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# Assessment of TiO<sub>2</sub> (nano)particles migration from food packaging materials to food simulants by *single particle* ICP-MS/MS using a high efficiency sample introduction system

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## Abstract

TiO<sub>2</sub> is the most widely used white pigment in plastics and food packaging industry, thus the question of its migration towards food and hence the impact on consumers is raised. Since recent research indicate its potential toxicity, it is necessary to study TiO<sub>2</sub> contamination as a consequence of food storage. For this purpose, plastic containers from commercially-available dairy products and custom-made TiO<sub>2</sub>-spiked polypropylene materials were put in contact with 50% (v/v) ethanol and 3% (w/v) acetic acid, which were used here as food simulants. The migration assays were carried out under standard contact conditions of packaging use (as recommended by Commission Regulation (EU) N° 10/2011 for food contact migration testing), and under conditions of extreme mechanical degradation of the packaging. The TiO<sub>2</sub> (nano)particles released in the food simulants were analysed by single particle inductively coupled plasma-tandem mass spectrometry in mass-shift mode and using a high efficiency sample introduction system (APEX™ Ω) to avoid matrix effects from food simulants. For the dairy product containers and for the spiked polypropylene, results showed release of TiO<sub>2</sub> particles of rather large sizes (average size: 164 and 175 nm, respectively) under mechanical degradation conditions, i.e when the polymeric structure is damaged. The highest amounts of TiO<sub>2</sub> were observed in 50% ethanol after 10 days of storage at 50 °C (0.62 ng cm<sup>-2</sup>) for the dairy product containers and after 1 day of storage at 50 °C (0.68 ng cm<sup>-2</sup>) for the spiked polypropylene. However, the level of Ti released in particle form was very small

compared to the total Ti content in the packaging and far below the acceptable migration limits set by European legislation. Release under standard contact conditions of use of the container was not measurable, thus the migration of TiO<sub>2</sub> particles from this packaging to dairy products among storage is expected to be negligible.

**Keywords:** TiO<sub>2</sub> nanoparticles, Migration, Food packaging, Single particle ICP-MS/MS

## 1. Introduction

Food packaging plastics contain a large number of organic and inorganic additives to enhance their appearance, storage properties and performance (Hahladakis et al., 2018; Singh et al., 2012; Wiesinger et al., 2021). Nanomaterials and nanoparticles (NPs) are extensively employed as plastic additives to improve the properties and create new functionalities of food packaging layers (Ahmad et al., 2023; Ashfaq et al., 2022; Dash et al., 2022). One of the most used additives in this industry is titanium dioxide (TiO<sub>2</sub>) (Turner & Filella, 2023), a white powder mainly used for its whitening and opacifying properties (Haider et al., 2019) generally at concentrations in the range of 0.5 to 5% in mass (Day, 1990); this additive is composed of particles ranging in size from < 100 nm (referred here as NPs) to microns level. In food packaging applications, TiO<sub>2</sub> also enhances antibacterial features in polyvinyl alcohols (PVOH) and antimicrobial properties in polyethylene-based films (PE) (Dash et al., 2022; Duncan, 2011) and prevent the food from oxidative degradations due to its ultraviolet light absorption properties (Xiao-e et al., 2004). In addition, TiO<sub>2</sub> was proved to be a crosslinking agent, which improves the plastics gas barrier and water resistance properties in active films (Alizadeh Sani et al., 2022; Zhang & Rhim, 2022).

According to European Union (EU) legislation, plastics intended to be used in contact with food may contain non-authorized substances in their structures as long as functional barriers prevent

any migration and ensure that the release yield is below a maximum level of  $0.01 \text{ mg kg}^{-1}$  in the food. Nevertheless, carcinogenic, mutagenic or reprotoxic (CMR) substances cannot be used in food packaging without authorization even in the presence of functional barriers (European Commission, 2011). To date,  $\text{TiO}_2$  is not concerned by this regulation due the discrepancies between studies regarding its toxicity (Carvalho Naves et al., 2018; El Yamani et al., 2022; Shi et al., 2022; Wu et al., 2020). However,  $\text{TiO}_2$  as food additive (E171, employed mainly used in form of *anatase* crystalline structure) was recently banned in the EU due to its potential genotoxicity by ingestion (European Commission, 2022; Younes et al., 2021) but it is still allowed in food packaging industry (mainly in form of *rutile* crystalline structure) (Turner & Filella, 2023). Therefore, food packaging may release  $\text{TiO}_2$  during storage, thereby entering the food chain and subsequently being ingested by consumers. Nevertheless, no specific migration limit (SML) for food packaging containing NPs has yet been defined in EU legislation (European Commission, 2011). Hence, it is important to investigate the migration of  $\text{TiO}_2$  from packaging during food storage (Souza & Fernando, 2016) and evaluate human exposure.

According to Störmer et al. (2017), migration of embedded NPs by diffusion is expected to be negligibly since the NPs  $> 5 \text{ nm}$  have limited potential to move within the polymer structure. Nevertheless, NPs may migrate from polymers by desorption from the polymer surface (Noonan et al., 2014), dissolution of the NPs (Lin et al., 2014) or degradation of the polymeric matrix by mechanical abrasion or heating (Addo Ntim et al., 2018). So far, only a few studies have investigated the release of  $\text{TiO}_2$  NPs from food contact materials (Addo Ntim et al., 2018; Bott et al., 2014; Enescu et al., 2020; Golja et al., 2017; Huang et al., 2017; Lin et al., 2014; Mackevica et al., 2016). A wide range of migration yields were reported for plastics materials, from of  $\sim 12 \mu\text{g kg}^{-1}$  to  $\sim 2 \text{ mg kg}^{-1}$  (Chen et al., 2019) of total Ti in food simulants (FSs) and  $\text{TiO}_2$  (nano)particle's sizes from 50 to 800 nm (Golja et al., 2017; Mackevica et al., 2016). Addo Ntim et al. (2018) observed higher release of  $\text{TiO}_2$  NPs with abrasion at levels up to  $10^8$  particles per  $\text{dm}^2$  from cookware coatings. Overall, acid FSs showed higher levels of  $\text{TiO}_2$  than alcoholic ones, and levels

TiO<sub>2</sub> increased with the duration and the storage temperature (Chen et al., 2019; Huang et al., 2017; Lin et al., 2014; Mackevica et al., 2016).

Several studies related to the migration of NPs other than TiO<sub>2</sub> (i.e. Ag, Au, CuO) were published in the last years (Bazilio et al., 2023; Gibbions et al., 2021; Paidari et al., 2021), but these data cannot be straightforwardly compared to TiO<sub>2</sub> migration for several reasons. First, because of the difference in size between the different types of NPs (TiO<sub>2</sub> typical sizes ~ 200 nm vs. Ag or CuO typically < 100 nm), which might influence the migration rates and the mechanism of migration (Ahari & Lahijani, 2021; Bazilio et al., 2023; Enescu et al., 2020). Second, because of the stability of the different NPs; for instance, Ag NPs tend to dissolve (in Ag<sup>+</sup>) in acidic media (Mackevica et al., 2016), which means that migration might occur by mechanisms such as diffusion inside the polymeric structure (Ahari & Lahijani, 2021). On the contrary, TiO<sub>2</sub> NPs are highly stable and larger size, hence their migration by diffusion (in the ionic form) is unlikely.

Migration also depends on the studied material, which explains why some studies reported high concentrations of released NPs, while others did not observe any migration (Corps Ricardo et al., 2021). The parameters that may affect the NPs migration yields are the type of polymer and its porosity, the structure (mono- or multi-layer), the micro-morphology of composite film, the size and concentration of particles in the plastic or the presence of a functional barrier (Ahari & Lahijani, 2021; Jokar et al., 2017; Tang et al., 2020).

Most studies on TiO<sub>2</sub> transfer to FSs have been carried out using transmission or scanning electron microscopy (TEM/SEM) (Lin et al., 2014; Mackevica et al., 2016) or relying on total Ti determination by ICP-MS after acidic digestion (Bott et al., 2014; Enescu et al., 2020; Golja et al., 2017; Huang et al., 2017; Lin et al., 2014). Amongst the emerging techniques for the characterization of NPs, single particle inductively coupled plasma-mass spectrometry (spICP-MS) allows characterisation and quantification of NPs in highly diluted environments even in complex matrices such as FSs. This approach allows to obtain the concentration in number of NPs and in

mass (if particle's density is known) and the size of these NPs (assuming the spherical shape of the particles).

The present study reports the quantification of TiO<sub>2</sub> NPs released from TiO<sub>2</sub>-spiked polypropylene plastics and from empty (never used) dairy products containers. The tests were performed using two FSs under two migration conditions, such as (i) in standard contact conditions, as recommended by the European Commission (European Commission, 2011), and (ii) in extreme mechanical degradation conditions. The FSs were analysed after different storage times in order to assess the evolution of migration with time. A previously published approach (Bastardo-Fernández et al., 2023) based on spICP-MS/MS using a high sensitivity desolvation system (APEX™ Ω) was used for the determination of the size and concentration of TiO<sub>2</sub> NPs in the FSs. The total content of Ti in these plastics was also determined by ICP-MS after acid digestion in order to assess the migration yield. The spiked polypropylene served as reference sample of known concentration.

## 2. Experimental

### 2.1. Instrumentation

For total Ti determination, a single quadrupole ICP-MS (iCapQ from Thermo Fisher Scientific, Courtaboeuf, France) equipped with a sea-spray borosilicate nebulizer and a quartz cyclonic spray chamber as sample introduction system was used.

An ICP-MS/MS (8900 type from Agilent Technologies, Les Ulis, France) using the single particle approach was employed throughout the TiO<sub>2</sub> NPs analysis. An APEX™ Ω (Elemental Scientific, Omaha, USA) was also used as high efficiency sample introduction system with the ICP-MS/MS. The APEX™ Ω consists of a quartz heated cyclonic spray chamber (140 °C), a Peltier-cooled condensing system (2 °C) and an ePTFE (expanded polytetrafluoroethylene) helical desolvation membrane (maintained at 155 °C). The purpose of the APEX™ Ω is to evaporate the aerosol droplets, which allows ICP-MS/MS measurement in the presence of solvents (used here as FSs) with recoveries of 85% on average. It also increases sensitivity (10 to 13-fold), allowing to

detect particles as small as 12 nm (limit of detection in size,  $LOD_{\text{size}}$ ), as shown in a previous study (Bastardo-Fernández et al., 2023).

The optimum ICP-MS conditions for the determination of total Ti in the plastic samples and the characterisation of  $TiO_2$  NPs in the FSs are given in Table 1.

A close microwave system (Ethos 1 from Thermo Fisher Scientific, Courtaboeuf, France) was employed for samples digestion in view of total Ti determination.

For the gravimetric preparation of all solutions and suspensions a vortex, a cup horn sonicator (Branson Ultrasonics Corp, VWR, Strasbourg, France) and two precision balances were used (AT200 and AT460 Delta Range, Mettler Toledo, Viroflay, France).

**Table 1.** Instrumental parameters for the characterisation of total Ti in plastics by ICP-MS and  $TiO_2$  NPs in food simulants by spICP-MS/MS.

	ICP-MS	APEX™-spICP-MS/MS
Instrument	Thermo iCapQ	Agilent 8900
Dwell time	200 - 400 ms	100 $\mu$ s
Acquisition time	40 s	1 min
Mass scan type	-	MS/MS (mass shift mode)
Nebulizer gas flow	$\approx 1.05 \text{ L min}^{-1}$	$\approx 0.80 \text{ L min}^{-1}$
Sample input flow	$0.35 - 0.50 \text{ mL min}^{-1}$	$0.35 - 0.50 \text{ mL min}^{-1}$
Torch i.d. injector	2.5 mm	1.5 mm
Gas mode	He	$O_2 + H_2$
Collision/reaction gas flow	He $\approx 4.5 - 5 \text{ mL min}^{-1}$	$O_2 \approx 0.15 \text{ mL min}^{-1}$ $H_2 \approx 7 \text{ mL min}^{-1}$
m/z (Q1)	$^{47}Ti^+$ , $^{48}Ti^+$ , $^{49}Ti^+$	-
m/z (Q1 $\rightarrow$ Q2)	-	$^{197}Au^+$ - $^{197}Au^+$ ; $^{48}Ti^+$ - $^{64}(TiO)^+$

## 2.2. Reagents

A Milli-Q™ system (Millipore S.A., St Quentin-en Yvelines, France) was used to obtain ultra-pure water (18.2  $M\Omega$ .cm, UPW).

Nitric acid (67-69%  $HNO_3$  (w/w), NORMATOM®, VWR Chemicals, Leuven, Belgium), hydrochloric acid (37%  $HCl$  (w/w) AnalaR NORMAPUR, VWR Chemicals, Fontenay-sous-Bois, France), hydrofluoric acid (47-51%  $HF$  (w/w), OPTIMA, Thermo Fisher Scientific, New Jersey, USA) and boric acid (99.999%  $H_3BO_3$ , trace metal basis, Sigma-Aldrich, Steinheim, Germany) were used throughout this study.

For the calibration of the ICP-MS system for Ti total determination, standard solutions of ionic Ti(IV) were prepared in 5% HNO<sub>3</sub> (v/v) and 0.25 g L<sup>-1</sup> H<sub>3</sub>BO<sub>3</sub> at concentrations of 50, 100, 150 and 200 µg L<sup>-1</sup>.

For the calibration of the spICP-MS/MS system for TiO<sub>2</sub> NPs analysis, standard calibration curves of ionic Au(III) (1000 µg mL<sup>-1</sup> in 20% HCl (v/v), LGC Standards, Molsheim, France) and Ti(IV) (1000 µg mL<sup>-1</sup> in 5% HNO<sub>3</sub> (v/v), LGC Standards, Teddington, UK and 1000 µg mL<sup>-1</sup> in 0.24% HF (v/v), SCP Science, Villebon-sur-Yvette, France) were prepared daily.

The suspensions of gold (Au) NPs of 40 nm and 60 nm that were analysed daily for the determination of size-based transport efficiency ( $\eta$ ) in spICP-MS/MS were purchased from BBI Solutions, Crumlin, UK.

Absolute ethanol (EtOH)  $\geq$  99% from Fisher Scientific, Loughborough, UK and glacial acetic acid (purity of 99.8 – 100.5 %, AnalaR NORMAPUR, VWR Chemicals, Fontenay-sous-Bois, France) were employed for the preparation of the FSs.

A TiO<sub>2</sub> powder refereed as NM-10200a from the European Commission (EC) Joint Research Center (JRC) (Ispra, Italy) being composed mainly of *anatase* was employed as a reference material for internal quality control. According to a characterisation carried out by JRC using TEM, the TiO<sub>2</sub> particles of NM-10200a have a mean diameter of 190.6  $\pm$  5.8 nm (European Commission. JRC, 2014). A different TiO<sub>2</sub> sample consisting of *rutile* particles coated with aluminium, which was provided by a global TiO<sub>2</sub> producer, was employed for spiking the plastic materials at different TiO<sub>2</sub> levels, as described in the section below.

### 2.3. Preparation of polypropylene materials spiked with known levels of TiO<sub>2</sub>

The polypropylene (PP) samples (batches) spiked with known levels of TiO<sub>2</sub> pigment (*rutile* form) used in this study were prepared at the Industrial Technical Centre for Plastics and Composites (IPC, Alençon, France). The target TiO<sub>2</sub> levels were 10 and 0.1 g kg<sup>-1</sup>, respectively (spiked-PP1 and spiked-PP2, respectively), which were used as high and low content PP materials for the migration

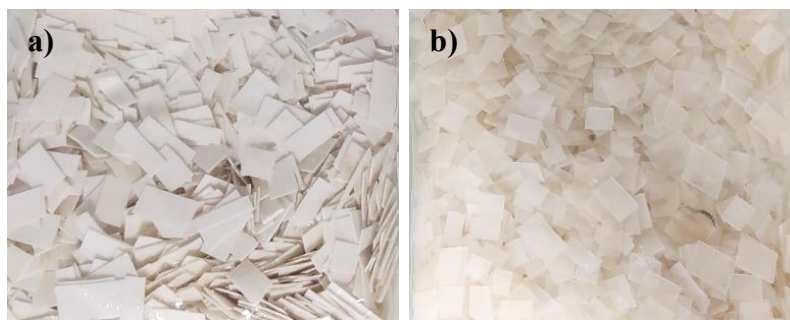


studies. PP was supplied by SABIC Innovative Plastics France under the reference PP 531Ph (melt flow rate (MFR) of  $0.30 \text{ g (10 min)}^{-1}$  ( $230 \text{ }^\circ\text{C}$ ;  $2.16 \text{ kg}$ ) and density  $0.905 \text{ g cm}^{-3}$ ). Samples of  $50 \text{ g}$  of PP were weighed using an analytical balance Sartorius A200-S with a closed chamber and an accuracy of  $0.001 \text{ g}$ . Blends were obtained by using a mixer HAAKE™ PolyLab OS RheoDrive 4 (Thermo Fisher Scientific, Courtaboeuf, France). The PP material and the  $\text{TiO}_2$  powder were introduced by the feeding zone in the mixing chamber composed by two counter-rotating paddles to mix the polymer material with a rotation speed of  $60 \text{ rpm}$  at  $190^\circ\text{C}$  during  $5 \text{ minutes}$ . The melt materials (extrudates) were manually removed from the mixing chamber. Each extrudate was then pressed by a heating-press (Carver 9893 CE, Indiana, USA) using a  $40 \text{ bar}$  pressure at  $210 \text{ }^\circ\text{C}$  during  $5 \text{ minutes}$  in order to obtain thin plastic sheets that were subsequently cut into small pieces. All these steps were carried out four times in order to obtain a total of  $200 \text{ g}$  per formulation (Table 2).

**Table 2.** Formulations of four sub-samples of PPs materials spiked with  $\text{TiO}_2$ .

Sub-sample	spiked-PP1				spiked-PP2			
	1	2	3	4	1	2	3	4
TiO <sub>2</sub> mass (g)	0.497	0.499	0.497	0.497	0.005	0.005	0.005	0.005
PP mass (g)	49.495	49.498	49.995	49.997	49.996	49.989	49.999	50.001
Batch mass (g)	49.992	49.997	49.995	49.997	50.001	49.994	50.004	50.007
Average TiO <sub>2</sub> mass fraction ( $\text{g kg}^{-1}$ )	9.951				0.098			
Total mass (g)	199.98				200.01			

All PP samples were then stored at  $23 \text{ }^\circ\text{C}$  under  $50\%$  relative humidity (RH) for at least four days before further characterisation. The final samples consisted in pieces of  $\approx 0.5 - 2 \text{ cm}^2$  of PP mono-layers and an average thickness of  $0.6 \pm 0.1 \text{ mm}$  and  $1.0 \pm 0.1 \text{ mm}$  ( $n = 10$ ) for spiked-PP1 and spiked-PP2, respectively (see Fig. 1); they served as an internal reference material with known  $\text{TiO}_2$  level to be used for migration studies. The homogeneity of these materials was confirmed by total Ti determination using ICP-MS (see Sup. Material S2).



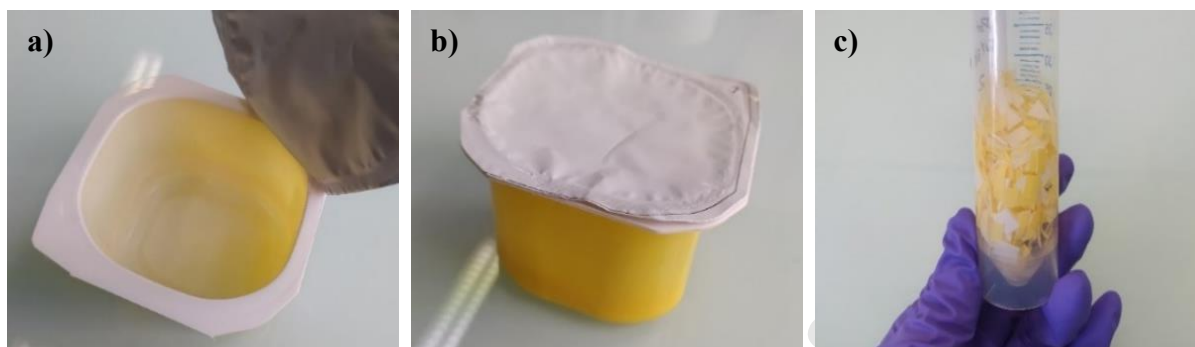
**Fig. 1.** Images of (a) spiked-PP1 ( $\sim 10 \text{ g kg}^{-1} \text{ TiO}_2$ ) and (b) spiked-PP2 ( $\sim 0.1 \text{ g kg}^{-1} \text{ TiO}_2$ ) samples. Note: The materials show different colour depending on the  $\text{TiO}_2$  level.

In addition, IPC provided also several empty (never used) dairy products containers (DPC) consisting of a  $\text{TiO}_2$ -based multi-layer of PP/PVOH/PP with an average thickness of  $0.3 \pm 0.1 \text{ mm}$ , which were also used for the migration study. These containers were from the same production batch of food packaging for common dairy products on the French market; their inner surface was white and the outer one was yellow. These containers were intended to be used for vanilla cream desserts, which can be stored for up to one month at a temperature of  $\sim 4 \text{ }^\circ\text{C}$  (if non-pasteurised) or up to six months at  $\sim 25 \text{ }^\circ\text{C}$  (if pasteurised). As stated above, the homogeneity of these materials was confirmed by total Ti determination using ICP-MS (see Sup. Material S2).

#### 2.4. Migration assays

In this work, a study of the migration of  $\text{TiO}_2$  (nano)particles from dairy products packaging into two FSs, namely 50% EtOH (v/v) (FS1) and 3% acetic acid (w/v) (FS2), was carried out using either standard contact and extreme degradation conditions during the storage. It is worth to note that FS1 simulates foods with a lipophilic character or that are able to extract lipophilic substances while FS2 simulates foodstuffs with a hydrophilic character, which are able to extract hydrophilic substances. Both are recommended by the EC as FSs for milk and fermented milk products, such as yoghurts, buttermilk and cream desserts (European Commission, 2011).  $\text{TiO}_2$  migration was evaluated from the inside and the outside of the DPC (in-DPC and out-DPC, respectively) and by immersion of cut pieces of the packaging in the FS (cut-DPC) (see Fig. 2), according to EC recommendations

(European Commission, 2011) on plastic materials and articles intended to come into contact with food.



**Fig. 2.** Preparations for dairy products packaging migration assays in (a) standard contact conditions (*in-DPC*), (b) external contact conditions (*out-DPC*) and (c) extreme degradation conditions (*cut-DPC*)

Figure 2a shows the plastic material (referred here as *in-DPC*) used to study the migration in standard (contact) conditions while Fig. 2c shows the type of plastic material (*cut-DPC*) used to assess the migration under extreme mechanical degradation conditions. Finally, the external side of the material (Fig. 2b, referred as *out-DPC*) was also employed to determine if the difference of migration between standard (*in-DPC*) and extreme (*cut-DPC*) conditions is caused by the external side (yellow surface) of the plastic container or by the cross-section created when cutting the packaging.

For the assays carried out using *in-DPC*, the lid was slightly opened by the corner of the container and 50 mL of each FSs was added into container. The lid was then closed and the container was carefully sealed with cellophane placing a weight on top to ensure there is no loss of solvent during assays.

For *out-DPC* samples, the label on the containers was removed and then it was placed into a 500 mL beaker and almost fully immersed (a weight was used for this purpose) into 100 mL of FS; the beaker was then sealed with cellophane to ensure there is no loss of solvent during assays.

For the sample *cut-DPC*, some of the DPC were cut into small pieces of  $\approx 0.25 - 0.50 \text{ cm}^2$  after removing the label and the cover. At least three containers were cut and thoroughly mixed before randomly sampling. An amount of  $\sim 3 \text{ g}$  of this (cut) material were placed in a PP

(centrifuge) tube, then 40 mL of FSs added and the tube was closed. The spiked-PP materials were treated in the same way as cut-DPC to study the migration in extreme degradation conditions.

Migration blanks (PP-control) of FS1 and FS2 were obtained in laboratory 50 mL PP flasks by using the procedure described above for in-DPC.

The mixture of samples and FSs prepared as describe above were kept in an oven at 50 °C during 10 days (D10) for DPC samples and 7 days (D7) for PP samples, respectively. The conditions employed here for the DPC materials cover all refrigerated storage times, and also, storage times of up to six months at room temperature according to the European Commission (2011) recommendations for migration assays.

The contact surface between the plastic materials and the FSs was measured at each sampling tome (D0, D0 + 15', D1 and D10).

Aliquots of 15 mL of FSs were sampled after 15 min of storage (D0 + 15') and also 24 h (D1) storage, respectively and then analysed in duplicate (the same day) by using the APEX™-spICP-MS/MS method. For this purpose, the FSs were diluted in order to acquire ~ 2000 spikes (nano)particles during an acquisition timeframe of 1 min.

All the migration experiments and the analyses of FSs described above were carried out in duplicate (n = 2).

## 2.5. Analytical procedures

### 2.5.1. Total TiO<sub>2</sub> content in the containers and spiked polypropylene

The total Ti content of the DPC and PP samples was determined by ICP-MS using the parameters reported in Table 1, following their digestion using a closed microwave digestion system as described hereafter.

For DPC samples, 0.12 g of material was weighed, cut into very small pieces (~ 2 mm<sup>2</sup>) and placed into the digestion vessel; then 0.2 mL of HF, 6 mL of HNO<sub>3</sub>, 1 mL of H<sub>2</sub>O<sub>2</sub> and 3 mL of UPW were added. For spiked-PP1 and spiked-PP2, 0.5 mL of HF, 8 mL of HNO<sub>3</sub> and 2 mL of

H<sub>2</sub>O<sub>2</sub> were used for digestion; the amount of digestion reagents were slightly larger compared to DPC as they were thicker than dairy products containers. The samples were digested during 45 min using a temperature gradient until 230 °C, where this temperature was kept for 10 min. The digested samples were transparent and no residual particles or precipitates were observed in all cases. Then, the residual HF was neutralised using 5 mL of a supersaturated solution of H<sub>3</sub>BO<sub>3</sub> at 62 g L<sup>-1</sup>, and the samples were prone to microwave radiation during 20 min at 160 °C (see Sup. Material S1). Finally, the neutralized samples were brought to 50 mL in UPW and diluted when necessary to match the linearity of the calibration curve. All digestions were performed in PFA flasks and dilutions performed gravimetrically.

The determination of total Ti was carried out using a single quadrupole ICP-MS and three titanium isotopes (<sup>47</sup>Ti, <sup>48</sup>Ti, and <sup>49</sup>Ti) were measured. The quantification was carried out by external calibration and the results are reported as the average of the concentration given by the three isotopes. The method uncertainty was 10% (k = 2) and the limit of quantification (LOQ) = 10 mg kg<sup>-1</sup>.

In order to calculate the migration yield of TiO<sub>2</sub> from the analysed plastics (PP and DPC) materials, the measured Ti level was converted to TiO<sub>2</sub> (TiO<sub>2</sub>/Ti mass fraction = 1.67) assuming that Ti in these samples is present exclusively in the form of TiO<sub>2</sub>.

The efficiency of the digestion procedure and the quantification by ICP-MS was assessed by analysing a similar PP material with known levels of Cd, Cr and Pb, which has made the object of a laboratory inter-comparison (Feng et al., 2010). The recoveries for these analytes in our study were 107.9 ± 10.8 %, 104.9 ± 10.5 % and 94.2 ± 9.4 % for Cd, Cr and Pb, respectively, which proves the method's trueness.

Finally, each digestion batch included a reagent blank to assess the eventual samples cross-contamination. The ICP-MS system was rinsed between samples with a solution of 5% (v/v) HNO<sub>3</sub> during 2 min.

### 2.5.2. Quantification of TiO<sub>2</sub>(nano)particles in food simulants by APEX<sup>TM</sup>-spICP-MS/MS

The spICP-MS/MS measurements for the characterisation of TiO<sub>2</sub> NPs in the FSs resulted from the migration studies were carried out using the method developed previously in our laboratory (Anses) (Bastardo-Fernández et al., 2023). Briefly, an ICP-MS/MS, operated in the mass-shift mode (using the mixture of O<sub>2</sub> + H<sub>2</sub> as reaction gas), was equipped with an APEX<sup>TM</sup> Ω as high efficiency sample introduction system. The APEX<sup>TM</sup> Ω was operated with a N<sub>2</sub> flow of  $\approx 3 - 8 \text{ mL min}^{-1}$  and an Ar membrane sweep flow of  $\approx 2.5 - 4.0 \text{ L min}^{-1}$ . The settings of the method are summarized in Table 1.

Briefly, the dispersions and ionic solutions were gravimetrically prepared in 50 mL PP vials. A dispersion of NM-10200a was prepared in UPW at  $500 \text{ mg L}^{-1}$ . This stock dispersion was stored for a maximum period of six months at room temperature and working dispersions of NM-10200a were daily prepared from it either in UPW or in the FS1 and FS2 (Bastardo-Fernández et al., 2023). Au NPs dispersions of 40 and 60 nm, respectively, were daily prepared in UPW after vortex agitation of the initial suspensions. The Au NPs and NM10200a dispersions were diluted in order to detect  $\sim 1000$  to  $2000$  particles during each spICP-MS/MS run (1 min).

Standard calibration solutions of ionic Au (III) were prepared in a mixture of 0.15% HCl (v/v) and 0.05% HNO<sub>3</sub> (v/v) at concentrations of: 0, 0.05, 0.5 and  $1.0 \text{ } \mu\text{g L}^{-1}$ . Standard calibration solutions of ionic Ti (IV) were prepared in 0.1% HNO<sub>3</sub> (v/v) at concentrations of: 0, 0.05, 0.5 and  $1.0 \text{ } \mu\text{g L}^{-1}$ .

Sample flow rate was gravimetrically measured three times per day of analysis and the average value used as the daily sample flow rate. Each sample (individual replicate) was analysed in triplicate under repeatability conditions. The rinsing procedure consisted of 10 s in 6% (v/v) HNO<sub>3</sub>, 120 s in a mixture of 4% HNO<sub>3</sub> (v/v) and 2% HCl (v/v) and 60 s in UPW in self-aspiration mode.

Data processing was performed in « single particle » mode using MassHunter ICP-MS/MS software in peak integration mode. Calibration coefficients for ionic Au and ionic Ti were obtained in Excel and used for data processing in the single particle software. Average  $\eta$  was calculated by

using the size approach (Pace et al., 2011) based on the analysis of Au NPs of 40 nm and 60 nm diameter, respectively.

TiO<sub>2</sub> NPs from NM-10200a were characterised assuming that particles consist mainly of *anatase* (particle density = 3.90 g cm<sup>-3</sup>), while for the migration suspensions it was assumed that TiO<sub>2</sub> NPs consist mainly of *rutile* (particle density = 4.23 g cm<sup>-3</sup>). For all NPs suspensions (Au or TiO<sub>2</sub>) it was assumed that particles are spherical.

For the samples, only the acquisitions consisting of at least 700 spikes (particles) per minute were considered quantifiable and representative of the distribution of NPs in the sample. The limits of quantification in number of counted particles (LOQ<sub>NP</sub>) and in mass concentration (LOQ<sub>mass</sub>) were calculated on the basis of this premise. The LOQ<sub>NP</sub> were 1.6 × 10<sup>7</sup> and 1.5 × 10<sup>7</sup> kg<sup>-1</sup> in FS1 and FS2, respectively. The LOQ<sub>NP</sub> obtained in our study are of the same order as the few found in the literature for TiO<sub>2</sub> (10<sup>5</sup>-10<sup>7</sup> kg<sup>-1</sup>) (Badalova et al., 2019; Vidmar et al., 2017, 2022).

For suspensions with  $C_p < LOQ_{NP}$ , the mean and median equivalent spherical diameters (ESD<sub>mean</sub> and ESD<sub>med</sub>) were not measured as they were considered non representative of the sample actual distribution. The LOQ<sub>mass</sub> was calculated from the LOQ<sub>NP</sub> considering the average ESD of the TiO<sub>2</sub> particles obtained for the samples with a  $C_p > LOQ_{NP}$ . The LOQ<sub>mass</sub> were therefore 170 and 201 ng kg<sup>-1</sup> in FS1 and FS2, respectively.

Finally, the limit of detection in size (LOD<sub>size</sub>) was determined as the smallest size of the particle size distribution (PSD) and it was 12 nm. It is also worth to note that the use of the forced analogue detection mode assured a reliable characterisation of the particles up to 800 nm (Bastardo-Fernández et al., 2023).

The uncertainties of the method (U, k = 2) were 42.3%, 28.5%, 11.5% and 11.8% for  $C_p$ ,  $C_m$ , ESD<sub>mean</sub> and ESD<sub>med</sub>, respectively for FS1 analysis and 31.1%, 45.1%, 5.8% and 9.0%, respectively, for FS2 (Bastardo-Fernández et al., 2023).

The NM-10200a material containing TiO<sub>2</sub> NPs was daily used for internal quality control (IQC) and also to determine the baseline and threshold minimal values, which were the same for all

the replicates of each sample and all storage times for the same sample. The IQC results ( $n = 3$ ) were satisfactory over all days of analysis with an average mean diameter of  $207 \pm 24$  nm and  $78.7 \pm 11.7$  % of recovery in FS1 and  $208 \pm 12$  nm and  $92.3 \pm 16.9$  % in FS2.

### 3. Results

#### *3.1. Evaluation of TiO<sub>2</sub> NPs migration from polypropylene based food contact materials spiked with TiO<sub>2</sub>*

##### 3.1.1. Determination of total Ti mass fraction in polypropylene based food contact materials spiked with TiO<sub>2</sub> by ICP-MS

The total content of Ti in the spiked-PPs was determined by ICP-MS after acidic digestion as described in the section 2.5.1. Three independent replicates of randomly selected pieces were prepared (digested) and the digests then analysed in triplicate by ICP-MS. The results showed that spiked-PP1 and spiked-PP2 contained  $9.7 \pm 1.1$  and  $0.12 \pm 0.01$  g kg<sup>-1</sup> ( $n = 3$ , U ( $k = 2$ )) of TiO<sub>2</sub>, respectively. These results correspond to a recovery of  $97.1 \pm 9.7$  % and  $124.0 \pm 12.4$  %, respectively, compared to the spiking levels (see section 2.3).

##### 3.1.2. Assessment of the migration of TiO<sub>2</sub> NPs from polypropylene based food contact materials spiked with TiO<sub>2</sub> by APEX™ Ω-spICP-MS/MS

In this section, the spICP-MS/MS approach reported previously (Bastardo-Fernández et al., 2023), see also section 2.5.2) was employed to determine the size and the concentration of TiO<sub>2</sub> particles from spiked-PPs released into the FSs. The assays were carried out by the analysis of two independent replicates, and each duplicate was analysed three times (3 instrumental replicates). The results were expressed per unit of mass of FS (kg<sup>-1</sup>) and per unit of contact surface (cm<sup>-2</sup>).

Table 3 shows the results for the spiked-PPs and the PP-control (blank for all the analysis, including DPC) in both FS1 and FS2.



**Table 3.** Average results ( $n = 2$ ) of  $C_p$ ,  $C_m$ ,  $ESD_{mean}$  and  $ESD_{med}$  for the determination of  $TiO_2$  migrated from PP-control, spiked-PP1 and spiked-PP2 samples to FS1<sup>a</sup> and FS2<sup>b</sup>.

Sample	Food simulant	Time of storage	$C_p$ ( $kg^{-1}$ )	$C_p$ ( $cm^{-2}$ )	$C_m$ ( $ng\ kg^{-1}$ )	$C_m$ ( $ng\ cm^{-2}$ )	$ESD_{mean}$ (nm)	$ESD_{med}$ (nm)
PP-control	FS1	D0 +	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		15'	$LOQ_{NP}$	$LOQ_{NP}$	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		D1	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
	FS2	D10	<	<	205	0.10	—	—
		D0 +	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		15'	$LOQ_{NP}$	$LOQ_{NP}$	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
spiked-PP1	FS1	D1	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		D7	$3.5 \times 10^7$	$5.8 \times 10^3$	873	0.15	184	175
		D0 +	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
	FS2	D1	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		D7	$4.1 \times 10^7$	$1.1 \times 10^4$	770	0.21	169	165
		D0 +	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
spiked-PP2	FS1	D1	$4.7 \times 10^7$	$1.5 \times 10^4$	1397	0.44	184	172
		D7	$2.4 \times 10^7$	$3.8 \times 10^3$	654	0.10	191	181
		D0 +	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
	FS2	D1	$5.3 \times 10^7$	$2.9 \times 10^4$	1082	0.59	168	164
		D7	$7.8 \times 10^7$	$3.1 \times 10^4$	1686	0.68	171	164
		D0 +	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
FS2	D1	$7.2 \times 10^7$	$2.1 \times 10^4$	1311	0.38	155	147	
	D7	$4.1 \times 10^7$	$1.1 \times 10^4$	770	0.21	169	165	
	D0 +	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—	

<sup>a</sup> FS1 = 50% EtOH (v/v)<sup>b</sup> FS2 = 3% acetic acid (w/v)

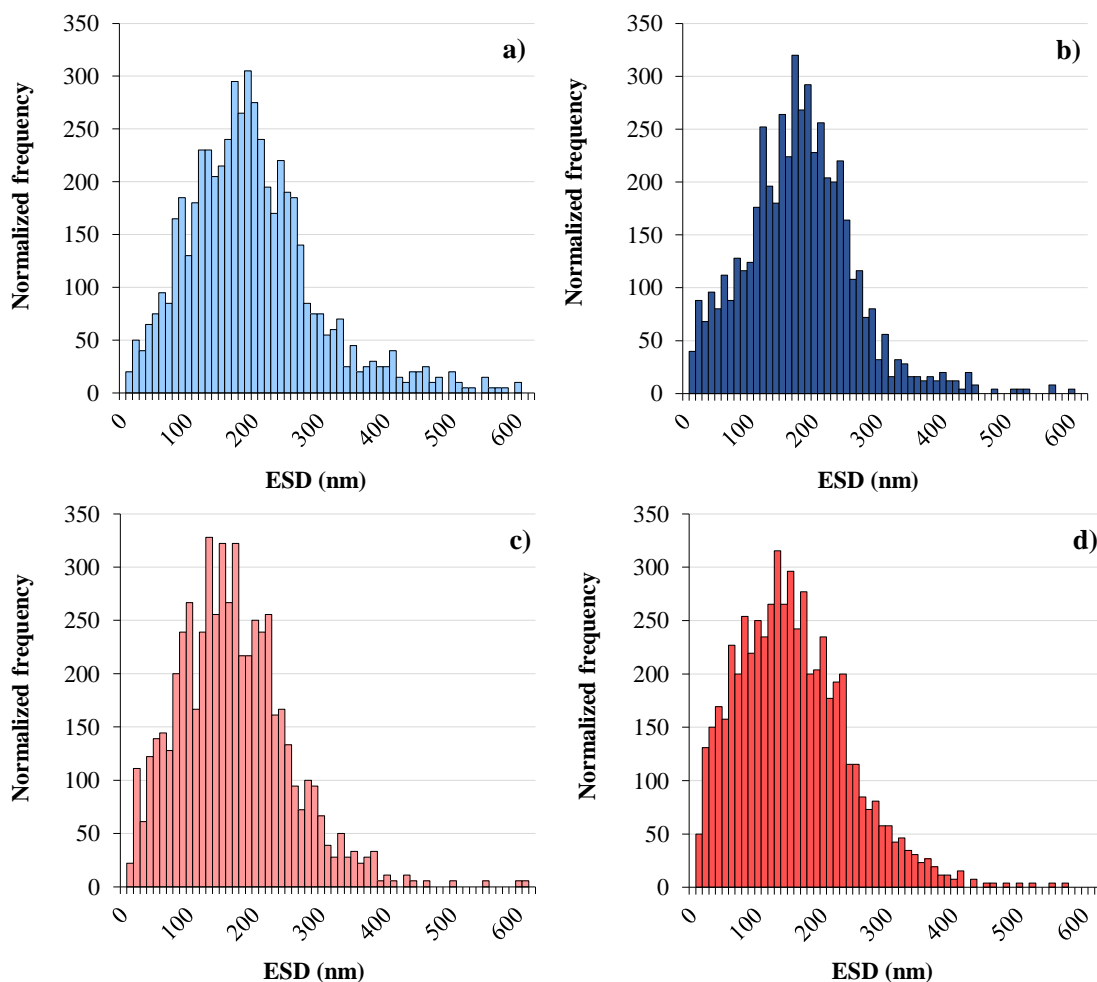
The data obtained for PP-control analysis confirmed the absence of  $TiO_2$  NPs in the assay tubes and in both FSs, with the exception of FS1-D10, which is slightly  $> LOQ_{mass}$ .

All the results for both spiked-PP1 and spike-PP2 were  $> LOQ_{mass}$  and  $LOQ_{NP}$  in FS1. The most significant release was observed at D1, being of  $1.3 \times 10^4$  and  $3.1 \times 10^4$  particles per  $cm^2$  for spiked-PP1 and spiked-PP2, respectively. At D7, there is a significant decrease of  $TiO_2$  levels compared to D1 (considering  $C_p$  and  $C_m$  uncertainties) for both samples. It is likely that the decrease in concentration in FS1 occurs due to a gradual destabilization of the  $TiO_2$  NPs (from the spiked-PPs) in the ethanol-based medium over time.

Very different behaviour was obtained in case of FS2 compared to FS1. While TiO<sub>2</sub> from spiked-PP1 and spike-PP2 was measurable in FS1 very shortly after the contact (D0 + 15'), the TiO<sub>2</sub> released in FS2 was very limited, and long contact duration was needed for the migration to occur (D7). In addition, for both spiked-PP1 and spike-PP2 the concentrations on D7 in FS2 were higher than the ones found in FS1 in any day:  $5.8 \times 10^3$  and  $2.1 \times 10^4$  particles per cm<sup>2</sup> of contact surface for spiked-PP1 and spike-PP2, respectively.

It is worth to note that although spiked-PP1 is 100-fold more concentrated in TiO<sub>2</sub> than spiked-PP2 (see paragraph 3.1.1), the results obtained for C<sub>p</sub> and C<sub>m</sub> were comparable. Moreover, the migration per surface area seems slightly higher for spiked-PP2 (51% higher on D1) than for spiked-PP1. Since spiked-PP2 is nearly twice as thick as spiked-PP1 (1.0 and 0.6 mm, respectively), this could be explained by the release of TiO<sub>2</sub> occurring mainly in the cut-edges of the spiked-PP, where the plastic has been mechanically altered.

Regarding the ESDs, in both FSs and for the two spiked-PPs the results were equivalent within uncertainty and their particles size distributions (PSD) at D7 were nearly identical with diameters ranging from 12 nm to 600 nm (Fig. 3). The average ESD<sub>mean</sub> calculated was 180 nm in FS1 and 170 nm in FS2.



**Fig. 3.** Particle size distributions (PSD) obtained from the migration of  $\text{TiO}_2$  NPs from spiked-PP1 in FS1 (a) and FS2 (b) and spiked-PP2 in FS1 (c) and FS2 (d) in contact conditions simulating a storage of 6 months between 0 and 25 °C (D10).

### 3.2. Evaluation of $\text{TiO}_2$ NPs migration from dairy products containers

#### 3.2.1. Determination of total Ti mass fraction in dairy products containers by ICP-MS

For total Ti mass fraction measurements, three independent replicates of DPC were analysed by ICP-MS (also in three instrumental replicates); the level of total Ti was  $7.8 \pm 0.8 \text{ g kg}^{-1}$  ( $n = 3$ ,  $U(k = 2)$ ), which corresponds to  $13.1 \pm 1.3 \text{ g kg}^{-1}$  of  $\text{TiO}_2$  assuming that all Ti comes from  $\text{TiO}_2$ .

Due to the lack of a  $\text{TiO}_2$  reference material, the results were validated by the analysis of the plastic spiked with NM-10200a, for which the recovery was  $96.8 \pm 9.7 \%$ . In addition, to compensate for possible matrix effect, one replicate was quantified using the standard addition method by adding 100, 200 and 400  $\mu\text{g L}^{-1}$  of ionic Ti to the final dilutions of a digested sample.

This approach confirmed that the TiO<sub>2</sub> content of the dairy products' containers was  $12.3 \pm 1.2 \text{ g kg}^{-1}$ , which proved the efficiency and trueness of the analytical procedure. Due the negligible difference in results between the external calibration and the standard addition results, the external calibration method was used for all quantifications due to its simplicity.

### 3.2.2. Assessment of the migration of TiO<sub>2</sub> NPs from dairy products containers by APEX™- spICP-MS/MS

In this section, spICP-MS/MS was employed to determine the size and the concentration of TiO<sub>2</sub> NPs migrated from dairy products containers to FSs, as previously explained (see section 3.1.2). The assays were carried out in duplicate (2 independent replicates), and each duplicate was analysed three time (3 instrumental replicates). Similarly to the case of spiked-PPs analysis, LOQ<sub>mass</sub> for the DPC were calculated from the LOQ<sub>NP</sub> using the average ESD of the TiO<sub>2</sub> obtained from the samples with a  $C_p > \text{LOQ}_{\text{NP}}$ . The experimental LOQ<sub>mass</sub> were therefore 166 and 135 ng kg<sup>-1</sup> for FS1 and FS2 analysis, respectively.

Table 4 shows the results in terms of  $C_p$ ,  $C_m$ , ESD<sub>mean</sub> and ESD<sub>med</sub> obtained for the TiO<sub>2</sub> migration from DPC to both FS1 and FS2; the results were expressed per unit of mass of FS (kg<sup>-1</sup>) and per unit of contact surface (cm<sup>-2</sup>).

**Table 4.** Average results ( $n = 2$ ) of  $C_p$ ,  $C_m$ ,  $ESD_{mean}$  and  $ESD_{med}$  for the determination of  $TiO_2$  migrated from in-DPC, out-DPC and cut-DPC samples to FS1<sup>a</sup> and FS2<sup>b</sup>.

Sample	Food simulant	Time of storage	$C_p$ ( $kg^{-1}$ )	$C_p$ ( $cm^{-2}$ )	$C_m$ ( $ng\ kg^{-1}$ )	$C_m$ ( $ng\ cm^{-2}$ )	$ESD_{mean}$ (nm)	$ESD_{med}$ (nm)
in-DPC	FS1	D0	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		15'	$LOQ_{NP}$	$LOQ_{NP}$				
		D1	<	<	274	0.20	—	—
	FS2	D10	<	<	219	0.15	—	—
		D0	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		15'	$LOQ_{NP}$	$LOQ_{NP}$				
out-DPC	FS1	D1	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		D10	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		D0	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
	FS2	D1	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		D10	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		D0	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
cut-DPC	FS1	D1	$1.3 \times 10^8$	$2.1 \times 10^4$	3317	0.53	174	165
		D10	$1.8 \times 10^8$	$2.5 \times 10^4$	4167	0.57	172	167
		D0	$2.9 \times 10^8$	$3.5 \times 10^4$	5100	0.62	160	157
	FS2	D1	<	<	< $LOQ_{mass}$	< $LOQ_{mass}$	—	—
		D10	$2.3 \times 10^7$	$4.0 \times 10^3$	399	0.07	155	149
		D0	$4.6 \times 10^7$	$6.0 \times 10^3$	834	0.11	160	155

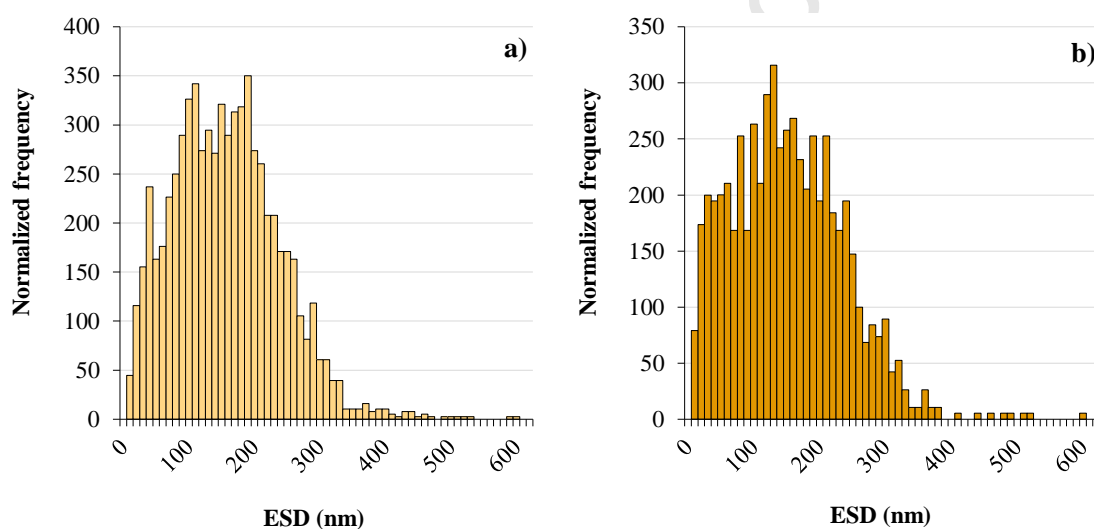
<sup>a</sup> FS1 = 50% EtOH (v/v)<sup>b</sup> FS2 = 3% acetic acid (w/v).

Most results for in-DPC and out-DPC were  $< LOQ_{NP}$  and  $LOQ_{mass}$ . Only  $C_m$  for in-DPC at D1 and D10 were  $> LOQ_{mass}$  in FS1, but it was comparable to the results obtained for PP-control in the same FS (see Table 3), hence indicating negligible migration.

Significant migration was observed only for cut-DPC, for both FS and all storage durations. In case of FS1 use, an increase in  $C_p$  and  $C_m$  can be observed with the increase in the contact duration even taking into account the uncertainties of 42.3% and 28.5% for  $C_p$  and  $C_m$ , respectively (see also Sup. Material S3). The data obtained for D10 was significantly different from the two

precedent days with  $3.5 \times 10^4$  particles released per  $\text{cm}^2$ , the highest migration yield observed. Similar to the spiked-PPs, in case of FS2, the release was proved to be slower and in smaller quantity than for FS1. At  $D0 + 15'$ , no  $\text{TiO}_2$  particles were detected, but at D1 and D10 a progression related to the duration of storage was also seen, ranging from  $4.0 \times 10^3 \text{ cm}^{-2}$  at D1 to  $6.0 \times 10^3 \text{ cm}^{-2}$  at D10 (see also Sup. Material S3).

The ESDs for cut-DPC samples in both FS1 and FS2 were equivalent within uncertainty, giving an average  $\text{ESD}_{\text{mean}}$  of 169 nm and 158 nm in FS1 and FS2, respectively. The PSDs at D10 were also comparable between the two FSs and showed particles from 12 nm up to 600 nm (Fig. 4).



**Fig. 4.** Particle size distributions (PSD) obtained from the migration of  $\text{TiO}_2$  NPs from cut-DPC in FS1 (a) and FS2 (b) after contact conditions simulating a storage of 6 months between 0 and 25 °C (D10).

#### 4. Discussion

It is worth to highlight that the  $\text{TiO}_2$  migration yields depend largely on the physical properties (viscosity, density, etc.) of the investigated material, the nature of the  $\text{TiO}_2$  pigment (size, shape) or the contact protocol operated (Ahari & Lahijani, 2021; Jokar et al., 2017; Tang et al., 2020), so the comparison of our results with those of the literature can be challenging. The highest reported levels are  $\sim 2 \text{ mg kg}^{-1}$  of total Ti using a food simulant consisting of 4% acetic acid and contact during 10 days at 40 °C (Chen et al., 2019). Despite the similarity with our contact conditions, this finding is significantly higher than our migration values. Other studies reported maximum Ti migration

amounts of  $1.4 \mu\text{g kg}^{-1}$  in FS consisting of 3% acetic acid and  $0.6 \mu\text{g kg}^{-1}$  in 50% ethanol after 8 hours at  $25 \text{ }^\circ\text{C}$  (Lin et al., 2014). It is worth to note that most of the studies regarding for  $\text{TiO}_2$  NPs migration from plastics reported greater migration yields in acidic FSs compared to ethanol-based FSs (Chen et al., 2019; Lin et al., 2014), which is different than our study. The increase of migration yield with the storage time observed in our study is also in agreement with the results reported by other authors (Chen et al., 2019; Huang et al., 2017).

The fact that  $\text{TiO}_2$  particles are not released from out-DPC and in-DPC could be explained by the potential presence of functional barriers in the dairy product both inside and outside of the packaging material in order to avoid the migration of  $\text{TiO}_2$  from the surface, even if the external part of the container is not intended to be in contact with food. Our results highlight that the migration observed (cut-DPC and spiked-PPs) is mostly caused by the release of  $\text{TiO}_2$  NPs from the cut-edges of the package in contact with the FSs, which is in agreement with Lin et al. (2014). In addition, no correlation was observed between the level of  $\text{TiO}_2$  in the two spiked-PPs and the migration yield, which rules out diffusion as main migration mechanism.

The migration of  $\text{TiO}_2$  NPs from the commercial containers investigated in this study can therefore be explained via two mechanisms: (i) desorption from the cut-edge surface/interface (Jokar et al., 2017) and (ii) material degradation due to the mechanical stress (Noonan et al., 2014). It seems likely that release from spiked-PPs also occurred as a result of the contact of cut-edges with the FSs after the cut either by one or the other mechanism, as also concluded by Enescu et al. (2020).

To better understand the migration mechanism of  $\text{TiO}_2$  (nano)particles from the materials to food simulants investigated in our study, the total Ti content migrated from cut-DPC sample to FS1 at D1 and D10 was analysed after evaporation of the FS and acid digestion of the dry sample. The total  $\text{TiO}_2$  mass fractions in the cut-DPC-FS1 at D1 and D10 ( $8.0 \pm 1.6$  and  $11.3 \pm 2.3 \mu\text{g kg}^{-1}$ , respectively) were approximately twice the concentration found by spICP-MS/MS in the same samples. The conversion of  $\text{TiO}_2$  NPs into  $\text{Ti(IV)}$  ions seems unlikely due to the low reactivity of

TiO<sub>2</sub> NPs (Skocaj et al., 2011), hence the lower levels obtained by spICP-MS/MS can be explained by a loss of TiO<sub>2</sub> in form of micro/nanoplastic particles generated by mechanical abrasion (Echegoyen & Nerín, 2013, Mackevica et al., 2016) during sample preparation and sedimentation in the vial or in the spray chamber during the analysis (Laborda et al., 2021). Conversely, in case of total Ti determination by ICP-MS, the entire amount of sample (including the eventual micro/nanoplastics fraction) is digested and further analysed.

The migration factors (MF) were calculated by rationing the C<sub>m</sub> (in ng of TiO<sub>2</sub> released per g of plastic) to the total mass fraction determined in the same plastics (see paragraphs 3.1.1 and 3.2.1). For the two spiked-PPs, the MFs were extremely low, even in the most energy condition (FS1-D1) being of 0.0002% for spiked-PP1 and 0.01% for spiked-PP2. Very low MFs were also obtained for cut-DPC at D10, with 0.0004% in FS1 and 0.00006% in FS2. It is worth to note that C<sub>p</sub> values of TiO<sub>2</sub> obtained in our study ( $\sim 10^6$  dm<sup>-2</sup>) are significantly lower than those obtained for ceramic cookware ( $\sim 10^8$  dm<sup>-2</sup>) (Addo Ntim et al., 2018).

In any case, taking into account the generic specific migration limit (SML) of 60 mg kg<sup>-1</sup> for the substances for which no SML is foreseen (i.e. TiO<sub>2</sub>), the DPCs meet the requirements of European legislation both for the case of standard and extreme mechanical degradation conditions, as well as the spiked-PPs prepared without functional barriers (European Commission, 2011).

## 5. Conclusions

This work reports the first study assessing TiO<sub>2</sub> (nano)particles migration from plastic dairy packaging to food simulants using an approach based on single particle ICP-MS capable to quantify the truly released (nano)particle fraction. The particulate TiO<sub>2</sub> fraction released from the investigated commercial food packaging and custom-made spiked polypropylene materials was shown to be higher in 50% ethanol than 3% acetic acid. However, in all studies scenarios, the migrated TiO<sub>2</sub> fraction was very low and mostly arising from the cut-edges hence occurring a result of mechanical degradation (in standard use of the materials, the release of TiO<sub>2</sub> (nano)particles was not measurable).



The results confirm that spICP-MS/MS in combination with a high efficiency desolvation system is able to detect/quantify very low fractions of release particle in migration studies and to characterise individual particles issued as a result of abrasion. Under extreme mechanical conditions, a fraction of TiO<sub>2</sub> is likely to be released along with nano/microplastic particles.

Finally, our study showed that despite the high content of TiO<sub>2</sub> (nano)particles in the dairy products packaging, the migration of TiO<sub>2</sub> from this type of materials to the dairy products during storage is expected to be negligible under standard use of the products.

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## Declaration of interests

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.

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**Table 5.** Instrumental parameters for the characterisation of total Ti in plastics by ICP-MS and TiO<sub>2</sub> NPs in food simulants by spICP-MS/MS.

	ICP-MS	APEX™-spICP-MS/MS
Instrument	Thermo iCapQ	Agilent 8900
Dwell time	200 - 400 ms	100 µs
Acquisition time	40 s	1 min
Mass scan type	-	MS/MS (mass shift mode)
Nebulizer gas flow	≈ 1.05 L min <sup>-1</sup>	≈ 0.80 L min <sup>-1</sup>
Sample input flow	0.35 - 0.50 mL min <sup>-1</sup>	0.35 - 0.50 mL min <sup>-1</sup>
Torch i.d. injector	2.5 mm	1.5 mm
Gas mode	He	O <sub>2</sub> + H <sub>2</sub>
Collision/reaction gas flow	He ≈ 4.5 - 5 mL min <sup>-1</sup>	O <sub>2</sub> ≈ 0.15 mL min <sup>-1</sup> H <sub>2</sub> ≈ 7 mL min <sup>-1</sup>
m/z (Q1)	<sup>47</sup> Ti <sup>+</sup> , <sup>48</sup> Ti <sup>+</sup> , <sup>49</sup> Ti <sup>+</sup>	-
m/z (Q1→Q2)	-	<sup>197</sup> Au <sup>+</sup> - <sup>197</sup> Au <sup>+</sup> ; <sup>48</sup> Ti <sup>+</sup> - <sup>64</sup> (TiO) <sup>+</sup>

**Table 6.** Formulations of four sub-samples of PPs materials spiked with TiO<sub>2</sub>.

Sub-sample	spiked-PP1				spiked-PP2			
	1	2	3	4	1	2	3	4
TiO <sub>2</sub> mass (g)	0.497	0.499	0.497	0.497	0.005	0.005	0.005	0.005
PP mass (g)	49.495	49.498	49.995	49.997	49.996	49.989	49.999	50.001
Batch mass (g)	49.992	49.997	49.995	49.997	50.001	49.994	50.004	50.007
Average TiO <sub>2</sub> mass fraction (g kg <sup>-1</sup> )	9.951				0.098			
Total mass (g)	199.98				200.01			

**Table 7.** Average results (n = 2) of C<sub>p</sub>, C<sub>m</sub>, ESD<sub>mean</sub> and ESD<sub>med</sub> for the determination of TiO<sub>2</sub> migrated from PP-control, spiked-PP1 and spiked-PP2 samples to FS1<sup>a</sup> and FS2<sup>b</sup>.

Sample	Food simulant	Time of storage	C <sub>p</sub> (kg <sup>-1</sup> )	C <sub>p</sub> (cm <sup>-2</sup> )	C <sub>m</sub> (ng kg <sup>-1</sup> )	C <sub>m</sub> (ng cm <sup>-2</sup> )	ESD <sub>mean</sub> (nm)	ESD <sub>med</sub> (nm)
PP-control	FS1	D0 + 15'	< LOQ <sub>NP</sub>	< LOQ <sub>NP</sub>	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	-	-
		D1	< LOQ <sub>NP</sub>	< LOQ <sub>NP</sub>	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	-	-
		D10	< LOQ <sub>NP</sub>	< LOQ <sub>NP</sub>	205	0.10	-	-



FS2	D0	+	<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	15'		LOQ <sub>NP</sub>	LOQ <sub>NP</sub>				
	D1		<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	D10		<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
spiked-PP1	FS1		4.7×10 <sup>7</sup>	1.5×10 <sup>4</sup>	1397	0.44	184	172
		D1	5.7×10 <sup>7</sup>	1.3×10 <sup>4</sup>	1931	0.45	195	185
		D7	2.4×10 <sup>7</sup>	3.8×10 <sup>3</sup>	654	0.10	191	181
FS2	D0	+	<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	15'		LOQ <sub>NP</sub>	LOQ <sub>NP</sub>				
	D1		<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	D7		3.5×10 <sup>7</sup>	5.8×10 <sup>3</sup>	873	0.15	184	175
spiked-PP2	FS1		5.3×10 <sup>7</sup>	2.9×10 <sup>4</sup>	1082	0.59	168	164
		D1	7.8×10 <sup>7</sup>	3.1×10 <sup>4</sup>	1686	0.68	171	164
		D7	4.1×10 <sup>7</sup>	1.1×10 <sup>4</sup>	770	0.21	169	165
FS2	D0	+	<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	15'		LOQ <sub>NP</sub>	LOQ <sub>NP</sub>				
	D1		<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	D7		7.2×10 <sup>7</sup>	2.1×10 <sup>4</sup>	1311	0.38	155	147

<sup>a</sup> FS1 = 50% EtOH (v/v)

<sup>b</sup> FS2 = 3% acetic acid (w/v)

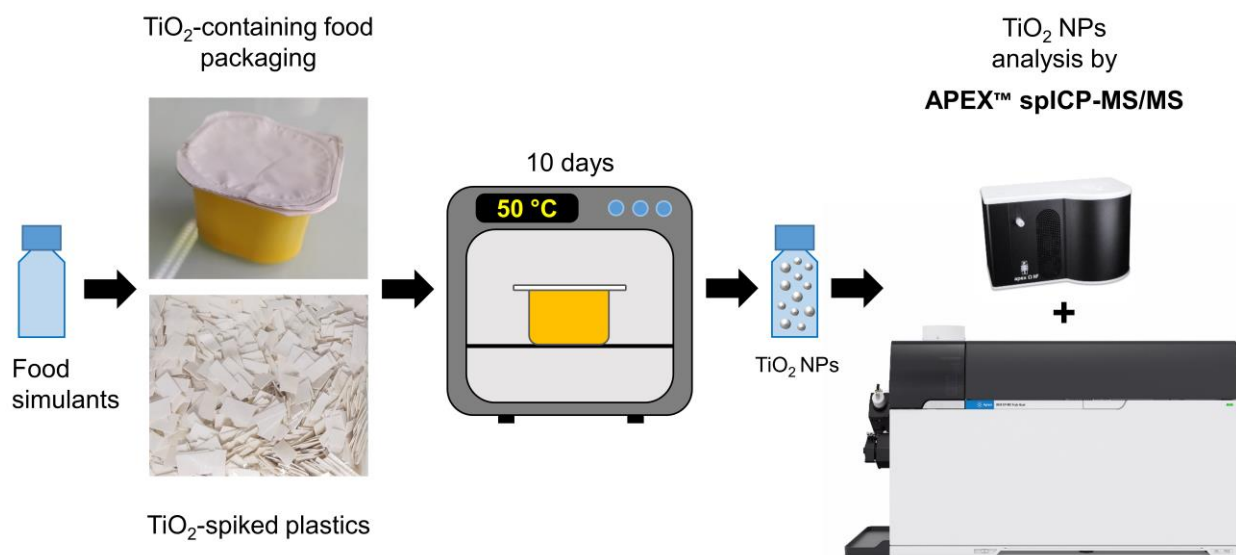
**Table 8.** Average results (n = 2) of C<sub>p</sub>, C<sub>m</sub>, ESD<sub>mean</sub> and ESD<sub>med</sub> for the determination of TiO<sub>2</sub> migrated from in-DPC, out-DPC and cut-DPC samples to FS1<sup>a</sup> and FS2<sup>b</sup>.

Sample	Food simulant	Time of storage	C <sub>p</sub> (kg <sup>-1</sup> )	C <sub>p</sub> (cm <sup>-2</sup> )	C <sub>m</sub> (ng kg <sup>-1</sup> )	C <sub>m</sub> (ng cm <sup>-2</sup> )	ESD <sub>mean</sub> (nm)	ESD <sub>med</sub> (nm)	
in-DPC	FS1	D0	+	<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
		15'		LOQ <sub>NP</sub>	LOQ <sub>NP</sub>				
		D1		<	<	274	0.20	—	—
	D10		<	<	219	0.15	—	—	
FS2	FS2	D0	+	<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
		15'		LOQ <sub>NP</sub>	LOQ <sub>NP</sub>				
		D1		<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	D10		<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—	
out-DPC	FS1	D0	+	<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
		15'		LOQ <sub>NP</sub>	LOQ <sub>NP</sub>				
		D1		<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	D10		<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—	

FS2	D0	+	<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	15'		LOQ <sub>NP</sub>	LOQ <sub>NP</sub>				
	D1		<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	D10		LOQ <sub>NP</sub>	LOQ <sub>NP</sub>	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
FS1	D0	+	1.3×10 <sup>8</sup>	2.1×10 <sup>4</sup>	3317	0.53	174	165
	15'							
	D1		1.8×10 <sup>8</sup>	2.5×10 <sup>4</sup>	4167	0.57	172	167
	D10		2.9×10 <sup>8</sup>	3.5×10 <sup>4</sup>	5100	0.62	160	157
cut-DPC	D0	+	<	<	< LOQ <sub>mass</sub>	< LOQ <sub>mass</sub>	—	—
	15'		LOQ <sub>NP</sub>	LOQ <sub>NP</sub>				
	D1		2.3×10 <sup>7</sup>	4.0×10 <sup>3</sup>	399	0.07	155	149
	D10		4.6×10 <sup>7</sup>	6.0×10 <sup>3</sup>	834	0.11	160	155

<sup>a</sup> FS1= 50% EtOH (v/v)

<sup>b</sup> FS2 = 3% acetic acid (w/v).



## Graphical abstract

### Highlights

- Assessment of TiO<sub>2</sub> NPs migration from food packaging upon storage.
- TiO<sub>2</sub> NPs in food simulants were characterised by APEX™-single particle ICP-MS/MS.
- Alcoholic based food simulants and storage time enhance migration.
- Higher levels of TiO<sub>2</sub> were released under mechanical degradation conditions.

- Very low migration yield of TiO<sub>2</sub> NPs from food packaging was noticed.

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