Determination of titanium dioxide nanoparticles in milk samples by single particle ICP-QQQ

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Introduction

Overview and importance Titanium dioxide (TiO_2) - classified as food additive E171 within the European Union- exhibit some characteristics that make it very attractive for the food industry; it is used as whitening and brightening agent in different foodstuffs. E171 mainly consists of microsized TiO2 particles, but might contain a certain nanosized fraction. However, there are some studies stating the potential toxic effects of TiO_2 nanoparticles to humans.

The European Commission published in 2011 a recommendation for the definition of a nanomaterial (2011/696/EU) suggesting that for regulatory purposes, the size distribution and number concentration of these nanomaterials should be known.

In this sense, ICP-MS, when used in single particle mode (sp-ICP-MS) has the potential to address all these questions. This, together with its simplicity of use, makes it the technique of choice for characterization of NPs in terms of size and concentration for regulatory purposes. In this vein, there is an ISO standard method for analysis of NPs employing sp-ICP-MS (ISO/TS 19590).

Titanium is a difficult element that presents many interferences that cannot be totally removed with single quadrupole instruments. In particular, ^{48}Ca represents an important interference for the most abundant Ti isotope, ^{48}Ti. For Ca-rich samples, such as milk, this interference can only be removed with the triple quad technology. Also, sulphur and phosphorus, that are present at high concentrations in milk, present important interferences for measuring ^{48}Ti, that can also be removed efficiently with ICP-QQQ.

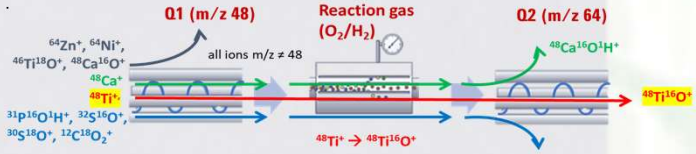
Objective: to demonstrate the usefulness of MS/MS technology in combination with reaction gases for the characterization of TiO_2 NPs in single particle mode in samples containing high concentrations of interferents, such as milk.

Experimental

Instrument and configuration

- Agilent 8900 ICP-QQQ, Advanced configuration.
- SPS 4 autosampler, MicroMist Nebulizer (concentric), Scott double-pass spray chamber, quartz torch (1.0 mm id)
- Nanoparticle Application Module of MassHunter software

Reaction gas mode: O_2/H_2



Instrumental settings

Parameter	Value
RF power	1550 W
Sampling depth	8 mm
Nebulizer gas	0.70 L/min
Sample uptake rate	0.35 mL/min
Dwell time	0.1 ms
Reaction cell gas	H_2 7ml/min O_2: 10%

Reference materials and standards

- 30 nm AuNP NIST (in water) was used for calculation of transport efficiency, based on "particle size method"
- Ionic Au standard was used to calculate response factor for gold (5 ng/mL in water)
- Ionic Ti standard (50 ng Ti/mL in diluted milk) was used to calculate response factor for titanium
- JRCNM 10200a: TiO_2 NPs, primary sized particles 115 nm, in solution around 230 nm, aggregates can go up to 700 nm. Composition: anatase (100%)

Further parameters

- Ratio between molar mass of particle and molar mass of analyte = 1.668
- Density of TiO_2 = 3.9 g/cm^3
- Assumption of spherical particle shape
- Flow rate: gravimetrically determined, N=2

Samples and samples/standards preparation

TiO_2 NPs standards were dissolved in MQ water, submitted to probe sonication and diluted to appropriate concentrations → Spike TiO_2 NPs to milk → 

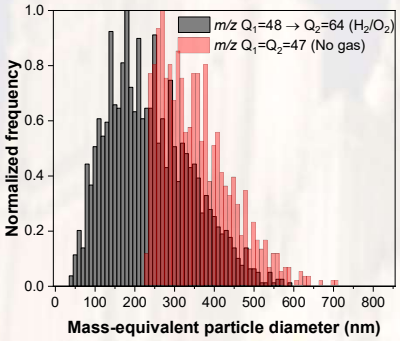
Skimmed milk with 0.1% fat Denmark, Arla

Estimated conc in milk (µg/mL):
- calcium (Ca): 1200
- sulfur (S): 300
- phosphorus (P): 950-1000

→ 100-times dilution with MQ water → **single particle ICP-QQQ analysis**

Results and Discussion

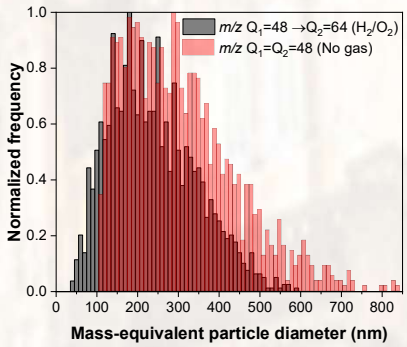
Comparison of measurements of TiO_2 NPs in milk in MS/MS mode with O_2/H_2 (48→64) and no gas mode (47→47)



Median diameter: 218 nm **(333 nm)**
Minimum particle diameter: 41 nm **(226 nm)**

Measurements for ^{47}Ti isotope –the one that could be measured free of interferences in SQ mode– were biased. Particles with lower sizes than 226 nm could not be detected, due to the low abundance of ^{47}Ti isotope, and therefore sensitivity was not enough to detect small particles. The use of O_2/H_2 as reaction gas in MS/MS mode enabled the measurement of ^{48}Ti isotope free of interferences and smaller particles could be detected.

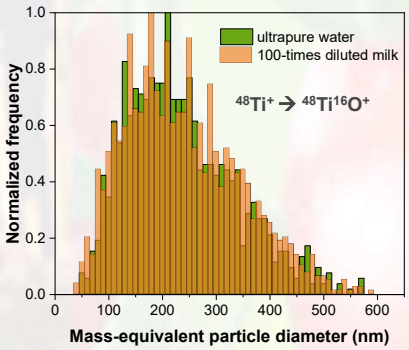
Comparison of measurements of TiO_2 NPs in milk in MS/MS mode with O_2/H_2 (48→64) and no gas mode (48→48)



Median diameter: 218 nm **(281 nm)**
Minimum particle diameter: 41 nm **(105 nm)**

Measurements for ^{48}Ti isotope with no reaction gas also provided biased results. Interferences present in milk could not be resolved and therefore backgrounds were very high, and particles smaller than 105 nm in diameter could not be detected. Again, the use of O_2/H_2 as reaction gas in MS/MS mode enabled the measurement of ^{48}Ti isotope and smaller particles could be detected.

Comparison of measurements of TiO_2 NPs in water and in milk matrix in MS/MS mode with O_2/H_2 as reaction gas



Median diameter: 226 nm **(218 nm)**
Minimum particle diameter: 36 nm **(41 nm)**

Results of size distributions for TiO_2 NPs were very similar in MQ water and in milk matrix. This means that the use of O_2/H_2 as reaction gas in MS/MS mode made possible the measurement of ^{48}Ti isotope almost free of interferences in milk matrix, to levels comparable to those in water, and the smaller particles could be detected.

Conclusions

- Single particle ICP-MS is a simple and powerful technique for the characterization of nanoparticles, provided that the composition and shape of the particles are known.
- The Agilent 8900 ICP-QQQ operating in MS/MS mode with O_2/H_2 cell gas is able to efficiently remove the isobaric and polyatomic interferences of ^{48}Ti in matrices containing high concentration of interferences, such as milk. Ti can be measured then at its most abundant isotope, which greatly reduces the particle size detection limit.
- The high sensitivity of the Agilent 8900 ICP-QQQ, combined with the short dwell times and the ability of operating in MS/MS mode makes possible the determination of nanoparticles of challenging composition and small sizes.
- The Nanoparticle Application Module of MassHunter software is very simple to use and facilitates all the data analysis related to single particle measurements