thermo scientific

Comprehensive Analysis of Nanoparticles using Single and Triple Quadrupole ICP-MS and a Dedicated Data Evaluation Tool

Daniel Kutscher, Shona McSheehy Ducos and Julian D. Wills, Thermo Fisher Scientific, Hanna-Kunath-Str. 11, Bremen, Germany 28199

ABSTRACT

Purpose: Demonstrate the possibility to directly determine the size distribution and particle number concentration of different nanoparticles using ICP-MS operated in the so-called single particle mode.

Methods: Different nanoparticles (e.g. made from gold or titanium dioxide) were analyzed using either single quadrupole ICP-MS or triple quadrupole ICP-MS. All parameters relevant for the measurement were determined automatically using a dedicated software module, the npQuant plug-in for the Thermo Scientific™ Qtegra™ Intelligent Scientific Data Solution software. To show validity of results, a dataset acquired using the npQuant plug-in was exported and evaluated in an independent, publically available software solution

Results: Excellent agreement with certified values was achieved. A comparison of the results obtained by the npQuant plug-in to a widely accepted spreadsheet solution also showed identical results. For TiO_2 particles, low detection limits (in terms of lowest detectable particle size) was achieved using triple quadrupole based ICP-MS.

INTRODUCTION

The direct sizing and counting of nanoparticles using single particle ICP-MS (spICP-MS) is an alternative to established techniques for particle characterization. However, for some materials such as silica or TiO_2, spectral interferences are still a limiting factor. In addition, the differences in data evaluation may slow the implementation of spICP-MS as a tool in routine analysis.
In order to enable comprehensive analysis of nanoparticles this presentation will show a completely integrated workflow solution based on the Qtegra Intelligent Scientific Data Solution software. The software plug-in allows also unexperienced users to set up methods through automatic determination of key input parameters and statistical evaluation of the data in order to recognize artefacts.

MATERIALS AND METHODS

Sample Preparation

Gold and silver nanoparticles with nominal diameters of 30 and 60 (Au, NIST reference materials 8012 and 8013) were used for instrument calibration and measurements. The particle solutions were diluted gravimetrically in ultrapure water to the right particle number concentration before measurement. In order to assure a suitable dispersion of the particles, all solutions were sonicated in an ultrasonic bath for 5 minutes before analysis. Commercially available TiO_2 particles were suspended and further diluted in water.

Test Method(s)

For the assessment of nanoparticle size information and number concentration, the main regulatory guideline is a recommendation issues by the European Commission, stating that "Nanomaterial means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate where 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range of 1nm-100nm"[1]

Mass Spectrometry

A Thermo Scientific™ iCAP™ RQ ICP-MS or iCAP TQ ICP-MS was used for all analyses. The typical operating parameters are summarized in Table 1:

TABLE 1. ICP-MS operating parameters single and triple quadrupole systems.

Parameter	iCAP RQ ICP-MS		iCAP TQ ICP-MS	
Forward Power	1550 W			
Nebulizer Gas Flow	1.05 L·min^{-1}		1.08 L·min^{-1}	
Mode	KED		TQ-O_2	
Gas Flow	100% He @ 4.8mL·min^{-1}		100% O_2 @ 0.4 mL·min^{-1}	
Cell Settings	QCell Bias	Quad Bias	QCell Bias	Quad Bias
	-18 V	-21 V	-7.5 V	-12 V
Dwell time	5 ms		10 ms	

Data Analysis

Acquisition and Evaluation of the data was accomplished using the npQuant plug-in for the Qtegra ISDS Software. Due to the instrument agnostic design of the software, the plug-in is compatible with all ICP-MS instruments operated through Qtegra ISDS, including both instruments of the iCAP Qnova Series™, the iCAP RQ and iCAP TQ ICP-MS. Also different peripherals, such as autosamplers from all major manufacturers, are supported in this application. The use of a dedicated plug-in for acquisition and evaluation of the data allows to hassle free mix different applications, for example, trace elemental quantification as the major application in routine analysis focused laboratories, and single particle ICP-MS as a new application of interest.

RESULTS

Established Test Methods for the Analysis of Nanoparticles

For the characterization of nanoparticles in different samples, there is a wide variety of different analytical methods available. It is important to understand that a single method will not be sufficient to establish a complete understanding of the nanoparticles under scrutiny. Among the portfolio of existing methods, the most important ones are listed in the following:

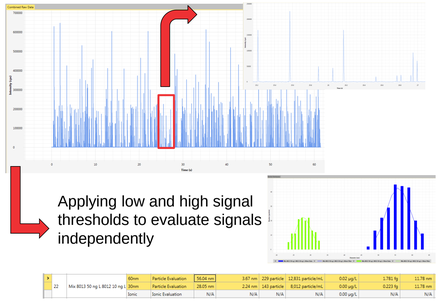
- **Microscopy (e.g. TEM):** Gold Standard for the analysis of particles as it allows to directly size and count particles. Due to direct visualization, also the true particle shape can be determined. However, sample preparation is required and analysis of a large number of particles is difficult.
- **Light Scattering (e.g. DLS):** Standard technique for particle sizing, allows to scan a large ensemble of particles quickly, however, limited with respect to the attainable (particle concentration based) detection limit.
- **Separation techniques (e.g. FFF, HDC):** Techniques to fractionate different size regimes in a sample. Whereas FFF can achieve very good resolution of different particle sizes, HDC is a fairly robust technique only very little affected by matrix effects.

Single particle ICP-MS nicely complements this portfolio of methods, as it allows to

- ✓ Scan a high number of particles in a short amount of time (e.g. 1000 particles per minute).
- ✓ A low number of particles per volume is a prerequisite for spICP-MS, often eliminating pre-concentration steps.
- ✓ ICP-MS is a very robust technique, hence sample preparation before analysis may be simplified.

A typical data set with resulting particle size and number information is shown in figure 1. The sample contained a mixture of 30 and 60nm gold nanoparticles.

FIGURE 1. Analysis of 30 nm and 60 nm gold nanoparticles present in the same sample. The npQuant plug-in allows to evaluate signals independently and hence discriminates the two particle sizes



VALIDATION OF RESULTS

In order to verify the correctness of the obtained results, the results obtained for the analysis of Au nanoparticles was exported and re-evaluated using the Single Particle Calculation tool (abbreviated as SPC in the following), a widely accepted solution for spICP-MS data evaluation based on a spreadsheet calculation software. This tool is available free of charge on the website stated as reference 3.

Transport Efficiency Determination

The results obtained for the determination of the transport efficiency are displayed in table 2, showing the results for both ways of estimation, either using the expected particle size or the expected particle number as a reference value. In a larger batch (50 unknown samples plus the required standards, 59 samples in total), 10 independent determinations of this parameter were performed overall. Please note that the SPC only estimates the transport efficiency using the expected particle number concentration, so that only this value is mentioned in the table.

Table 2. Results obtained for the determination of the transport efficiency.

N=10	npQuant - Particle number	npQuant – Particle mass	SPC - number
Average [%]	4.1	4.3	4.6
SD	0.3	0.04	0.3
RSD [%]	7.3	0.9	6.5

As can be seen from the results, both ways of calculating the transport efficiency in npQuant agree with each other, and furthermore as expected the transport efficiency does also agree well with the value determined using the SPC as a reference calculation tool. It is also evident that the assessment of the transport efficiency using the particle mass shows less variations in a larger batch as it is not as dependent on the conditions of the sample solution (particles may agglomerate over time).

Nanoparticle size and number concentration

In a similar way, the particle size and number determination was verified against the SPC. The reference particles were analyzed (6 repetitions), and the data was processed using both npQuant and the SPC. The average of the calculated particle size and the detected number of particle signals (which is subsequently converted into the number concentration in the sample) are shown in table 2. Please note that the number of detected particles is slightly lower for npQuant, as, in contrast to the SPC, low and high threshold values are used to discriminate a given signal range for evaluation.

The particle solution was analyzed under optimum concentration conditions (approx. 50 ng · L^{-1} for NIST 8013), so that the expected particle number should be approximately 23,000 #·mL^{-1} with slight variations possible between individual preparations. Table 3 shows the results.

Table 3. Results obtained for the determination of the transport efficiency.

Repetition		SPC	npQuant
1	Size [nm]	52	53
	# · mL^{-1}	21,818	21,062
2	Size [nm]	53	54
	# · mL^{-1}	23,163	21,944
3	Size [nm]	54	54
	# · mL^{-1}	24,324	23,505
4	Size [nm]	54	54
	# · mL^{-1}	24,018	23,258
5	Size [nm]	53	54
	# · mL^{-1}	26,218	25,797
6	Size [nm]	53	54
	# · mL^{-1}	21,696	21,876

Both particle size and particle number concentration determined using npQuant or the SPC did not show any significant variation when a t-test was applied (P>0.05). The values determined are virtually identical taking into account the aforementioned difference in data collection.

ANALYSIS OF TiO_2 PARTICLES USING TRIPLE QUADRUPOLE ICP-MS

The analysis of Titanium is particularly challenging due to the isobaric overlap of ^{48}Ca and polyatomic interferences from SO^+ and POH^+ on the most abundant Ti isotope, ^{48}Ti. To overcome these interferences, a combination of using reactive gases inside the collision/reaction cell system and previous mass filtration of ions reaching the cell, can be applied. The additional mass filtration step is mandatory to reduce potential side reactions of other ions in the ion beam, which would potentially create new interferences. However, this can only be accomplished using a triple quadrupole instrument.

For the analysis of Ti, the use of ammonia as a reactive gas and a mass shift of Ti to a cluster ion with one or more gas molecules attached to it, is the most effective way of reducing the impact of the common interferences. Especially in biological or food samples, high concentrations of Ca can be found, leading to a significant interference contribution. Figure 2 shows how the iCAP TQ ICP-MS can overcome these interferences.

FIGURE 2. Analysis of ^{48}Ti using triple quadrupole ICP-MS with ammonia or oxygen as reactive gas.

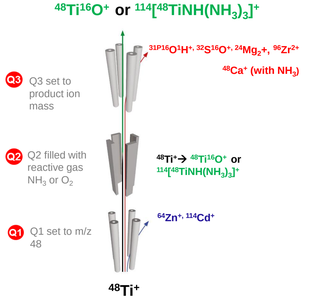
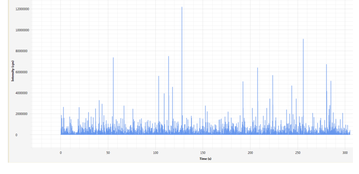


Figure 3 shows the raw data obtained for the analysis of TiO_2 nanoparticles. According to the supplier, the particles were having a wide size distribution with an average size below 150nm. As no Ca was present, the particles were analyzed using O_2 as a reactive gas and utilizing triple quadrupole technology.

FIGURE 3. Analysis of ^{48}Ti using triple quadrupole ICP-MS with ammonia or oxygen as reactive gas.



The resulting particle size distribution reveals the inhomogeneous nature of the particles. Comparing the sample with and without thorough sonication in an ultrasonic bath, one can easily recognize that only after sonication, particles tend to de-agglomerate, so that a distinct fraction of smaller nanoparticles (size below 50 nm) can be recognized. Following reference 1, this material could potentially be classified as a nanomaterial.

FIGURE 3. Particle size distribution for TiO_2 nanoparticles without (left) and with (right) sonication before analysis.

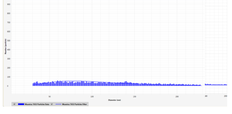


Table 4. Size and number concentration for TiO_2 particles with and without sonication. The particle size detection limit is accessed in every single run and this value is a representative average.

	Average Particle Size [nm]	Particle Number concentration #·mL^{-1}	Particle size detection limit [nm]
Without Sonication	114 ±61	94,000	26 ±7
With Sonication	57 ±38	175,000	

CONCLUSIONS

- The npQuant plug-in for Qtegra ISDS allows to analyze all types of nanomaterials in a simple and intuitive workflow. All required input parameters can be determined automatically and users are guided to find optimum acquisition conditions for their analysis.
- The use of triple quadrupole ICP-MS greatly helps to overcome challenging interferences on some analytes, including isobaric interferences, which are difficult to overcome using single quadrupole ICP-MS instruments.

REFERENCES

1. Definition of a Nanomaterial, http://ec.europa.eu/environment/chemicals/nanotech/faq/definition_en.htm
2. Application Note 43330, Thermo Fisher Scientific.
3. Rikilt Website, https://www.wur.nl/en/show/Single-Particle-Calculation-tool.htm

ACKNOWLEDGEMENTS

Part of this work has been carried out within the Nanodefine Project (European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement no. 604347). S. Böhme, C. Cascio, H. Marvin and M. van der Lee from RIKILT – Institute of Food Safety (WUR, The Netherlands) are acknowledged for conducting parts of the experimental work and scientific exchange. Dr. Jörg Bettmer and Silvia Candás Zapico are acknowledged for conducting the analysis of TiO_2 nanoparticles and also for scientific exchange.

TRADEMARKS/LICENSING

Thermo Fisher SCIENTIFIC