Exposure assessment of nanotitanium oxide powder handling using real-time size-selective particle number concentration measurements and X-ray fluorescence spectrometry —The possibility of exposure to nonagglomerated nanomaterials during the handling of nanomaterial fine powders—

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Abstract: In this study, airborne particles were collected using filters, and the particle number concentrations were measured in two nanotitanium dioxide (nanoTiO₂)-manufacturing plants. Real-time particle size measurements were performed using both optical and scanning mobility particle sizer and X-ray fluorescence spectrometry (XRF). The respirable particles collected using filters were used to analyze Ti concentrations in the workplace air of two factories engaged in nanoTiO₂ powder bagging processes. The XRF analysis revealed sufficient sensitivity to measure 0.03 mg/m³, which is 1/10 the concentration of the recommended occupational exposure limit of nanoTiO₂ in both stationary sampling and personal exposure sampling settings. In a factory where outside air was directly introduced, micron-sized aggregated particles were generated because of factory operations; however, nanosized and submicron-sized particles were not observed owing to high background concentrations of incidental nanoparticles. Alternatively, in another factory where particles from the outside air were removed using a high-efficiency particulate air filter, work-related nanoparticles were released. The findings of this study suggest that in nanoparticle powder handling processes, a nanoparticle exposure risk exists in the form of nonagglomerated state in nanoparticle powder handling processes.

Key words: TiO₂, Nonagglomerated nanoparticles, Nanomaterial, Industrial hygiene, Work environment, Nanotitanium dioxide, Exposure assessment

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Introduction

Over the last two decades, risks to workers from nanomaterial exposure have become an important topic of interest in the field of occupational health\(^1\)\(^–\)\(^9\). These risks come from two factors. First, nanomaterials constitute a new type of material introduced into the workplace, and their health risks have hitherto been unknown\(^3\)\(^,\)\(^8\)\(^,\)\(^9\). Second, the negative health effects of small particles with sizes of <100 nm in atmospheric air, known as incidental nanoparticles, have already been established in epidemiological studies\(^10\)\(^–\)\(^13\).

Exposure surveys targeting workers handling engineered nanomaterials have been conducted in response to concerns about the health risks posed by engineered nanoparticles. For instance, we conducted exposure surveys in factories handling carbon nanotubes\(^14\)\(^,\)\(^15\) and carbon black\(^15\). Similar to carbon-based nanomaterials, it is important to evaluate workers’ exposure to nanotitanium dioxide (nanoTiO\(_2\))\(^1\)\(^–\)\(^2\),\(^16\)\(^–\)\(^19\).

TiO\(_2\) is used in paints, varnishes, lacquer, paper, plastics, ceramics, printing ink, and fundamental industrial materials\(^1\)\(^–\)\(^2\). NanoTiO\(_2\) particles, with diameters of <0.1 µm, are used to improve optical and chemical properties such as ultraviolet light absorption and catalyst photochemical efficiency. To quantify exposure to nanomaterials, we used a combination of particle number and size measurements, as well as chemical analysis. Measurements of particle number and size provide real-time exposure data related to workers’ activities. However, from our experiences\(^14\)\(^,\)\(^15\), measuring the changes in the nanosized particle concentration with respect to nanomaterial handling has been difficult owing to the high background concentration of incidental nanoparticles. Based on mass concentration evaluations, most industrial nanomaterials are found in the workplace as submicron-sized aggregated particles, with TiO\(_2\) being no exception. Some influential researchers believe that these toxic responses attributed to engineered nanoTiO\(_2\) particles\(^8\)\(^,\)\(^20\)\(^,\)\(^21\) are not correlated with the mass-based concentration but the total surface area. The US National Institute for Occupational Safety and Health (NIOSH)\(^20\) and the Japan Society for Occupational Health (JSOH)\(^21\) have published a recommended exposure limit (REL) and occupational exposure limit (OEL) of 0.3 mg/m\(^3\) for nanoTiO\(_2\) particles. This viewpoint is solely on mass-based concentrations as it has not been accepted and is difficult to confirm due to constraints in measurement technology. However, we assert that it is necessary to establish whether industrial nanomaterials are exposed as engineered nanoparticles because the effects of incidental nanoparticles on health have also been reported\(^10\)\(^–\)\(^13\), and it remains unclear whether agglomerated or nonagglomerated (single) particles carry the same hazards\(^3\)\(^,\)\(^8\)\(^,\)\(^9\). However, quantifying nanosized particles and agglomerates from nanomaterials is difficult. It is essential to assess the exposure to nanosized particles in order to take effective health protection measures for workers because even the same primary particle sizes may have different toxicities if they have various agglomerate sizes\(^22\). As this question has yet to be clearly answered, knowing whether workers are exposed to nonagglomerated nanosized particles remains an important topic in the field of occupational health.

For investigating exposure to nanoTiO\(_2\), we used X-ray fluorescence spectrometry (XRF) as the most suitable chemical analysis method, combined with particle size measurements. The XRF measurement has been adopted as the official method by the US Environmental Protection Agency (EPA)\(^23\) and the Ministry of the Environment of Japan\(^24\) as an analytical method for detecting trace metal containing particles in the ambient atmosphere. These protocols of XRF offer sufficient precision\(^23\)\(^,\)\(^24\) to be viable for the measurement of nanoTiO\(_2\) in the workplace at the 1/10 concentration recommended as the OEL\(^20\)\(^,\)\(^21\). XRF also has an advantage over conventional metal analysis methods, such as atomic absorption spectrometry\(^25\), inductively coupled optical emission spectrometry, and inductively coupled mass spectrometry. These methods require sample digestion before introducing into the analytical devices. Such wet chemical methods for analyzing the TiO\(_2\) concentration entail the decomposition of concentrated sulfuric acid. However, numerous industrial nanoTiO\(_2\) applications feature hydrophobic surface treatments, making the decomposition of sulfuric acid difficult. XRF can be employed to assess solid samples and avoid the issue of acid decomposition\(^23\)\(^,\)\(^24\).

The Ministry of Health, Labour and Welfare (MHLW) and the Japan Industrial Safety and Health Association (JISHA) provided us with the opportunity to measure particle release during the nano-TiO\(_2\) powder bagging process in two nano-TiO\(_2\)-manufacturing plants: one that was conventional plant and another where the air-derived background particles were actively removed. Based on our field survey, we note that the presence of some nonagglomerated nanoparticles comprising the nanomaterials. In this study, we highlight the exposure risks of nanoparticles to workers who are handling nanomaterials in their workplaces. We also demonstrate the use of XRF analyses of TiO\(_2\) for evaluating the occupational exposure risk of nanoTiO\(_2\).
Materials and Methods

We conducted a field survey in two nanoTiO₂-manufacturing factories, hereinafter referred to as factory A (FA) and factory B (FB). These two factories belong to the same chemical company in Japan. During the bagging process of rutile nano-TiO₂ powder, filtration was employed to conduct size-selective particle number concentration measurements and airborne respirable particle collection assessments. The TiO₂ concentration in the filtered airborne dust samples was then analyzed in a laboratory using XRF.

Sample collection devices and analytical instrument

Size-selective particle number concentrations were measured using a portable scanning mobility particle sizer (SMPS: NanoScan 3910 TSI Inc., Shoreview, MN, USA) and an optical particle sizer (OPS: TSI 3330, TSI Inc.). The observed particle sizes were in the range of 10–400 and 300–1,000 nm using SMPS and OPS, respectively. Their operating parameters are presented in Table 1. All particles were assumed to be spherical, and their densities were equivalent to the bulk TiO₂ density (4.9 g/cm³) to convert the number concentrations into mass concentrations. Airborne particles were collected using polyvinyl chloride (PVC) membrane filters (GLA 5000, Pall, USA) by employing an NW354 sampler (Sibata Scientific Technology, Souka, Saitama, Japan) equipped with an LV-40 sampling pump (Sibata Scientific Technology). The NW354 sampler is an impactor-based, size-selective, low-volume air sampler, showing a calibration curve corresponding to the respirable particles defined in ISO7708: 1995[20]. The sampling air flow rate was 20 l/min, and the diameter of the PVC membrane filter was 35 mm. Electroconductive silicone tubing was used to extend the sampling inlets in SMPS and OPS near the inlet of the NW354 sampler. The heights of the sampling locations were ~1.2 and ~2 m away from the hoppers, respectively. Fig. 1 presents the installation of one of the sampling devices. Sampled PVC membrane filters were analyzed using an EDXL-300 energy-dispersive XRF spectrometer (Rigaku, Akishima, Tokyo, Japan). XRF analysis was conducted using the absolute calibration method. Moreover, the calibration curve made with the standard series samples were prepared as follows: the rutile TiO₂ reagent (Fujifilm Wako Pure Chemical, Osaka, Japan) was suspended in pure water and spiked onto the designed filter media for liquid sample XRF analysis (UltarCarry light®, Rigaku), with TiO₂ masses of 0, 10, 25, 50, 100, and 250 μg in the filters.

Details of the field for sample collection and measurement

Particle concentrations were measured, and airborne particles were collected during the bagging process of three types of hydrophobic-treated rutile nanoTiO₂, of which two were from FA and the other from FB. FA synthesized TiO₂ using the sulfuric acid method and had surface treatment facilities, where hydrophobic-treated TiO₂ products were fabricated. We measured the particle concentration and collected particles in two bagging rooms of FA-a and FA-b. The bagging process in both rooms entailed a gravity-driven powder falling into paper bags, with a local exhaust ventilation (LEV) system and combined hoppers in operation. Workers fed TiO₂ powder from the hopper into paper bags whose tops were open. Following powder filling, the worker (or another worker) adjusted the
Fig. 1. Layout of bagging tasks and measurement and sampling location in FA-a and photographs of sampler and particle number concentration measurement devices. A: top and B: side views of the layout of the workers and factory devices and ventilation. C: photograph of samplers. D: photograph of sampling pump and particle size and number measurement devices.
weight of TiO₂ using hand ladles. Finally, the top of the bags was stitched using a sewing machine and stacked on pallets for shipment. Fig. 1 and 2 present the sampling process in FA-a and FA-b, respectively. The LEV system in the FA-a bagging room differed from that in the FA-b bagging room, comprising a push–pull type. The alignment of the push–pull ventilation system in FA-a is presented in Fig. 1B. The air for ventilation in the LEV system in FA was directly drawn from the ambient atmosphere without performing further filtration of atmospheric particulate matter.

The other factory, FB, had some facilities for the surface treatment of fine particles for synthesizing ingredients for cosmetics. To avoid ambient-pollutant contamination and ensure the grade of the cosmetics, high-efficiency particulate air (HEPA)-filtered air was introduced through the ventilation systems. The bagging process was performed, with the related instrument and LEV systems in operation, in a clean room, which was continually supplied with the HEPA-filtered air. There were two ventilators and vibrating sieve-combined hoppers in the bagging room. Following filling and weight adjustments, the powdered product was placed in a plastic bag, and the bag was compressed in a
small, ventilated box to decrease the volume. Finally, the bag was closed using a rubber ring and individually placed in a cardboard box. On the day when our measurements were conducted, two bagging operations were performed in sequence. First, nanoTiO$_2$ was bagged in one of the hoppers (FB-a) and nanoZnO was bagged in another hopper (FB-b). The two bagging operations were performed alternatively by the same team of workers. Two sets of SMPS and OPS were located near both hoppers, and the NW354 sampler was located near FB-a, shown in Fig. 3.

Results

$\text{TiO}_2$ concentrations in the workplaces

Fig. 4 presents filters with sampled particles on the surface. The color of the filters with sampled particles in FA was a darker gray than that in FB. This indicates that fewer particles are originating from the background in FB than in FA. The color of the filter face could be a qualitative index of particle concentrations from the outside air, as the outside air contains numerous colored particles derived from black soot or other combustion origin particles$^{15}$.

The TiO$_2$ content in the sampled particles was measured via XRF analysis and converted to the particle number concentration, which was measured using OPS; the results are presented in Table 2. In FA, the particle concentration of TiO$_2$ was not obtained quantitatively due to the high background concentrations. Therefore, Table 2 presents the estimated values obtained using OPS in FB only. The order of the TiO$_2$ concentration in the three sampled locations, namely, FA-a, FA-b, and FB, was almost the same. Alternatively, in FB, the order of the TiO$_2$ concentration obtained using XRF analysis differed from that estimated using the optical counting method.

Time course studies of the size distribution of particles in workplaces

Fig. 5, 6, and 7 present the contour maps and particle number concentrations of classified size ranges, showing the time course of the particle size distribution in FA-a, FA-b, and FB, respectively. Horizontal black bands (count 0) can be observed in the center of all contour maps. Occasionally, a similar zero band was observed using the NanoScan, which was attributed to a technical error because the particle size was close to the upper limit of the particle size range of the device. Note that this error did not affect the results of our measurements.

With respect to the operation performed in FA, submicron-sized and nanosized particles were detected using SMPS and OPS; however, no relationship was observed between changes in airborne concentrations and bagging tasks with/without the push–pull ventilation system, which are shown in Fig. 5 and Fig. 6, respectively. Fig. 5 depicts the data acquired in FA-a with the push–pull ventilation system. The background concentrations of particles <100 nm in B1 and B2 (backgrounds) were generally higher than those in A1 and A2 (near the bagging task). The nanoparticle concentrations in A1 and A2 were slightly lower than...
Table 2. TiO₂ concentrations in the workplace air as titanium measured by X-ray fluorescence spectrometry and estimated TiO₂ concentrations from optical particle counting by means of OPS

| Sample ID | (A) TiO₂ conc. on filters† | (B) Sampled volume/L | (C) TiO₂ conc. in workplace air†, ‡ | (D) Estimated TiO₂ concentration from OPS counts† |
|-----------|---------------------------|---------------------|------------------------------------|-----------------------------------------------|
| FA-a      | 24.0 ± 0.07*             | 2,147               | 0.055                              | N/A‡‡                                         |
| FA-b      | 9.0 ± 0.04*              | 1,479               | 0.030                              | N/A‡‡                                         |
| FB        | 4.2 ± 0.03*              | 2,086               | 0.098                              | 0.23                                          |

† The concentrations units are (A): μg/cm² as Ti, (C): mg/m³ as Ti, respectively.
* Statistical errors of X-ray counts.
‡ (C) [mg/m³] = (A) [μg/cm²]/1,000 [μg/mg] × 4.19 [cm²]/((B)/1,000 [L/m³]).
Here: 4.19 cm² is the effective filtering face of NW354.
‡‡ N/A: Not available. The particle number concentrations of FA-a and FA-b were not clearly differentiated from the background concentrations.

Fig. 4. Photographs of filters colored due to particle collecting. 1: sampling in Fa-A, 2: sampling in Fa-B, 3: sampling in FB-a, respectively.
concentration of nanoparticles did not change. One peak could be observed in the SMPS result near (*). Some noise peaks associated with air turbulence were also observed when moving the devices, indicating that the particle concentration did not change.

Fig. 6 presents the data acquired in FA-b without the push–pull ventilation system.

Moreover, operations related to submicron- and nano-sized particle releases were performed in FB (Fig. 7). There those in B1 and B2 due to the effect of the push–pull ventilation system. However, it was difficult to confirm the generation of particles during work, which did not significantly differ from the background level. The measurement point B was moved to another section because of operations other than bagging, in the same room at a certain distance from the workplace (marked (*) in B1 and B2 in Fig. 5). A change in the concentration of large particles was observed as the distance from the workplace increased. However, the concentration of nanoparticles did not change. One peak could be observed in the SMPS result near (*). Some noise peaks associated with air turbulence were also observed when moving the devices, indicating that the particle concentration did not change.

Fig. 6 presents the data acquired in FA-b without the push–pull ventilation system.

Moreover, operations related to submicron- and nano-sized particle releases were performed in FB (Fig. 7).
Fig. 6. Contour map and particle number concentrations with classified size ranges showing the time course of particle size distribution in FA-b. *V: Vacuum cleaner operated.
were two hoppers in FB, and two bagging operations were conducted in sequence. The first operation was the nano-TiO$_2$ bagging process in FB-a, and the second operation was the nano-ZnO bagging process in FB-b. During the first operation, the release of nanoparticles was observed at FB-a, where bagging occurred, as well as FB-b, approximately 3 m away from the bagging location. However, the difference was not statistically significant. During the second operation, a similar trend was observed in the airborne particle concentration; however, the number concentration in the case of the nano-ZnO bagging process was lower than that in the case of the nano-TiO$_2$ bagging process. Based on the size-selective particle number concentration, the calculated contribution of nanoTiO$_2$ (<100 nm) in terms

Fig. 7. Contour maps (A1, B1) and particle number concentrations with classified size ranges (A2, B2) showing the time course of particle size distribution in FB-a and FB-b. A: sampled near hopper a (FB-a) from which nanotitanium dioxide put into the plastic bags. B: sampled near hopper b (FB-b) from which nanozinc oxide put into the plastic bags. (*): Individual nanoparticle release observed.
of exposure near the two hoppers was 0.03%.

Discussion

As presented in Table 2, the order of magnitude of the measured and XRF results of the TiO₂ concentration estimated using the OPS count values was the same. However, due to a lack of data, such as particle shape and bulk density, the values for OPS calculation differed. In the cases of the XRF analysis of filtered samples, the sample thickness can induce analytical errors. We measured the same PVC-filtered samples using a different XRF instrument with lower X-ray power in a previous study. The intensity of the XRF signals of the substrate on which the PVC filter was placed was sufficient. As a result, we believe that the thickness of the apparatus used in this study was sufficient for X-ray observation of PVC-filtered samples. The estimated lower limit of quantitation (LOQ) of the measurement obtained from the calibration curve was approximately 0.12 μg/cm². The Ti concentrations in the filtered sample ranged between 4.2 and 24 μg/cm², which were sufficiently larger than the LOQ values. The LOQ value was approximately 0.0029 mg/m³ based on stationary sampling with a low-volume air sampler, assuming an air volume of 200 l sampled at a flow rate of 20 l/min for 10 min, with an effective collection area of approximately 4.91 cm² (using the 35-mm-diameter filter). Furthermore, the calculated LOQ value of personal exposure to Ti in airborne particles was approximately 0.0008 mg/m³ in a typical personal airborne particle sampler, assuming an air volume of 480 l sampled at a flow rate of 2.0 l/min for 4 h, with an effective collection area of approximately 3.14 cm² (using the 25-mm-diameter filter). The estimated LOQ values were lower than 0.03 mg/m³, which is the 1/10 concentration of the recommended OEL value of 0.3 mg/m³. Therefore, the XRF analysis was useful in both stationary measurement and personal exposure measurement applications.

The results indicate that XRF analysis is well suited for the evaluation of occupational TiO₂ exposure risks during powder bagging processes. However, the XRF analysis presented in this study has the following limitations. In the case of a solid-sample analysis without dissolution, the accuracy of the analysis is determined by the sample thickness and the size and shape of the sample particles. In this instance, the calibration curve was obtained by preparing a standard sample set by adding suspension liquid to the medium, and the results may show some deviations. However, we believe that the analytical procedure using XRF is a useful method for the evaluation of TiO₂ exposure risk because the wet analysis of chemical-resistant TiO₂ and the gravimetric determination of high concentrations of workplace background particles are extremely difficult with a high frequency.

The FA result suggests that the particle number measurement is not a viable option for evaluating nanomaterial exposure in a factory where nonfiltered outdoor air is introduced due to high concentrations of environmental particles. This result is consistent with the findings of many previous studies. The concentrations of both nanosized and submicron-sized particles fluctuate with the changes in the concentrations of background particles. The concentration of micron-sized particles closely corresponds to operations performed by workers and serves as a good index for relative exposure. However, the result of particle number concentration cannot be directly converted into the evaluation of mass concentration. In the result presented in Table 2, the estimated result of the particle number concentration considerably differs from the analyzed XRF result because the assumed values of the particle shape and density did not match those of the real TiO₂ particles in the workplace. Because of loose agglomeration, the bulk-specific gravity of larger, micron-sized particles is expected to considerably differ from the density of TiO₂, even though micron-sized particles make a greater contribution than nanoparticles to mass concentrations in the workplace environment. Due to current knowledge limitations, the particle number concentration measurement for quantitative exposure evaluations necessitates simultaneous microscopic observations and/or chemical analyses. The particle number concentration measurement has limited applicability to relative risk estimations, i.e., task improvements and ventilation effect evaluation.

Fig. 7 presents considerable qualitative information on the behavior of nanoparticles in the workplace. The elimination of background particles indicates the existence of nonagglomerated nanoparticles in the vicinity of employees, not only near the working hopper but also 3 m away from the bagging position; nevertheless, it does not provide quantitative information. As can be seen from the upper graph of Fig. 7, the NanoScan result is sometimes 0 during the nanoTiO₂ bagging process, possibly due to the rapid concentration fluctuation during scanning, the overflow of larger particle elimination cyclones, and DMA errors attributed to the electrostatic charging of particles because of powder falling from the hopper. Consequently, it is difficult to quantitatively assess the exposure risk of nanoparticles using NanoScan, even in the absence of background particles during the powder bagging process.
Conclusions

In this study, we observed the behaviors of nanoTiO$_2$ particles in two nanomaterial-handling factories and employed nanoparticle-measuring methods to measure the particle number concentration. The following results were obtained: 1) nonagglomerated particles with sizes of <100 nm or small aggregated particles of TiO$_2$ will be released while handling nanoTiO$_2$ powders; 2) in the presence of both nanosized and submicron-sized particles, the separable particle concentration measurements of the workplace air would be somewhat unsuitable for the particles present in the background air; and 3) XRF analysis is an effective method for evaluating TiO$_2$ exposure.

Conflict of Interest

The authors have no conflicts of interest to declare.

Acknowledgments

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