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Nota Técnica

ANALYTICAL METHOD VALIDATION FOR THE IDENTIFICATION AND QUANTIFICATION OF DISSOLVED GOLD AND GOLD NANOPARTICLES IN COSMETICS PRODUCTS BY SINGLE PARTICLE INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY

Lisia M. G. dos Santos[a,*], Cristiane Barata-Silva[a], Santos A. Vicentini Neto[a], Mayssa A. Fonseca[a], Carolina D. Magalhães[a], Josino.C. Moreira[b] and Silvana C. Jacob[a]

[a]Departamento de Química, Instituto Nacional de Controle de Qualidade em Saúde, Fiocruz, 21040-900 Rio de Janeiro – RJ, Brasil

[b]Centro de Estudos da Saúde do Trabalhador e Ecologia Humana, Escola Nacional de Saúde Pública, Fiocruz, 21041-210 Rio de Janeiro – RJ, Brasil

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Nanoparticle (NP) applications have recently gained more space in the development of many products, especially in cosmetology. The aim of the present study was to validate a single particle inductively coupled plasma mass spectrometry technique for the detection and quantification of gold nanoparticles (AuNPs) and gold ions (Au (i)) in different cosmetics currently marketed in Brazil. The size limit of detection for pure AuNPs was 22 nm, and a concentration limit of detection of 2.3×10^6 particles g^{-1} was achieved. The limit of detection for total gold was 0.02 μg L^{-1} obtained in standard mode conditions. The recovery achieved was 98% for dissolved Au and 109% for AuNPs; the relative standard deviation was <5%. This validated method was applied to cosmetic products (n = 10) from different national and international industrial producers. Most cosmetics analysed contained quantifiable amounts of dissolved gold (< 0.005-2.1 μg g^{-1}) and only four contained quantifiable amounts AuNPs the variability of the results detected (< LOD – 9.3×10^8 particles g^{-1}). The products that contained the greatest amount of these metallic NPs were the artisanal products. The results demonstrate the importance of adequate quality control for cosmetics to ensure consumer safety.

Keywords*:* gold nanoparticles; cosmetics; single particle mode; ICP-MS; health surveillance.

INTRODUCTION

Nanotechnology is currently considered an innovative science resulting from technological development that made it possible to reduce particle sizes to the nanoscale (10^{-9} m).[1] Nanomaterials are a product of this new technology, and metallic nanoparticles (NPs) are the most used in consumer products, whose number-size distribution ranges from 1 to 100 nm in at least 50% of the particles in the three external dimensions.[2–4]

NPs are being used in a large number of products. The pioneering products in terms of the development of NP use in cosmetics were sunscreens containing titanium dioxide (TiO_2) in the form of engineered nanoparticles (ENPs). The objective was to promote physical protection against UVA and UVB radiation and to provide the ability to become invisible after application.[5] Silver nanoparticles (AgNPs) are also being applied to clothing and packaging due to their antimicrobial activity. Gold nanoparticles (AuNPs) have been widely researched and applied in cosmetology. More recently, they have been used in cosmetics and toiletries as anti-wrinkle agents, an application that makes AuNPs the main agent in combating loss of skin elasticity.[6–8] Some biological AuNP properties have been reported, including anti-inflammatory and antioxidant activities on different macromolecules – for example, fibroblasts and collagen.[6,7] Thus, the AuNP-mediated action on ageing skin processes occurs by inhibition of the deleterious effects of the final products of advanced glycation (AGEs) responsible for collagen degradation and, thus, skin ageing.[8]

The production and commercialisation of AuNP-containing cosmetics is currently not regulated by competent bodies, such as the Brazilian National Health Surveillance Agency (ANVISA).[9] This is due to a lack of standardised and validated methodologies, besides the fact that sample preparation is an important factor for analysis. In all cases, the sample must be carefully purified to remove all excess reagents or undesired by-products. Characterisation of nanomaterials presents several challenges. Of note, the selection of the proper method to obtain a homogeneous sample and the appropriate analytical method are key to obtaining reliable data.[9]

Given the lack of regulation, the creation of specific legislation for the development and commercialisation of NPs applied in the health area is warranted.[9] This legislation gap is a worldwide issue, and efforts are being made to create guidelines for manufacturing, toxicity studies and quality control of these products, as well as documents that support the development of regulations for the inspection of NP-containing products, as carried out by the multinational project NanoReg.[10]

From the analytical point of view, the need to apply a combination of methods to determine the necessary characteristics of the used NPs is essential to understand potential adverse effects from exposure. For this endeavour, single particle inductively coupled plasma mass spectrometry (spICP-MS) associated with a separation method or even alone seems to be a useful technique.[11] This analytical technique has been widely used to identify and quantify metallic NPs in samples from different sources.[12] The 'single particle' module allows real-time data acquisition and provides information such as dissolved ion concentration (ug L^{-1}), average dissolved ion count, number of NPs per millilitre, particle diameter, sample size distribution, average size, the most frequent size and the number of peaks detected in the data acquisition period. This information is instantly processed, and different types of histograms are provided.[13,14]

An important aspect to consider is the reliability of the analytical measurements performed by the laboratories. One way to guarantee sufficient reliability is through the validation of analytical methods. This endeavour requires establishing parameters described in ISO 17025:2017, such as linearity and working range, precision,

*e-mail: lisia.gobbo@incqs.fiocruz.br

selectivity, detection limit and accuracy.[15] Therefore, the aim of this study comprised the development and validation of an analytical method for the analysis of AuNP-containing cosmetics currently marketed in Brazil. Furthermore, the results will provide technical and scientific information for quality control sanitary inspection and regulatory standard implementation for cosmetics.

MATERIAL AND METHODS

Instrumentation

The experiments were performed on a NexION 300D ICP-MS (Perkin Elmer, USA). The ICP-MS was equipped with a concentric nebulizer type Meinhard, glass cyclonic nebuliser chamber, cone, skimmer and nickel hyper-skimmer. Argon gas with a minimum purity of 99.996% was supplied by White Martins (São Paulo, Brazil). ICP-MS instrumental and data acquisition parameters are listed in Table 1.

Table 1. Default single particle inductively coupled plasma mass spectrometry instrumental and data acquisition parameters

Instrumental parameters		
RF Power	1400 W	
Argon gas flow rate		
Plasma	18 $Lmin^{-1}$	
Auxiliary	1.2 $Lmin^{-1}$	
Nebulizer	1 $Lmin^{-1}$	
Data acquisition parameters		
Measurement unit	Standard	Single particle detection
Point per spectral peak	1	1
Sweeps	20	1
Dwell time	50 ms	50 µs
Readings per replicate	1	2000.000
Integration time	1 s	100 s
Isotope Monitored	^{197}Au	^{197}Au

Measuring single particles with ICP-MS is quite different to measuring dissolved species. The most important factor when measuring single particles is the speed at which data can be acquired (dwell time) that should be in the order of microseconds, rapid data acquisition and elimination of the settling time between measurements. For single-particle ICP-MS analysis, continuous data acquisition at a dwell time shorter than or equal to 100 µs is the most important instrumental requirement for precise nanoparticle counting and sizing.[14]

Standards

Monodisperse AuNP suspensions were prepared from commercially available solutions. AuNPs measuring 49.6 ± 2.1 nm and with 1.02×10^7 particles/mL; 27.1 ± 1.1 nm and with 9.8×10^6 particles/mL and 99.4.6 ± 3.0 nm and with 1.02×10^7 particles/mL were obtained from NanoComposix (San Diego, CA, USA). After dilution 100-fold and before each analysis, the suspensions were sonicated and vortexed for 1 min.

Transport efficiency (TE) was determined using 50 nm AuNPs, which was sonicated for 1 min and diluted 100-fold in deionized water (Milli-Q Advantage, Molsheim, France), to a final nominal concentration of 1×10^6 particles/mL.

A standard 999 ± 2 µg mL^{-1} dissolved Au stock solution in 5% HCl (Sigma-Aldrich, Saint Louis, MO, USA) was used to prepare an intermediate 0.1 µg mL^{-1} solution. The calibration curve was prepared in 15 mL Falcon flasks by means of successive dilutions in ultrapure water of this solution in a linear range from 0.0005 to 0.02 µg mL^{-1}.

Samples

The samples were acquired on the national market in different commercial establishments located in the Brazilian states of Rio de Janeiro and Minas Gerais. A sample of each cosmetic samples of different acquisition values and from different producers, both industrial and artisanal, were selected. All manufacturers stated on their products' labels that they contained AuNPs or colloidal Au. Eight national brand samples and two international brand samples marketed in Brazil were analyzed, three of which comprised artisanal products (soap, body lotion and facial cream) – that is, produced individually and to order, in a small production site by the same manufacturer. Only two international brands were acquired due to price, which limited the comparison of results. All were identified and characterized by a numerical sequence; their main characteristics are described in Table 2.

Table 2. National and international cosmetics produced both industrially and artisanally, marketed in Brazil and acquired in the states of Rio de Janeiro and Minas Gerais in 2019

Samples	Products	Origin	Type	State Au on label
Sample 1	Face mask	Brazil	Industrial	Yes
Sample 2	Face mask	Brazil	Industrial	Yes
Sample 3	Face mask	Brazil	Industrial	Yes
Sample 4	Face mask	Brazil	Industrial	Yes
Sample 5	Face mask	Brazil	Industrial	Yes
Sample 6	Cream	Brazil	Artisanal	Yes (50nm)
Sample 7	Soap	Brazil	Artisanal	Yes (50nm)
Sample 8	Lotion	Brazil	Artisanal	Yes (50nm)
Sample 9	Face mask	China	Industrial	Yes
Sample 10	Face mask	China	Industrial	Yes

Sample preparation

AuNPs

The cosmetics used herein are considered complex matrices because they contain numerous components that may interact in ways that are difficult to understand and with a reduced possibility of separating the AuNPs from the other constituents.[10,16]

To obtain the best preparation methodology, firstly, different reagents were evaluated: 1% dimethyl sulfoxide (DMSO) solution, 10% tetramethylammonium hydroxide (TMAH) solution and deionized water; the best result was obtained with deionized water. Then, the ultrasound and centrifugation times were optimized. In addition, different volumes of conductor and amounts of sample used in the extraction were tested. The small amount of sample used respected the ratio between the volume of solvent and the amount of mass, in order to obtain the maximum interaction and migration of the analytes to the liquid phase. Once the sample preparation methodology for AuNP analysis was optimized, the samples were submitted to the process as described below. The results of preparation are not described in this work.

About 0.02 g of the sample was weighed in triplicate and each triplicate analysed five times and placed in a polypropylene Falcon tube with 5 mL water. The samples were then submitted to ultrasound treatment for 2 h, centrifugation at 5,000 rpm for 30 min and filtration through 0.22 μm pore membranes.[16,17] The filtration step was used to removed unwanted organic matter and larger particle fractions. Particle losses may occur depending on the particle size and surface coating interaction with the filter material, but this loss was overlooked in this study. Furthermore, to assess the sonification time on AuNP standards were added before this stage and no significant losses were observed as shown by the recovery study. After filtration, each sample were sonicated and vortexed for 1 min. A blank solution containing only ultrapure water, with no added sample, was subjected to the same extraction process.

Total Au analysis

Sample preparation for total Au determination included acid microwave digestion using a SpeedWave microwave (Berghof, Germany), as described by Santos *et al.*,[18] for 45 min at a maximum temperature of 200°C and 90 W power. Briefly, approximately 0.5 g of each sample was weighed in duplicate and each duplicate analysed five times. All samples were placed in Teflon-type plastic tubes with 2 mL ultrapure water (Millipore, Brazil), 2 mL supra pure nitric acid 65% (p/v) (Merck, Germany) and 2 mL hydrogen peroxide 30% (v/v) (Merck, Germany) and then microwaved. After cooling, the samples were transferred to 15 mL volumetric Falcon flasks, and ultrapure water was added. Then the samples were diluted 15-fold to obtain an acid concentration around 1.2%

Validation

The validation parameters assessed herein are in accordance to those described in the guidance document on Analytical Method Validation by the Brazilian INMETRO (DOQ-CGCRE-008) and ISO 17025.[15,19]

The analytical performance of the method was evaluated for each sample batch, through recovery assessments, where a known amount of 50 nm AuNP standard (1.1×10^5 particles/mL) was added to a control sample. The limit of detection (LOD) was calculated by reading a blank (ultrapure water) [20] that was prepared like the samples. The recovery and precision were assessed by analyte addition with different concentrations and sizes of standards AuNP and and dissolved Au in a mask sample. The preparation of the added samples was carried out according to what is described in the item sample preparation for nanoparticles and total gold.

Statistical analyses

Descriptive statistics were obtained using Microsoft Excel 2010, including the arithmetic mean, median, standard deviation (SD), Student's *t*-test and analysis of variance (ANOVA). The measurement uncertainties were estimated by the 'bottom-up' mode, where the final combined uncertainties of all stages of the analytical procedure were considered: sample preparation, standards preparation, analytical curve that was based on the ordinary least squares regression and the uncertainty associated with the repeatability of the methodology that is associated with random effects and was measured from repeated experiments and quantified by the standard deviation of the response.[21] Once the final combined uncertainties were calculated and the coverage factor k (k = 2) was defined for a 95% confidence level, the final expanded uncertainty was calculated.[19]

RESULTS AND DISCUSSION

Validation

The instrumental parameters that were optimised at the beginning of the analysis are sample flow rate (0.18 mL/min), dwell time (50 μs) and integration time (100 s). TE was calculated by waste collection method, where TE was indirectly determined by dividing the total aspirated sample volume by the volume difference between the sample uptake and waste stream, 60 s after the aspiration.[22] This process was repeated during three different runs. For each run, the method produced similar efficiency; the variation in results was less than 5%, proving this method to be an easy and accurate. The obtained result was 6.19 %.

In addition, TE was evaluated using an AuNP suspension in a mask sample that was subjected to the extraction process. The result (6.08%) was compared with the value obtained with water and there was no statistically significant difference, showing that the viscosity and density of the extracted samples are similar to that of water.

Selectivity

The selectivity of the technique was evaluated by determining the total concentrations of Au in standard mode in a suspension of NPs just diluted in water and after acidic digestion by microwave.[12] Table 3 presents the results obtained.

Based on these results, both procedures are statistically equal, assessed through Student's *t*-test at 5% significance level, proving that the ICP-MS selectivity is independent of the physicochemical properties of the Au and that the observed matrix effect was not significant – the difference was < 20%.[12]

In addition, two distinct groups were prepared, containing Au ions: a group consisting of the matrix of interest (group 1) and known quantity of the analyte, and another group composed of water and analyte (group 2). Through the results obtained, the Snedecor F-test of homogeneity of variances and Student's *t*-test for comparison of means were applied, with a 95% confidence level.[19] The value obtained in the t test (t calculated = 0,4064) was less than the expected value (t critic = 2.4469) and it can be concluded that the matrix does not have a statistically significant effect on the result with a 95% confidence.

Linearity

Seven analytical curves were prepared using an Au standard dissolved at concentrations from 0.00005 to 0.02 μg mL^{-1}; the solutions were measurement in spICP-MS mode. To define the mass flow curve for quantifying the NP, the dissolved Au concentrations were correlated to the Au mass with reference to each reading ('dwell time').[20] The linearity was proven with the help of the worksheet

Table 3. Analysis of standards a gold nanoparticle suspension (with different sizes) in the standard mode. Data are expressed as mean ± standard deviation ($n = 3$)

Standard	30 nm	50 nm	100 nm
	Mass concentration/μgmL^{-1}		
Acid digestion	$1.6 \times 10^{-4} \pm 0.4 \times 10^{-5}$	$1.5 \times 10^{-4} \pm 0.4 \times 10^{-5}$	$2.0 \times 10^{-4} \pm 0.1 \times 10^{-5}$
Suspension	$1.4 \times 10^{-4} \pm 0.2 \times 10^{-4}$	$1.3 \times 10^{-4} \pm 0.1 \times 10^{-4}$	$1.6 \times 10^{-4} \pm 0.1 \times 10^{-4}$

entitled "Worksheet for Assessing Assumptions" prepared by Bazilio et al.[23] An ANOVA to confirm the linearity of the constructed curve with aqueous standards, in single particle mode, presented a p value < 0.001, indicating that the curve regression is significant (p > 0.05 would indicate no linearity deviation). The coefficient of determination (R^2) was > 0.9990, indicating that the analytical curve presents adequate linearity according to INMETRO specifications.[19,23]

LOD for NPs

AuNP identification and quantification by spICP-MS depends on two factors: (i) the size of the NP, which must be large enough to generate a number of ions detectable by the spectrometer; and (ii) the numerical NP concentration, which must be high enough to allow counting a minimum number of events.[19] Therefore, two LODs are calculated: the size LOD (LOD_d, for the diameter of solid NPs) and the concentration of the number of NPs LOD (LOD_{NP}).

LOD_d and LOD_{NP} were calculated by reading the blank (n = 10) under a residence time, TE, flow rate and count number of peaks.[20] The LOD_d was 22 nm. The LOD_{NP} was 2.3×10^6 particles/g. These results are in accordance with other studies in the literature and suitable for the type of sample assessed herein.[12,13]

LOD for total Au

The LOD for total Au, 0.005 μg g^{-1}, was calculated, in the standard mode, from the ratio of three times the standard deviation blank (ultrapure water) divided by the sensitivity.[16] The limit of quantification (LOQ) was obtained experimentally, defined as the first point of the calibration curve (0.025 μg g^{-1}). Both values are suitable for this study and demonstrated adequate sensitivity for the applied technique.

Accuracy and precision

To assess the method's accuracy and precision, the sample containing the lowest concentration of AuNPs and gold ions was selected and solutions were prepared containing AuNPs and dissolved Au. The Au (i) concentration was chosen to be in the middle of the calibration curve (1.0×10^{-3} μg mL^{-1}) and the AuNP concentration the lowest that can be detected (1.0×10^5 particles mL^{-1}); it was not possible to evaluate more than one concentration due to the amount of sample available. Five independent solutions were prepared and analysed in single-particle mode. The average number of particles determined for each standard was compared with expected values. The results are presented in Table 4.

The obtained recoveries are within the acceptable range of 40%-120% for dissolved Au according to the standard operating procedure of the Instituto Nacional de Controle de Qualidade em Saúde (INCQS) inorganic elements laboratory and INMETRO guidance document.[19,24] The percent relative standard deviation (% RSD) of < 10% is also in line with previous guidance.[14] Furthermore, the most frequent size detected is consistent with the size of the added particles. The particles per millilitre recovery obtained for complex matrices such as face masks is suitable for the study. According to a bibliographic survey, accuracy studies must be evaluated using certified reference material, because factors such as matrix, size, density, stoichiometry and the type of NP directly influence recovery values.[12,14,25] The RSD > 10% can be justified by the AuNPs intrinsic property of agglomerating to form complexes which can cause a lack of homogeneity in the samples.

Method uncertainty

Estimation of the uncertainty of a test result can help determine the critical points in an analytical procedure, being necessary to determine the factors that can influence the final result. Some of these main factors are the preparation of analytical standards, dilution of samples, measurements made using equipment (repeatability), and the quantification procedure by calibration.[21] The relative uncertainty for the determination of Au ions in the single-particle mode was 71%. The items that most contributed to the relative uncertainty were sample preparation (48%) and analytical curve preparation (38%). With regard to determining the number of NPs, the relative uncertainty of 54% was most influenced by the analytical curve (53%) and repeatability (36%).

AuNP spICP-MS detection and quantification in cosmetics

The samples were subjected to the extraction process with water for AuNP analysis under the previously described experimental conditions and for Au analysis in the form of Au ions [Au(i)] through microwave-assisted acid digestion. AuNPs and Au(i) detection and quantification were carried out under the experimental conditions defined in the validation section. Each sample was prepared in triplicate and five independent measurement were taken for each replicate – i.e. 15 results were generated for each cosmetic and used to calculate the means and relative standard deviations displayed in Table 5.

Most analysed cosmetics (70%) contained quantifiable dissolved Au thus confirming the presence of this element in their formulations. Although one of the ingredients in these cosmetics is Au, about 60% of this ion was not present in the form of NPs, as stated on the label, or it was present in amounts below the LOD of spICP-MS, with regard to both size and concentration.

The ideal condition for NP assessments would require no sample preparation, but in complex samples such as cosmetics, in addition to sample preparation, factors such as storage time, type of storage, handling, transport, temperature and the matrix can influence the stability of NPs by changing the concentration of the number of particles and size. This is the great challenge of working with the final product because researchers do not have control over these factors.

Samples 6 and 8, the only artisanal products analysed in this study, were the only ones that declared the size of AuNPs used in the manufacturing process (50 nm). This information was corroborated by the results, where the AuNP size range varied from 40 to 60 nm, considering the occurrence of the NP agglomeration phenomenon present in the final formulation. The AuNP size range for sample 7,

Table 4. Accuracy and precision evaluation for dissolved gold and gold nanoparticles (AuNPs), determined in single particle detection mode (n = 5)

Sample	Added Au(i) μg mL^{-1}	Measured Au(i) mg mL^{-1}	Added AuNP particles/mL	Measured AuNP - particles/mL	Most frequent size (nm)	% REC	% RSD
Face mask	-	$1.2 \times 10^{-4} \pm 2 \times 10^{-5}$	-	$< 1.1 \times 10^5$	-	-	-
Face mask + 50 nm AuNPs	-	-	1.0×10^5	$1.2 \times 10^5 \pm 1.0 \times 10^4$	42 ± 5	109	4.5
Face mask + 50 nm AuNPs	1.0×10^{-3}	$1.3 \times 10^{-3} \pm 8 \times 10^{-5}$	1.0×10^5	$1.3 \times 10^5 \pm 2.5 \times 10^4$	47 ± 2	Au(i), 118% AuNPs, 115%	Au(i), 6% AuNPs, 11%

Note: Au(i), gold ions; % REC, per cent recovered; % RSD, per cent relative standard deviation; - not added and/or measured.

Table 5. Results for cosmetics that manufacturers claim to contain gold nanoparticles (AuNPs) (n = 3)

Samples	Au(i) (μg g^{-1})	Most frequent size (nm)	Particle concentration (particles/g)	Most frequent size range (nm)	% particles/g
Sample 1	0.015 ± 0.002	< LOD_d	< LOD_{NP}	–	–
Sample 2	0.05 ± 0.02	24	2.3 x 10^8 ± 2.6 × 10^7	20-40	46
Sample 3	0.0081 ± 0.0001	< LOD_d	< LOD_{NP}	–	–
Sample 4	< 0.005	< LOD_d	< LOD_{NP}	–	–
Sample 5	0.037 ± 0.006	40	1.8 x 10^8 ± 2.3 × 10^6	20-40	30
Sample 6	0.89 ± 0.01	47	9.3 x 10^8 ± 4.6 × 10^7	41-60	69.5
Sample 7			Not possible to analyse		
Sample 8	2.128 ± 0.009	60	4.8 × 10^8 ± 5.5 × 10^6	40-60	32
Sample 9	< 0.005	< LOD_d	< LOD_{NP}	–	–
Sample 10	< 0.005	< LOD_d	< LOD_{NP}	–	–

Note: Au(i), gold ion; LOD_d, nanoparticle size limit of detection; LOD_{NP}, number of nanoparticles limit of quantification, - not detected.

however, could not be identified because foam formed during the sonication step that prevented introduction of the sample into the ICP-MS, which can be explained by the composition of the samples (soap). Therefore, this sample could not be analysed. In samples 9 and 10 (imported), it was not possible to detect AuNPs and Au (i), either due to the limitation of the analysis methodology or the absence of these in the composition, which made it impossible to compare them with the samples purchased in Brazil.

Given that no regulation of products related to health interests that use nanotechnology has been published or implemented, there is no obligation for producers to inform consumers about the use of this technology on their product labels.[9] According to the European Union Commission Recommendation No. 2011/696/EU of 18 October 2011,[2] the results must be presented in the form of number of particles with a certain size by the total number of particles,[7] which facilitates classifying a product as a nanomaterial. In addition, inspection agencies have not defined what parameters, such as good manufacturing practices, are required during the production and in the quality and toxicological control of these cosmetics, thus allowing producers to only carry out the previously recommended tests for traditional cosmetics, without assessing the health risks of this innovative technology.[26]

There was a similarity between the different products containing NPs in terms of NP diameter. This may indicate agreement for these selected and analysed cosmetics concerning the manufacturing process with regard to the size range of the AuNPs that must be added to the product to ensure cutaneous penetrability in a given skin region and, thus, the intended effect. Previous studies have reported that AuNP skin permeability is inversely proportional to the size of the NPs – that is, smaller NPs reach deeper skin regions, while larger NPs are retained mainly in the epidermis and dermis.[27,28]

The number of AuNPs contained in each millilitre of sample could only be determined in 40% of the analysed cosmetics using the described method. The products that contained the greatest amount of these metallic NPs were the artisanal products, indicating they either have greater activities attributed to AuNPs, such as anti-inflammatory, anti-oxidant and skin ageing retardant actions, as described in the literature,[6–8] or generate still unknown toxic effects for this type of formulation and application.[29,30] However, the differences observed among the analysed samples demonstrate that the consumer population is exposed to a cosmetic composition heterogeneity, which can lead to toxic health effects when metallic NPs are present in higher concentrations. These high concentrations may either lead to the formation of Au 'clusters' in different types of cells and interaction with DNA,[29] or to a lack of the effects promised by such products.[6–8]

CONCLUSIONS

With the advent of nanotechnology, there has been a significant increase in cosmetics that include new ingredients classified as NPs in their composition. This technological innovation has brought a series of advantages for products related to health and aesthetics, although there is also a need for more rigorous production and cautious use, in addition to quality assessments and the control of toxicological risks. In this regard, the development and implementation of methodologies that verify the quality of these products has become a scientific challenge to meet the current need for inspection laboratories.

The spICP-MS technique allowed for the identification of the type of NP present in the analysed sample and a validation study indicates it is possible to quantify NPs in cosmetics with adequate precision and accuracy. The technique presented high uncertainty, although this factor does not prevent the method from being used as a routine in laboratories for the analysis of NPs in products of sanitary interest.

Concerning sample preparation, an essential step to obtain reliable results, the best methodology should be assessed according to the type of matrix to be analysed. In this study, water was the best extractor solvent: it exhibited satisfactory recovery and lower costs and waste production. However, filtration (0.22 μm) was needed after extraction in all experiments due to the presence of precipitates that could cause analytical interferences.

This study contributes to strengthen the literature on the application of nanotechnology in products of sanitary interest, thus providing technical-scientific support for the sanitary inspection of quality control carried out by the competent bodies and implementation of regulatory standards in this field of activity.

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