Borneo Journal of Pharmacy
Vol 5 Issue 1 February 2022
Page 21 – 26

http://journal.umpalangkaraya.ac.id/index.php/bjop/article/view/2708
DOI: https://doi.org/10.33084/bjop.v5i1.2708
e-ISSN: 2621-4814

Short Communication

Control of the Nanoparticles Content in Cosmetic Medicines

Marina Viktorivna Rakhimova[1*]
Igor Nikolaevich Bondarenko [2]
Oleg Grigorovitsh Avrunin [2]
Andrii I. Fedosov [1]
Irina A. Sych [1]
Vitaliy Dmitrievich Yaremenko[1]
Olha O. Vislous [1]
Lina O. Perekhoda [1]

[1]Department of Pharmacy, National University of Pharmacy, Kharkiv, Kharkiv Oblast, Ukraine

[2]Department of Biomedical Engineering, Kharkiv National University of Radio Electronics, Kharkiv, Kharkiv Oblast, Ukraine

*email: rakhimovamv@gmail.com

Keywords:
Acousto-magnetic method
Determination of the concentration
Nanocosmetics

Abstract

The safety of nanoparticles used in medical cosmetology and dermatology raises significant concerns. One of the tasks of analyzing the concentration of nanoparticles that must be solved for the practical analysis of the quality of products with nanoparticles is the quantitative analysis of the content of nanoparticles. The research objectives were developing the simplified method for determining the quantitative content of magnetic nanoparticles in the sample and experimental testing the sensitivity of a previously developed acousto-magnetic method (AMM) for practical use for the samples prepared as a colloidal solution of cosmetic medicines with nanoparticles. The object of the study was a model colloidal solution containing a certain amount of magnetite nanoparticles. The possibility of using the simplified AMM method at a therapeutically permissible concentration of magnetic nanoparticles has been proven. Comparison of the used technique with other methods of measuring the concentration of magnetic nanoparticles showed several advantages of the AMM method. It is possible to create a device for practical use in the future.

Received: September 11th, 2021
Revised: January 11th, 2022
Accepted: January 27th, 2022
Published: February 28th, 2022

INTRODUCTION

The currently observed increased interest in metal nanoparticles (NPs) is caused by discovering their unique physical and chemical properties features of biological action, which often differ from the properties of this substance in a macrodispersed form. Good prospects are for metal NPs in medicine, particularly dermatology. A new direction of developing nano preparation is forming a complex between known drugs and NPs, which gives the possibility of a deeper penetration of such complex drugs into the pathological process. To maximize the benefits of nanoscale materials, accurate control of their concentration is a necessary condition. In particular, this is necessary regarding magnetic drug targeting to maximize the efficacy and minimize the toxicity of the nanomaterials. Towards this significant yet chronic problem, various strategies are currently under development[1].

Some of the concentration determination methods apply to the ensemble of physical properties of dispersions of NPs (for example, light absorption), while others, such as microscopy and sensors, directly count individual particles. The UV-Vis spectroscopy[2], turbidimetry[3], and dynamic light scattering (DLS)[4] are three optical methods that measure the intensity of light upon absorption or scattering by nanoparticles. The turbidimetry method measures a decrease in the intensity of the incident light caused by light scattering of nanoparticle suspensions. The values measured by these methods are ensemble properties of nanoparticle suspensions, which can reflect averaged concentrations with statistical significance. The

limitations of these three methods lie in the complexity of measuring extinction/scattering coefficient or employing a reference sample with a known concentration.

Laser-induced breakdown detection (LIBD) is another method measuring the plasma generation from nanoparticles irradiated by an intense, focused laser in a suspension. It has a wide application in various particles of different sizes, but a special laser system is required to ensure the breakdown of nanoparticles. Unlike measuring ensemble quantities of nanoparticle dispersions, several techniques enable counting individual nanoparticles under direct visualization[5].

Resistive-pulsed sensing, inductively coupled plasma mass spectrometry (ICPMS), and light scattering particle counter are three methods that can count particles. They provide concentration information based on the signal pulses from a sensor, and a standard reference sample is usually required for calibration. The ICPMS is a highly sensitive and rapid analytical technique for elemental analysis at ultra-low concentrations. The samples in traditional ICPMS are usually metal ions dissolved in solution, and the concentration of total metal can be calculated based on the averaged intensity of the ion peak over a measuring period[6].

Mössbauer spectroscopy is widely used to determine magnetic NPs (MNPs). The methods based on the analysis of X-ray diffraction data have a reasonably wide range of determined parameters (phase composition, structure, average size, and morphological characteristics of nanocrystals. However, using this method can lead to significant errors due to the influence of various factors on the effect of broadening of diffraction maxima and others. When the Mössbauer spectroscopy method is used for measurements at 4.2 K, the nanoparticles typically exhibit well-defined but complicated hyperfine spectra that may present some evaluation problems but eventually yield reliable results. The different situation was when nanoparticles of Fe_3O_4 (magnetite) and gamma-Fe_2O_3 (maghemite) had been studied by Mössbauer spectroscopy at room temperature when they are superparamagnetic. The magnetic hyperfine fields were averaged to zero, making Mössbauer spectroscopy useless for the characterization of superparamagnetic NPs[7].

Among the magnetic NPs suitable for use in medicine, particles of iron oxide Fe_3O_4 can be distinguished due to their biological compatibility with biological objects. These particles are superparamagnetic and cannot be studied by the Mössbauer spectroscopy method at room temperature. The characterization of magnetic iron oxide NPs is important for their use as contrast agents in magnetic resonance imaging, as carriers for magnetic drug targeting, for local hyperthermia. Magnetic resonance imaging (MRI) can be used for magnetic particles concentration determination[8].

Magnetic nanoparticles change the electromagnetic excitation spectra of organic molecules of the human body. Registration of these spectra by MRI provides information on the distribution of particles in space and, consequently, the concentration of drugs coupled with them. The special features of the MRI method are the high cost and the associated with it less availability and give information about NPs distribution. Analysis of existing methods shows no universal method for determining the concentration of NPs of various types[9]. Each of the listed methods has both certain advantages over others and limitations. In particular, developing a more straightforward method applicable to *in vivo* and *in vitro* use for superparamagnetic nanostructures at room temperature is important. This study aims to describes a simplified acoustomagnetic method (AMM) of detecting magnetic particles concentration[10] and experimental procedure for determining the concentration of MNPs in a colloidal solution that is the model of the cosmetic products with MNPs both *in vivo* and *in vitro* that is important in dermatology as the possibility of penetration through the skin, in particular through the sebaceous glands and hair follicles. Such carriers provide long-term drug release and protect it from degradation.

MATERIALS AND METHODS

Materials

The object of study was a colloidal solution of nanoparticles based on Fe_3O_4 in a mixture of oleic acid and kerosene, a model sample of a cosmetic product colloidal solution. The average particle size with magnetite was 50-150 nm, size of Fe_3O_4 was much less. Oleic acid prevents powder particles from sticking together in solution, and kerosene provides the necessary viscosity. For biophysical applications, it is recommended to use a solution with a concentration of nanoparticles not more

than 5%. In our experiments, the weight concentration of the actual magnetite was no more than 0.15%. The viscosity of the suspension was chosen close to the viscosity of the blood (5×10^{-3} poise).

Methods

The experimental verification of the applicability of the AMM method was carried out using the setup shown in **Figure 1**. The scheme consists of three component blocks (**A**, **B**, and **C**), allowing to determine the concentration of nanoparticles in a vessel with a studied medium. Block **A** is a conditional image of a plot of a model studied medium with nanoparticles affected by a constant magnetic field H_d and ultrasonic radiation (**US**). The result of these actions is the generation under the action of US on magnetic particles of an alternating magnetic field H_a, depending on the concentration of the nanoparticles in the indicated studied medium. Block **B** is a sensitive device for measuring the field H_a. Block **C** is a recorder of the value H_a. Ultrasonic radiation has induced excitation of vibrations of magnetic nanoparticles in the target area of the sample, located in the external uniform constant magnetic field H_d. Oscillations of the particle ensemble oriented (polarized) by H_d field caused the appearance in the surrounding space of the alternating magnetic field H_a with a frequency of **US**. The magnetic flux of this field depends on the concentration of nanoparticles in the studied region and can be measured by a sensitive detector located outside this region. As such a detector, it can be used a superconducting quantum magnetometer, which, as is known, has the highest sensitivity and dynamic measurement range among the known types of magnetometers[11]. In the experiments with a model of a cosmetic product due to the higher permissible content of magnetite nanoparticles, which themselves do not belong to highly toxic additives, a highly sensitive voltmeter was used. In addition, in practice, the possibility to use a sensor with a lower sensitivity compared to the superconducting quantum magnetometer will make the AMM technique available for practical use in the future.

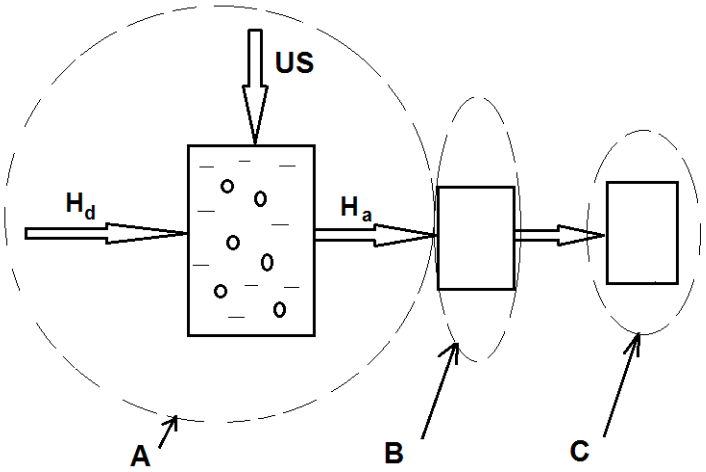

Figure 1. Block diagram of a measuring system

RESULTS AND DISCUSSION

Voltage (**U**) on the induction coil of unit **B** resulted from the excitation of oscillations of magnetic nanoparticles in the target area of the medium under the action of ultrasonic radiation. Accordingly to the Faraday's law on electromagnetic induction, the resulting **U** should be proportional to the magnitude of the nanoparticles' total magnetic field at the detector's location and their speed relative to the detector[12]. In turn, field H_a and **U** are proportional to the concentration (**K**) of the nanoparticles in the moving solution. In the specific case of the described experimental installation, the solution with the nanoparticles was moved using an ultrasonic wave, and the magnetic moments of the nanoparticles were oriented along the required direction by constant magnetic field H_d. In this case, the speed of movement of the nanoparticles is proportional to the power of the ultrasound. The magnitude of the **U** is proportional to the concentration of nanoparticles in the field of action of **US** and

magnetic field H_d and the **US** intensity (**I**). Dependence of the **U** at the induction coil on the **I** of ultrasound can be described by the **Equation [1]**:

$$U = k N I \qquad [1]$$

In which the parameter **k** characterizes the magnetic field properties in the coil area, the **N** number of the magnetic nanoparticles creates a magnetic field when all nanoparticles are oriented in the direction perpendicular to the plane of the coil by uniform constant magnetic field H_d. The value of **K** of the magnetic nanoparticles is equal to as described in **Equation [2]**:

$$K = (\mathbf{N\,V\,\rho/m})\ \mathbf{100}\% \qquad [2]$$

In which **V**, **ρ**, and **m** are the volume of one nanoparticle, its specific weight, and the total mass of the solution, respectively. The increase of the voltage on the induction coil proportionally to the **I** of the ultrasound confirmed the possibility of the magnetic particles registration using an acoustomagnetic method to measure the quantitative value of the concentration of the magnetic particles (**Figure 2**).

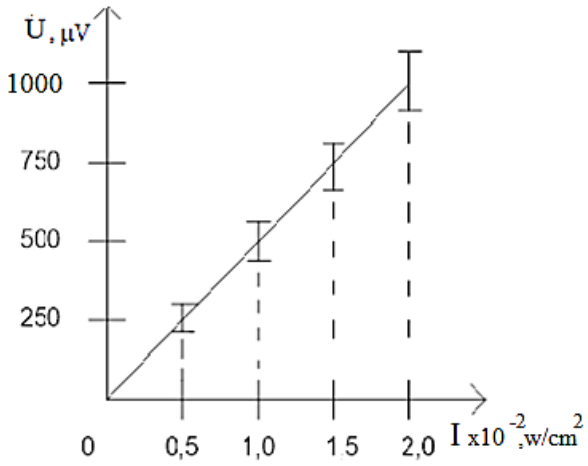

Figure 2. Dependence of the effective value of the alternating voltage U on the US intensity I

CONCLUSION

It is proposed to use a simplified method for determining the concentration of the cosmetic preparations when superconducting magnetometer usage is replaced by the highly sensitive voltmeter, which makes it possible to exclude the use of cryogenic liquid and makes the proposed method more accessible in practice for quality control of cosmetic preparations. Also, it has been experimentally shown that the sensitivity of detecting the response of an ensemble of MNPs using the selected measurement scheme is sufficient at the therapeutic dose with nanoparticles, which may be contained in a cosmetic product. The chosen method has several advantages over Mössbauer spectroscopy since it allows the concentration of superparamagnetic MNPs to be measured at room temperature, as Mössbauer spectroscopy is useless at this condition. Compared to MRI, the chosen technique is a direct method for determining the magnetic field's concentration and magnitude is significantly lower than it is used for MRI. Unlike most techniques, the chosen method allows its use not only for *in vitro* measurements but also for *in vivo* measurements at the penetration of MNPs through the skin in dermatology.

ACKNOWLEDGMENT

None.

AUTHORS' CONTRIBUTION

All authors have an equal contribution in carrying out this study.

DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors have declared no conflict of interest.

REFERENCES

1. Sukhanova A, Bozrova S, Sokolov P, Berestovoy M, Karaulov A, Nabiev I. Dependence of Nanoparticle Toxicity on Their Physical and Chemical Properties. Nanoscale Res Lett. 2018;13(1):44. doi:10.1186/s11671-018-2457-x

2. Jain PK, Lee KS, El-Sayed IH, El-Sayed MA. Calculated absorption and scattering properties of gold nanoparticles of different size, shape, and composition: applications in biological imaging and biomedicine. J Phys Chem B. 2006;110(14):7238-48. doi:10.1021/jp057170o

3. Khlebtsov BN, Khanadeev VA, Khlebtsov NG. Determination of the Size, Concentration, and Refractive Index of Silica Nanoparticles from Turbidity Spectra. Langmuir. 2008;24(16):8964-70. doi:10.1021/la8010053

4. Liu X, Dai Q, Austin L, Coutts J, Knowles G, Zou J, et al. A one-step homogeneous immunoassay for cancer biomarker detection using gold nanoparticle probes coupled with dynamic light scattering. J Am Chem Soc. 2018;130(9):2780-2. doi:10.1021/ja711298b

5. De Giacomo A, Koral C, Valenza G, Gaudiuso R, Dell'Aglio M. Nanoparticle Enhanced Laser-Induced Breakdown Spectroscopy for Microdrop Analysis at subppm Level. Anal Chem. 2016;88(10):5251-7. doi:10.1021/acs.analchem.6b00324

6. Zhang R, Zhao H. Small-Angle Particle Counting Coupled Photometry for Real-Time Detection of Respirable Particle Size Segmentation Mass Concentration. Sensors. 2021;21(17):5977. doi:10.3390/s21175977

7. Mourdikoudis S, Pallares RM, Thanh NTK. Characterization techniques for nanoparticles: comparison and complementarity upon studying nanoparticle properties. Nanoscale. 2018;10:12871-934. doi:10.1039/C8NR02278J

8. Hurley KR, Ring HL, Kang H, Klein ND, Haynes CL. Characterization of Magnetic Nanoparticles in Biological Matrices. Anal Chem. 2015;87(23):11611-9. doi:10.1021/acs.analchem.5b02229

9. Khan I, Saeed K, Khan I. Nanoparticles: Properties, applications and toxicities. Arab J Chem. 2019;12(7):908-31. doi:10.1016/j.arabjc.2017.05.011

10. Bondarenko SI, Avrunin OG, Bondarenko IS, Krevsun AV, Koverya VP, Rakhimova MV. On the measurements of magnetic nanoparticle concentration in a biological medium using a superconducting quantum magnetometer. Low Temp Phys. 2020;46:1094. doi:10.1063/10.0002152

11. Avrunin OG, Bondarenko IS, Bondarenko SI, Semenets VV, inventors; Kharkiv National University of Radio Electronics, assignee. Method for the remote recognition of the manifestation of magnetic nanoparticles in a biological environment. Ukraine patent 137159. 2019 Oct 10 [cited 2021 Sep 10]. 19 p.

12. Smith RT, Jjunju FPM, Young IS, Taylor S, Maher S. A physical model for low-frequency electromagnetic induction in the near field based on direct interaction between transmitter and receiver electrons. Proc Math Phys Eng Sci. 2016;472(2191):20160338. doi:10.1098/rspa.2016.0338