D	N.D	N.D	0.020	0.020	0.020	N.A	N.D	0.020	0.020	N.A	N.A	N.A	N.A	N.A	0.05
PFHxA	0.012	N.D	N.D	0.007	0.007	0.007	N.D	0.001	0.002	0.007	0.013	0.017	0.0001	0.0002	0.510	0.01
PFHpA	0.003	0.003	0.023	0.002	0.002	0.002	N.A	0.040	0.005	0.003	N.A	N.A	N.A	N.A	N.A	1
PFOA	0.006	0.009	N.D	0.002	0.0002	0.0002	N.D	0.0004	0.005	0.011	0.031	0.0003	N.D	N.D	0.0003	1
PFNA	0.0004	0.001	N.D	0.0002	0.0002	0.0002	N.A	0.019	0.005	0.010	0.005	N.A	N.A	N.A	N.A	10
PFDA	0.001	N.D	0.003	0.0001	0.0001	0.0001	N.A	0.001	0.0001	0.004	0.007	N.A	N.A	N.A	N.A	10
PFUnDA	N.D	N.D	N.D	0.014	0.014	0.014	N.A	0.004	0.014	0.014	0.008	N.A	N.A	N.A	N.A	4
PFDoA	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	0.011	N.A	N.A	N.A	N.A	3
PFTrDA	N.D	N.D	N.D	0.0002	0.0002	0.001	N.A	0.017	0.0002	0.0002	0.000	N.A	N.A	N.A	N.A	3
PFOS	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A.	N.A.	N.A.	0.015	N.A	N.A	N.A	N.A	2
PFDS	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A.	N.A.	N.A.	0.006	N.A	N.A	N.A	N.A	2
6:2 FTOH	N.A	N.A	N.A	N.A	N.A	N.A	0.024	0.225	31.01	1.080	12.89	1.930	3.525	52.89	0.576	0.02
8:2 FTOH	N.A	N.A	N.A	N.A	N.A	N.A	N.D	0.204	16.97	1.348	14.47	2.816	16.011	32.20	0.552	0.04
10:2 FTOH	N.A	N.A	N.A	N.A	N.A	N.A	0.054	0.087	6.345	1.567	7.40	2.678	17.859	14.58	0.606	0.04

* N.A. (not analyzed i.e., was not included in the studies)
** N.D. (not detected i.e., was analyzed but not detected in the samples)

this exposure assessment is based on a limited number of studies that were performed between 2008 and 2013. No further migration studies were available in the literature search that met the criteria decided upon to keep the approach as realistic as possible (analysis in real food, realistic contact with FCMs, and differentiation between before and after contact with the FCMs). In recent years, the paper and board FCMs changed considerably. Efforts have been made to improve the control procedures and put pressure on the packaging manufacturers (Carnero et al., 2021). Based on the Montreal Protocol, Cousins et al. (2019) determined that the substitution of PFAS with less risky substances is efficient enough to maintain the required functionalities of FCMs. As a consequence, several studies reported that the content of PFAS found in FCMs and the number of PFAS treated FCMs have declined (Elizalde et al., 2018; Granby et al., 2018), especially in FCMs that gained a lot of attention due to high levels of detected PFAS (e.g., popcorn bags). Additionally, a shift from longer chained PFAS e.g., PFOS to shorter chain ones e.g., PFBA occurred. The reason for this change was the assumption that these alternative PFAS show a more preferable toxicological and environmental profile (Kwiatkowski et al., 2020) and the declaration of PFOA and PFOS as persistent organic pollutants (Downie et al., 2012). Toxicological data regarding these replacements, however, does not support this theory (Kwiatkowski et al., 2020; Nian et al., 2020; Rericha et al., 2022). This, for instance, resulted in the voluntary phase-out of 6:2 FTOH use in US food packaging production by three manufactures by the end of 2023 (Boucher, 2020).

Nonetheless, the performed literature-based risk assessment illustrates the variety of PFAS found to migrate into food products from FCMs. Not only PFCAs/PFSAs but also FTOHs contribute to the dietary PFAS exposure of the consumer and potentially cause adverse health effects, especially for children. Therefore, comprehensive ways to assess potential health risks, such as the RPF approach or toxicological reference values that consider more than 4 PFAS, are required to avoid an underestimation of the PFAS exposure. Additionally, these predicted exposure scenarios consider only a small number of targeted PFAS that is typically included for the performance of migration tests and subsequent risk assessment. Even with a comprehensive approach for the risk assessment, this could lead to an underestimation of PFAS exposure from FCMs. To avoid this underestimation, some countries like Denmark decided to categorically ban the use of PFAS for FCMs that do not have barriers between PFAS and the food contact area (Danish Veterinary and Food Administration, 2019). Even so, until a global solution is found for the more stringent regulation of PFAS in paper based FCMs more research is required to ensure consumer safety.

5. Conclusion

Numerous reviews investigated the risk of the presence of PFAS in food. However, to the authors' knowledge, this is the first article discussing the entire process of PFAS migration from paper based FCMs into real food and the corresponding risk for the consumer. The risk estimation showed that PFAS migration from FCMs can contribute to the dietary exposure of the consumer to PFAS thereby possibly impacting human health. Application of either total PFAS or PFOA equivalents approaches to estimate the dietary exposure exceeded the TWI of 4.4 ng/kg bw/week for Σ (PFAS4). This indicates the potential severity of PFAS migration from FCMs into foods.

Furthermore, knowledge regarding the migration behavior of PFAS from paper based FCMs is scarce. Experimental conditions (contact time and migration temperature), characteristic of the PFAS (PFAS class and/or carbon chain length), and composition of the food matrix (fats, emulsifiers, etc.) can expedite the migration into food products. Particularly, high-temperature applications of FCMs with emulsifier rich food matrices (e.g., baking of muffins) appeared to have a high risk of PFAS migration. Nonetheless, detailed explanations and confirmatory experiments would help gain in-depth knowledge of the parameters that influence migration of PFAS into food and therefore help to prevent it.

Table 4
Dietary exposure estimates for the weekly intake of PFAS migrated from FCMs in different food items and total weekly intake.

	Total PFAS				Sum (PFAS3)				PFOA Equivalent			
	Average Consumer [ng/kg bw/week]		High intake consumer [ng/kg bw/week]		Average Consumer [ng/kg bw/week]		High intake consumer [ng/kg bw/week]		Average Consumer [ng/kg bw/week]		High intake consumer [ng/kg bw/week]	
Food items	Children	Adults	Children	Adults	Children	Adults	Children	Adults	Children	Adults	Children	Adults
Popcorn	2567*	1540*	8727*	5647*	0.0092*	0.0055*	0.0313*	0.0202*	102.7*	61.62*	349.2*	225.9*
Apple pie	0.156	0.048	0.3352	0.099	0.0964	0.0296	0.2066	0.0611	0.182	0.056	0.389	0.115
Pirogue	0.316	0.092	0.6284	0.186	0.0000	0.0000	0.0000	0.0000	0.690	0.201	1.372	0.405
Oatmeal	0.039	0.069	0.0787	0.069	0.0015	0.0026	0.0030	0.0026	0.053	0.093	0.106	0.093
Potato chips	0.266	0.142	0.7413	0.358	0.0012	0.0006	0.0034	0.0016	0.191	0.102	0.534	0.258
Fries	0.405	0.289	0.9433	0.599	0.0033	0.0024	0.0078	0.0049	0.546	0.390	1.272	0.808
Sugar	0.080	0.057	0.2453	0.183	0.0000	0.0000	0.0000	0.0000	0.003	0.002	0.009	0.006
Pizza	7.117	4.898	15.99	11.05	0.2288	0.1575	0.5141	0.3553	3.785	2.605	8.505	5.878
Muffins	316.4	110.6	441.7	266.9	0.0539	0.0188	0.1454	0.0454	9.700	3.389	26.18	8.180
Burger	35.9	23.66	13.13	46.74	0.1887	0.1243	0.3850	0.2457	3.143	2.070	6.40	4.091
Butter	48.80	21.96	125.4	61.00	0.0701	0.0315	0.2313	0.0876	1.947	0.876	6.426	2.434
Cheese	25.55	7.30	39.90	18.77	0.0010	0.0003	0.0030	0.0008	0.889	0.254	2.557	0.653
Potatoes	390.0	164.9	921.5	424.1	0.0000	0.0000	0.0000	0.0000	14.87	6.286	35.12	16.164
Bread	823.3	383.8	1539	1005	0.0000	0.0000	0.0000	0.0000	24.19	11.28	62.13	29.53
Fish finger	12.10	7.385	24.51	11.94	0.0018	0.0011	0.0036	0.0018	0.341	0.208	0.691	0.337
Total weekly intake	1660.5	725.1	4240.8	1846.7	0.66	0.37	1.50	0.81	27.81	60.53	151.70	68.95

* Values excluded for calculation of total weekly intake

However, some other factors that could affect PFAS migration have not been found in the literatures: properties of the material e.g., thickness, composition, unusual use or misuse of the packaging, etc.

Future research on this topic should also focus on including more classes of PFAS (especially FTOHs) and investigating more relevant factors that could influence the degree of PFAS migration. Since paper and board materials will be more and more spotlighted as plastic alternatives in the coming years, there is an immediate need for synchronization of migration studies. This could be achieved through the improvement of general guidelines regarding migration tests for paper and cardboard FCMs. Considering the ubiquity of PFAS in the environment along with their toxicity, it is crucial to reduce their presence in foods through strict, categorical regulations.

CRediT authorship contribution statement

Michaela Lerch: Methodology, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization, Validation, Software, Writing – editing, **Romy Fengler:** Resources, Writing – review & editing, **Gina-Reine Mbog**: Writing – initial draft, Writing – review & editing, **Khanh Hoang Nguyen:** Writing – review & editing, Methodology, Supervision, Resources, **Kit Granby:** Conceptualization, Funding acquisition, Supervision, Project administration, Methodology, Resources, Writing – review & editing,

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.fpsl.2022.100992.

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