TiO₂ particles in seafood and surimi products: Attention should be paid to their exposure and uptake through foods

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HIGHLIGHTS

- Relatively high total Ti contents were detected in seafood and surimi products.
- Smaller TiO₂ particles were identified in seafood and surimi products.
- Exposure assessment to TiO₂ particles through food consumption was performed.

GRAPHICAL ABSTRACT

Seafood and Surimi Products

nTiO₂ SEM Image

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ABSTRACT

The sustainable development of nanotechnology requires a thorough understanding of the life cycle of synthesized nanomaterials, including environmental release, deposition, exposure, and potential health risks. Titanium dioxide (TiO₂) materials containing nanosized TiO₂ (nTiO₂) are commonly used as food additives. Thus, dietary intake through foods is the most important route for the exposure of TiO₂ materials. Given the toxic effects of nTiO₂ on the gastrointestinal tract and other tissues, it is imperative to investigate their sources and concentrations in popular foods. Therefore, we conducted a survey on TiO₂ particles in white-colored seafood and surimi products in Beijing. Our data indicated that the total Ti levels reached 6–12 µg/g (dry weight) in some white-colored seafood products, such as squid and cuttlefish, whereas relatively low concentrations were observed in jellyfish at approximately 1–3 µg/g

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(dry weight). For the locally favorite surimi-based food products in the market, the Ti concentrations ranged from 2 to 81 $\mu\text{g/g}$ (dry weight). The exposure assessment showed that the average daily intake of TiO_2 particles through foods varied from 0.02 to 3.09 $\mu\text{g TiO}_2/\text{kg}_{\text{bw}}/\text{day}$, reflected by the Ti concentrations in this study, and that young people of age 20–30 showed the highest exposure level. Together, these results show relatively high concentrations of TiO_2 particles in some seafood and surimi products available in the market, and our findings therefore call for attention on TiO_2 particle exposure and uptake through daily foods.

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1. Introduction

Engineered nanomaterials (ENMs) are defined as materials that possess a size ranging from 1 to 100 nm in at least one dimension (Roco, 2003). Owing to their unique physiochemical properties, ENMs have been increasingly produced and widely applied in many fields, such as biomedicine, personal care products and health products, and food processing and packaging (Lu et al., 2013). One of the most frequently used ENMs is titanium dioxide nanoparticles (nTiO_2), which have numerous applications in paints, cosmetics, foods, environmental remediation materials, to mention a few (Allen et al., 2005; Auffan et al., 2010; Yang et al., 2014; Varshney et al., 2016). The estimated total production of nTiO_2 in the US will reach approximately 2.5 million metric tons by 2025 (Robichaud et al., 2009). Because of the diverse applications and huge yields, the environmental release of nTiO_2 is inevitable during production, transportation, storage, use, and final disposal (Gottschalk et al., 2013), resulting in the potential damages to the ecosystem and thereby posing a threat to living organisms and human beings (Lu et al., 2013; Srivastava et al., 2015).

TiO_2 powders mostly containing nTiO_2 are commonly used in the food industry as additives to improve the quality and taste of food (Buettner and Valentine, 2012). According to the sanitary standards in the UK and China, as much as needed TiO_2 particles can be used in the crisp shells of candies. Thus, TiO_2 particles can reach the mg/g level in chewing gums, drink mixes, and candies with hard shells (Weir et al., 2012; Chen et al., 2013). It has been reported that TiO_2 powders exhibit better bactericidal and fungicidal effects on a wide range of microorganisms than common germicides, which makes these materials favorable food additives for perishable and white-colored seafood (Chawengkijwanich and Hayata, 2008; Chorianopoulos et al., 2011). In addition, TiO_2 particles are applied in surimi-based foods to improve gel texture and sensory quality (Benjakul et al., 2004). Therefore, dietary exposure to TiO_2 powders containing nTiO_2 is considered a notable and direct nTiO_2 uptake route in humans. Although the toxicity of nTiO_2 through oral exposure has been reported (Bergin and Witzmann, 2013; Jovanović, 2015), this important and direct uptake pathway has not received sufficient attention thus far, and the current reports on the realistic exposure levels of TiO_2 particles in food products are rather limited (Weir et al., 2012; Chen et al., 2013; Lomer et al., 2000). Thus, it is imperative to investigate the sources and realistic concentrations of TiO_2 particles in popular foods available in the market. Moreover, for more accurate risk assessments on the dietary intake of TiO_2 particles, it is necessary to analyze their exposure levels in commonly consumed foods.

This study aimed to uncover the realistic exposure levels of TiO_2 particles in white-colored seafood products and surimi products readily available in the markets in Beijing. These products are the two types of favorite local foods, and are produced and consumed in large quantities (Smith et al., 2010; Guenneugues and Ianelli, 2013). In this study, unexpected high Ti levels were found in food

samples, and TiO_2 particles with various sizes including nTiO_2 were identified. This study unveils a previously unidentified exposure route of TiO_2 particles through food consumption.

2. Materials and methods

2.1. Chemicals and materials

High-purity nitric acid, hydrogen peroxide, and hydrofluoric acid were obtained from Sinopharm Chemical Reagent Co. (Beijing, China). The food-grade TiO_2 (i.e., E171) and industrial-grade TiO_2 (i.e., P25) were purchased from a large commercial supplier in China. E171 is a white food colorant with designation from the European Union and is also known as C177891 or Pigment White 6 (PW6) elsewhere, while P25 is the material mostly used in scientific research. Both reference TiO_2 samples were in powdered form. The stock suspensions of these TiO_2 powders were prepared by adding them into ultrapure water from a Milli-Q Gradient system (SAS-67120, Millipore, Molsheim, France), followed by sonication using an ultrasonic cleaner (KQ5200DE, ShuMei, KunShan, Jiangsu, China) for 30 min at 40 kHz.

2.2. Sample collection

Five most popular aquatic product wholesale markets located at different districts in Beijing were selected as the representative sampling sites. These markets are direct suppliers for supermarkets, restaurants, and local residents. Three seafood products (namely, jellyfish, squid, and cuttlefish) were randomly bought from vendors in each wholesale market. For the surimi products, which are processed seafood made from boneless and minced fish muscle tissue, we selected the most commonly consumed ones in the markets, including crab sticks, fish balls, beef balls, and several other seafood extenders, from six different brands. All the sampled products were collected in triplicate.

Samples were kept in ice ($<4^\circ\text{C}$) and taken to the laboratory immediately. Before digestion for analysis, the samples were rinsed with ultrapure water. The dry weights of the samples were determined by drying them at 50°C for 48–72 h. Thereafter, the aquatic samples and surimi products were ground into fine powders for the quantification of Ti contents and characterization of TiO_2 particles.

2.3. Digestion and elemental analysis of samples

Ti contents in each sample were quantified using an inductively coupled plasma mass spectrometer (ICP-MS, 8800 series, Agilent Technologies, Santa Clara, CA), according to a previously developed approach (Weir et al., 2012). All the powdered samples of dry weight of approximately 0.5 g were homogenized in a solution containing 6 mL of 65% nitric acid, 2 mL of 30% hydrogen peroxide, and 2 mL of 40% hydrofluoric acid, and digested at 190°C for 35 min using a Microwave Accelerated Reaction System (MARS)

Express instrument (PyNN110015, CEM Corporation, Matthews, NC). After cooling down to room temperature, the digested mixtures were transferred to Teflon beakers and heated on a hot plate at 180 °C to remove excess acid. The remaining contents in the beakers were then transferred to 5 mL volumetric tubes by rinsing the beaker sides and bottom with 2% nitric acid. Finally, the obtained samples were stored at 4 °C prior to the analysis of Ti concentrations.

2.4. Characterization of nTiO₂

To visualize nanoparticles, nTiO₂ in food samples were extracted and imaged using a field emission scanning electron microscope (FE-SEM, SU-8020 Series, Hitachi, Japan) equipped with an energy-dispersive X-ray spectrometer (EDX, Model 550i, IXRF Systems, Austin, TX). Briefly, the powdered samples were completely dispersed in ultrapure water and collected using 0.22-μm cellulose acetate filters, as previously described (Gondikas et al., 2014). Subsequently, the filter membranes were dried overnight and incinerated in a muffle furnace (SGM016/104, Si Gema, Luoyang, Henan, China) at 550 °C for 3 h, as determined previously (Gondikas et al., 2014). This processing aimed to remove the organic matrices and concentrate the samples. A small amount of ashes was then used for SEM characterization and elemental composition analysis with EDX. The standard TiO₂ powders (E171 and P25) were processed and analyzed in a similar way as that of

2.6. Human exposure assessment

Human exposure to TiO₂ particles was predicted from food consumption-frequency data obtained by a face-to-face questionnaire. Food consumption-frequency questionnaire was randomly issued to residents. A total of 500 participants (n = 500), of whom approximately half were male and half were female aged 10–50 years and 50 + years, were invited to fill in the questionnaire that included questions about frequency (total times in a year), consumption (grams consumed every time), and body weight (kilograms). A returned survey was considered valid only if all the questions were answered; in this study, 93.6% surveys were complete. On the basis of Ti concentrations detected in aquatic products and surimi-based foods, a realistic exposure model was created. In this model, the used relative molecular masses of Ti and TiO₂ were 47.87 and 79.88, respectively. The detected Ti contents were first converted to TiO₂ concentrations by multiplying the values with 1.67, assuming that all present Ti existed as TiO₂. Thereafter, the average TiO₂ concentrations were calculated to be 3.05, 15.65, 13.74, and 6.84 μg/g in jellyfish, squid, cuttlefish, and surimi products, respectively. Next, the consumption of TiO₂ per day in different products was calculated by multiplying the average TiO₂ concentration (μg/g), consumption (g/time), and frequency (times/year), which were obtained from the questionnaires, and then dividing it by 365 days and body weight. The formula used to calculate the exposure level is expressed as follows:

$$\text{exposure level} = \frac{\text{average TiO}_2 \text{ concentration } (\mu\text{g/g}) \times \text{consumption}(\text{g/time}) \times \text{frequency}(\text{time/year})}{\text{body weight}(\text{kg}) \times 365(\text{day})}$$

the food samples. To further substantiate the identification of TiO₂ particles, the standards and powdered samples were dissolved in ethanol and loaded onto silicon wafers. After air-drying, they were assessed using a confocal Raman spectroscopy system (InVia, Renishaw, Gloucestershire, UK), as described previously (Liu et al., 2011).

2.5. Size discrimination of TiO₂ particles

Smaller TiO₂ particles extracted from surimi products of two brands with relatively high total Ti contents were subjected to size discrimination, as described in a previous report (Weir et al., 2012). Briefly, 0.5 g of powdered samples was added into Teflon beakers and treated with 10 mL of 30% hydrogen peroxide and 0.5 mL of 65% HNO₃ at 110 °C to digest the organic matters in the samples. In fact, the processing during this step did not change the size of TiO₂ particles (Weir et al., 2012). The digestion was terminated when the volumes of the remaining contents in the beakers were less than 0.5 mL. After cooling down to room temperature, approximately 20 mL of 2% nitric acid was used to rinse the beaker sides and bottom, and 0.1 M NaOH was then used to adjust the pH to around 7, ensuring that the filters would not be damaged during filtration. After filtering through 0.45-μm nylon filters, TiO₂ particles smaller than 0.45 μm were collected, followed by acid digestion. Finally, the total Ti contents in the digested samples were analyzed using the ICP-MS, as described in 2.3. By dividing these values by the total Ti contents in their corresponding 0.5 g samples, the percentage of smaller-sized TiO₂ particles was obtained.

2.7. Statistical analysis

Data were represented as mean ± standard derivation (SD), and independent *t*-test or one-way ANOVA test was used to analyze the experimental data using the SPSS software. In the current study, the statistical significance was set with *P* < 0.05 or *P* < 0.001.

3. Results and discussion

3.1. High Ti contents were detected in seafood and surimi products

As shown in Fig. 1A, the concentrations of TiO₂ particles, as reflected by Ti contents, were between 1 and 12 μg/g dry weight in seafood samples. Ti contents in squids and cuttlefish that ranged from 6 to 12 μg/g dry weight were higher than those in jellyfish with 1–3 μg/g dry weight (Fig. 1A, *P* < 0.001). Similar to seafood samples, the Ti concentrations in the surimi-based samples ranged from 2 to 81 μg/g dry weight (Fig. 1B). For crab stick and crisp sausage samples, highest Ti contents were found in brand #2 and #1 than the other brands, respectively (Fig. 1B, *P* < 0.001). These results indicate that these white-colored seafood and surimi products contained considerable amounts of TiO₂ particles.

Our findings were consistent with those of previous studies that identified Ti contents in a number of popular foods (Weir et al., 2012; Chen et al., 2013; Lomer et al., 2000). In a previous study, 25 food products were sampled in the UK including white-colored confectionery and sauces. Among these samples, 12 were found to contain TiO₂ particles with concentrations ranging from 0.045 to 224.7 mg/g (a maximum level was detected in the sauce named

Fig. 1. Normalized Ti contents in seafood and surimi products. (A) Seafood products, namely jellyfish, squid, and cuttlefish, were obtained from three popular wholesale markets in Beijing ($n = 3$). (B) Surimi products were from six commercial brands, with the maximum TiO_2 concentration observed in crab sticks ($n = 3$).

Italian dressing) (Lomer et al., 2000). A large survey of 89 foods in the US showed that the top 20 products containing TiO_2 particles included drink mixes, pudding, and candies with hard outer shells, with TiO_2 concentrations ranging from 0.96 to 6.00 mg/g (the Ti contents in the literature were converted to TiO_2 concentrations by multiplying the values with 1.67) (Weir et al., 2012). In chewing gum products with hard shells, high concentrations of TiO_2 (1.51–3.88 mg/g) were detected consistently (Chen et al., 2013). To compare our data with those in the literature, the Ti contents were converted to TiO_2 masses, assuming that all Ti existed as TiO_2 . The calculated results revealed that the TiO_2 concentrations ranged from 1.67 to 20.04 $\mu\text{g/g}$ for seafood products and 3.34–135.27 $\mu\text{g/g}$ for surimi products (data not shown). Our results suggest that the TiO_2 levels in these products were much lower than those in candies with hard outer shells, as reported in previous studies (Weir et al., 2012). However, the TiO_2 concentrations detected in our study were comparable or even higher than those in candies without hard outer shells, baked goods, chocolate, grains, and dairy, with the TiO_2 concentrations ranging from 0.41 to 18.20 $\mu\text{g/g}$ (the Ti levels have been converted to TiO_2 concentrations) (Weir et al., 2012). Therefore, apart from sweets and candies, the consumption of white-colored seafood and surimi products is a prominent uptake route for TiO_2 particles. In terms of uptake mass, this is particularly noteworthy because people consume much larger amounts of foods than candies. To this end, although the actual contents of TiO_2 particles in seafood and surimi products are not as high as those in some candies, their contribution to the overall

Fig. 2. Identification of nTiO_2 in consumer products. (A) SEM images and EDX spectra of P25 and E171 TiO_2 particles. (B) SEM images and EDX spectra of powdered seafood and surimi products. The red lines showed the places where the EDX spectra were collected. All the samples were concentrated on 0.22- μm cellulose acetate membranes and ashed at 550 $^{\circ}\text{C}$ for 3 h prior to SEM and EDX analyses.

uptake of TiO_2 particles would be high because of the consumption of larger amounts of these products.

3.2. Identification of nTiO_2 in seafood and surimi products

The presence of nTiO_2 in food samples was assessed by electron microscope. E171 and P25 were used to identify the morphology, size, and chemical elements of TiO_2 particles, as the reference

Fig. 3. Raman spectra of E171, P25, seafood, and surimi products. The Raman spectral peak positions for food samples were consistent with the mode of anatase. It has been known that the phase of E171 is pure anatase, while P25 has an anatase/rutile mixed-phase.

Fig. 4. Percentage of smaller-sized TiO_2 particles. Fractions that can pass through 0.45- μm nylon filters were quantified in surimi products from two commercial brands with higher total Ti contents ($n = 3$). Asterisk (*) in crisp sausage for brand #1 denotes $P < 0.05$ compared to crab stick, fish ball, and shrimp ball. And asterisk (*) in crab stick for brand #2 indicates $P < 0.05$ compared to all other surimi products.

materials. The representative SEM images of the reference n TiO_2 samples and the particles separated from food samples were compared in Fig. 2. The particles in seafood and surimi samples had a similar shape as that of E171. The particles of P25 and E171 appeared to be homogenous, with sizes of approximately 50 and 50–200 nm, respectively (Fig. 2A), which is in agreement with previous reports (Yang et al., 2014). By contrast, the particles separated from the food samples showed a significant aggregation of individual particles with sizes in the range of 50–200 nm (Fig. 2B). The EDX analysis showed that the both Ti and O elements were found in the particles from seafood and surimi samples,

similar to the reference n TiO_2 particles (Fig. 2A and B). The elements Na, P, Cl, and Ca were also observed in the EDX spectra, which might have been derived from other food additives, such as NaCl, or inorganic components in the original organisms. Furthermore, the presence of TiO_2 particles was confirmed by confocal micro-Raman spectroscopy. As shown in Fig. 3, the Raman spectral peak positions of the particles from food samples were almost identical to those of the reference TiO_2 particles. The particles manifested the characteristic mode of B_{1g} , $A_{1g} + B_{2g}$, and E_g (Fig. 3), which were in accordance with the mode of anatase in a previous study (Quanjuan Xiang, 2011). It has been reported that P25 contains both anatase and rutile phases in a ratio of approximately 4:1 to 3:1, whereas E171 consists of the anatase phase only (Ohtani et al., 2010; Klingenfuss, 2014). These results support that the particles detected in the food samples contained mainly TiO_2 particles with an anatase phase.

3.3. Differentiation of smaller TiO_2 particles in food samples

To separate the small TiO_2 particles at the nano/microscale, we used a previously reported method (Weir et al., 2012). Specifically, we used 0.45- μm filters to obtain small particles in surimi products of two commercial brands with relatively high Ti concentrations (Fig. 1B). As shown in Fig. 4, more than approximately 30% TiO_2 particles from surimi samples were small, and the proportion was different for different surimi samples and brands. Brand #1 showed more smaller-sized TiO_2 particles in fish ball, shrimp ball ($P < 0.05$), and beef ball than brand #2, whereas brand #2 revealed more smaller-sized TiO_2 particles in crab stick and crisp sausage (Fig. 4). Moreover, for brand #1, among the surimi products, the lowest percentage was found in crisp sausage (~30%), compared to those from other surimi products (Fig. 4, $P < 0.05$, except for beef ball). For brand #2, crab stick contained the highest percentage of smaller-sized TiO_2 particles, relative to all other products (Fig. 4, $P < 0.05$). Overall, these results indicate that small TiO_2 particles

Fig. 5. Calculated daily consumption of TiO_2 particles. Exposure assessment was based on food consumption-frequency questionnaires filled by residents ($n = 500$) for (A) jellyfish, (B) cuttlefish, (C) squid, and (D) surimi products.

could readily be retained in food samples. The presence of TiO₂ particles, especially those of smaller size, in popular foods may increase the possible exposure of consumers to TiO₂ particles through food consumption.

3.4. Human exposure to TiO₂ particles through food consumption

We evaluated the human daily exposure levels of TiO₂ particles through consumption of seafood and surimi-based products. Fig. 5 shows the calculated results, with exposure levels of 0.02–0.20 µg TiO₂/kg_{bw}/day from jellyfish (Fig. 5A), 0.09–0.59 µg TiO₂/kg_{bw}/day from cuttlefish (Fig. 5B), 0.52–2.24 µg TiO₂/kg_{bw}/day from squid (Fig. 5C), and 0.22–3.09 µg TiO₂/kg_{bw}/day from surimi products (Fig. 5D). Among these foods, squid and surimi products appeared to result in higher exposure levels ($P < 0.001$). Furthermore, younger people aged 20–30 years were assumed to be exposed to higher levels of TiO₂ particles from seafood and surimi-based foods than other age groups ($P < 0.001$), likely due to the higher consumption of these foods by this population. Additionally, the daily exposure level of male consumers from the age group of 20–30 was higher than that of female consumers ($P < 0.001$). Given the large standard deviations in consumer groups, individual exposure levels to TiO₂ particles greatly depended on the dietary habits, and a small change in the dietary intake could result in a considerable increase in the consumed mass. Nevertheless, these results suggest that considerable exposure should surely be concerned upon the intake of TiO₂ particles through the consumption of seafood and surimi-based food products.

Based on a risk assessment evaluation, the health effects were predicted from a lifelong daily intake of 1.7 µg nTiO₂/kg_{bw}/day through food, supplements, and toothpaste (Heringa et al., 2016), as nTiO₂ can be absorbed by the gastrointestinal tract and pass through the mucus pores to enter other organs (Jovanović, 2015). With limited elimination rate, nTiO₂ accumulated in the gastrointestinal tract and other organs can cause adverse biological effects, including disturbances in the metabolism and gut microorganisms (Jovanović, 2015; Heringa et al., 2016; Bu et al., 2010). Therefore, considering that 36% of food-grade TiO₂ particles (referred to as E171) are nanosized (Weir et al., 2012), detrimental health effects due to the long-term intake of nTiO₂ through seafood products and surimi-based foods, even though at low doses, cannot be excluded. Thus, the uptake of TiO₂ particles through food products should receive more attention.

4. Conclusions

We detected relatively high Ti concentrations in seafood and surimi-based food products and found that TiO₂ particles including nTiO₂ and their aggregates accounted for a considerable fraction of the total Ti concentration. The human exposure assessments indicated that the consumption of these types of foods could be an important route for the uptake of TiO₂ particles, especially for younger people aged 20–30 years. Our findings further signified the need to raise public awareness on TiO₂ particles uptake through food consumption. Therefore, this study reveals a previously unidentified route for the release and accumulation of synthesized TiO₂ nanomaterials in the real world and may offer more bases for their environmental health risk evaluation.

Competing interests

There is no potential conflict of interests to disclose.

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