Reference Materials for Optical Nanosensor Systems: Reduced Glutathione and Chloramphenicol

Anna A. Yushina and Mikhail K. Alenichev

Abstract The research presents an approach to developing in-house reference materials (IHRMs) for a nanosensor system based on dynamic light scattering and fluorescence for qualitative and quantitative determination of the food contaminant antibiotic chloramphenicol (laevomycetin) and reduced glutathione, a marker for ischemic stroke and several other diseases. Chloramphenicol and reduced glutathione were chosen as candidate materials. The certification procedure based on the calculation and experimental method of preparation was employed to establish the certified value of the IHRM. During the tests, the metrological characteristics of the reference material were determined. The certified value of the mass fraction of the IHRM for reduced glutathione is 98.5%, and the expanded uncertainty of the certified value with the coverage factor $k = 2$ is $\pm$ 0.3%. The certified value of the mass concentration of the IHRM for chloramphenicol is 10.0 g/dm^3, and the expanded uncertainty of the certified value with the coverage factor $k = 2$ is $\pm$ 4.0%. The use of the developed IHRMs demonstrated their applicability for calibration of optical nanosensor systems based on dynamic light scattering and fluorescence. It is assumed that the developed in-house reference materials can be further certified as certified reference materials (CRM) and used for verification, calibration, and graduation of compact detection devices of the "point of care diagnostics" type designed for express tests right on the sampling site.

Keywords Reference material · Optical nanosensor system · Disease marker · Food contaminant · Dynamic light scattering · Fluorescence

A. A. Yushina (✉) · M. K. Alenichev
All-Russian Scientific Research Institute for Optical and Physical Measurements (VNIIOFI), Ozernaya st. 46, Moscow 119361, Russia
e-mail: yushina@vniiofi.ru

M. K. Alenichev
e-mail: alenichev@vniiofi.ru

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Introduction

The development direction of optical nanosensor systems has been burgeoning lately as the unique optical properties of nanoscale objects permit implementing highly sensitive detection of chemical substances, microorganisms, and biological molecules, including chemical contaminants of food, environmental media, and disease markers [1]. In many cases such systems provide a means of performing rapid tests directly on the sampling site (i.e. point of care diagnostics). The basis for optical nanosensors is the measurement of light absorption, fluorescence, or light scattering by nanoparticles interacting with the analyte [2].

Optical nanosensor systems based on the surface plasmon resonance effect [3] and various fluorescence effects such as fluorescence resonance energy transfer (FRET) [4, 5], the effect of excitation energy transfer from fluorophore [6, 7], or the inner filter effect [8, 9] are particularly common. In addition, there is a large amount of nanosensor systems based on dynamic light scattering (DLS) [10–12]. Nanosensor systems intended for quantitative analysis require the construction of calibration curves. For this purpose, reference materials of corresponding analytes are necessary. The requirements specified for reference materials for nanosensor systems include the correspondence of concentration ranges, the preparation simplicity of working solutions from standard reference materials, stability, purity, resistance to external influences, and culture media coordination. Ideally, the matrix of the standard reference material should correspond to the matrix of the sample which is going to be analysed later. Unfortunately, this condition is not always realizable in actual practice.

Optical nanosystems based on DLS and fluorescence were designed in the All-Russian Research Institute for Optical and Physical Measurements (VNIIOFI, Moscow) [1, 13]. The system based on DLS was developed employing the competition assay approach. It is aimed at detecting the antibiotic chloramphenicol (whose trade name is laevomycetin), an antimicrobial medicinal product, which is a dangerous contaminant of food, drinking water, and wastewater [14]. The fluorescent nanosystems were designed to detect and quantify reduced glutathione, a marker for ischemic stroke and several other diseases. These systems are based on the FRET effect and the effect of quantum dots excitation energy transfer. To provide metrological support of the measurements taken with optical nanosensor systems based on DLS and fluorescence, it was necessary to develop reference materials meeting the requirements formulated above and permitting the reproduction of mass concentrations of reduced glutathione and chloramphenicol.

This paper is an investigation into the feasibility of developing in-house reference materials (IHRM) intended for the metrological support of measurement procedures for chloramphenicol and reduced glutathione. The certified values of the mass concentrations of these analytes were determined through the mass measurement results obtained with an analytical balance traceable to the state primary reference material (SPRM) of mass and volume. The measurements were performed

with the help of dispensers traceable to the SPRM of fluid volume. The metrological characteristics of the precision balances and dispensers available at the All-Russian Research Institute for Optical and Physical Measurements (VNIIOFI) enable providing expanded uncertainties of the certified values of mass concentration which do not exceed 4.0% for chloramphenicol and 0.3% for reduced glutathione.

Materials and Methods

Characteristics of the Certified Reference Materials

Reduced Glutathione

Glutathione (γ-L-Glutamyl-*L*-cysteinylglycine) is a tripeptide (γ-glutamyl-*L*-cysteinyglycine) consisting of glutamic acid residues, cysteine, and glycine. It is a white crystalline powder or colorless crystals and is highly soluble in water and practically insoluble in methanol and diethyl ether [15].

Commercially available Sigma-Aldrich product CAS No. 70–18-8, cat. no. PHR1359[1] with at least 98.5% purity was chosen as the candidate material for preparing the IHRM for reduced glutathione. It is a secondary reference material developed in accordance with ISO 17034 [16] and ISO/IEC 17,025 [17]. The secondary reference material was prepared gravimetrically using a balance certified and calibrated as specified in the ISO 17025 requirements. All calibrations used NIST traceable weights calibrated in compliance with the NIST standards in a laboratory accredited according to ISO 17025. Metrological traceability to the corresponding primary standard is achieved via direct comparison.

No research of the uniformity estimation of the candidate for the IHRM was performed as its application involves single dissolution in deionized water and utilization of the entire quantity of the IHRM material from the test tube.

Chloramphenicol

Chloramphenicol (Chloramphenicolum) is an antibiotic in the form of a white crystalline powder, thin crystals, or oblong plates. It is highly soluble in ethanol, soluble in ethyl acetate, and poorly soluble in water [18].

[1] Pharmaceutical Secondary Standard; Certified Reference Material Glutathione 70–18-8. https://www.sigmaaldrich.com/catalog/product/sial/phr1359?lang=en&region=RU.

Commercially available Sigma-Aldrich product CAS No. 56–75-7, cat. no. C0378[2] with at least 98.0% (99%) purity was chosen as the candidate material for developing the IHRM for chloramphenicol.

Ethanol complying with State Standard (GOST) 5962–2013 was chosen as the solvent [19]. Since chloramphenicol molecules are evenly distributed throughout the entire solution volume due to Brownian diffusion in liquids and the identical charges of molecules, which is caused by the high solubility of chloramphenicol in ethanol, close distances between chloramphenicol molecules are ensured. For this reason, no research of the uniformity estimation of the candidate material for the IHRM was performed. The IHRM, consequently, is a true solution; there are no sources of uncertainly connected with its inhomogeneity.

For these reference materials the category "in-house reference material" was selected.

Determination of the Certified Values of the Reference Materials and Estimation of the Expanded Uncertainty of the Certified Values

Reduced Glutathione

The certified value of the IHRM was determined by the manufacturer (accredited in accordance with ISO/IEC 17,025) of the material chosen for the IHRM. The certification procedure based on the application of the reference material for reduced glutathione of the USA pharmacopoeia (the US glutathione standard) was employed to estimate the certified mass fraction value of the IHRM for reduced glutathione.

High-performance liquid chromatography was used to determine the certified mass fraction value of reduced glutathione.

Arrangements for measurements:

- Column: Ascentis Express C18, 4.6 × 50 mm, 2.7 μm
- Mobile phase: 6.8 g/l of K_2HPO_4 and 2.02 g/l of sodium heptanesulphonate in water (pH 3.3)–methanol (96:4)
- Flow rate: 1 ml/min
- Temperature: 30°C
- Sample volume: 3 μl
- Detection wavelength: 210 nm

In accordance with this certification procedure, the reference standard for glutathione of the United States Pharmacopoeia (USP) USP LOT R106J0 with the

[2] Pharmaceutical Secondary Standard; Certified Reference Material Glutathione 70-18-8. https://www.sigmaaldrich.com/catalog/product/sial/phr1359?lang=en&region=RU (Accessed 15 April 2021).

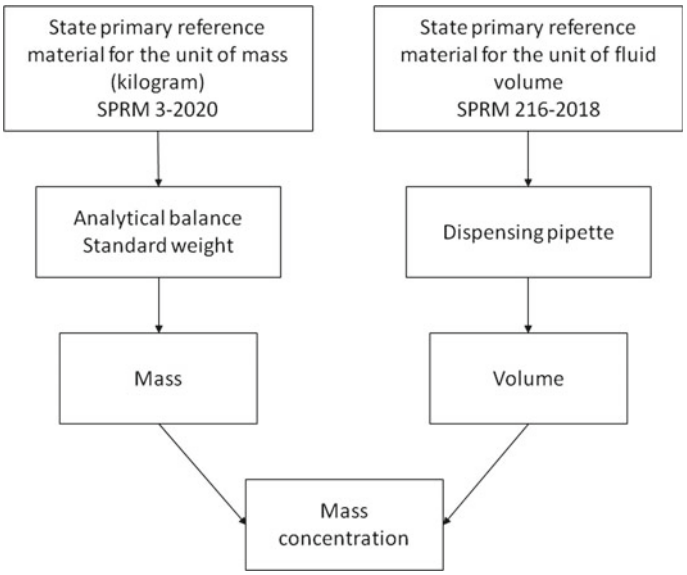

Fig. 1 Diagram of the metrological traceability of chloramphenicol mass concentration measurements

reduced glutathione content of 0.99 mg/mg was used for a preliminary calibration of a high-performance liquid chromatograph. The calibration was followed by a mass fraction measurement of the reduced glutathione in the material of the IHRM under development.

The metrological traceability of the IHRM certified value is estimated in relation to the reduced glutathione reference material of the United States Pharmacopoeia.

Chloramphenicol

The certified value of the candidate material for developing the IHRM for chloramphenicol was established by calculation according to the preparation procedure. The traceability of the mass concentration values was ensured using instruments for mass measurement (an analytical balance) traceable to the state primary reference material of the unit of mass SPRM 3–2020[3] and instruments for measuring the volume of fluid (a dispenser) traceable to the state primary reference material of the unit of fluid volume SPRM 216–2018.[4] The diagram in Fig. 1 shows the metrological traceability of the measurement results of chloramphenicol mass concentration.

[3] SPRM 3–2020 State primary reference material of the unit of mass (kilogram). https://fgis.gost.ru/fundmetrology/registry/12/items/1385582.

[4] SPRM 216–2018 State primary reference material of the unit of fluid volume in the range of 1.0·10-9 m^3 to 1.0 $м^3$. https://fgis.gost.ru/fundmetrology/registry/12/items/397905.

To determine the certified value of the IHRM for chloramphenicol mass concentration, the certification procedure based on the calculation and experimental method of preparation [20] was employed. The following measuring instruments were used to establish the certified values of chloramphenicol mass concentration:

- General-purpose weighing scale of class 1 accuracy to State Standard GOST OIML R 76-1-2011 [21] with the maximum permissible absolute measurement error of a single weighing not more than ±0.0001 g.
- One-milligram standard weight[5] as per State Standard GOST OIML R 111-1-2009 [22].
- Adjustable volume dispensing pipette covering ranges of 1000 to 10,000 mcl.[6] The maximum permissible systematic component of the basic relative error is ±1.0%. The maximum permissible mean-square deviation of the random component of relative error is 1.0%.
- Microclimate tester Meteoskop-M.[7]

A 0.05 chloramphenicol weighed sample was placed into a pre-weighed glass weighing bottle with a cap with a capacity of at least 10 cm^3. Then 5 cm^3 of ethanol was added using an adjustable dispensing pipette. The weighing bottle was capped, and its content was thoroughly mixed until the chloramphenicol completely dissolved in the ethanol. After that, the resulting solution was put into a container for storing the IHRM.

To measure the mass of the chloramphenicol weighed sample and the non-dissolved remainder of the chloramphenicol in the glass weighing bottle with a cap, the weighing procedure was performed as follows:

The weighing bottle with a cap was placed onto the weighing pan and weighed five times. A one-milligram standard weight was added to the same weighing pan (the actual mass was 1.001 mg) and weighed together with the capped weighing bottle five times.

The sensitivity of one reading of the scales *(δm)* was calculated according to Eq. (1):

$$\delta m = \frac{1mg}{(n_{b+w} - n_b)}, \tag{1}$$

where n_{b+w} is the mean number of discrete readings while weighing a capped weighing bottle with the standard weight; n_b is the mean number of discrete readings while weighing a clean weighing bottle.

[5] Class E1, E2, F1, F2, and M1 weights (number in the state register 36068-07). https://fgis.gost.ru/fundmetrology/registry/4/items/345346.

[6] Single- and multi-channel adjustable pipettes (number in the state register 37432-13). https://fgis.gost.ru/fundmetrology/registry/4/items/346979.

[7] Microclimate testers (number in the state register 32,014–11). https://fgis.gost.ru/fundmetrology/registry/4/items/340205.

The standard weight was removed from the weighing pan. The chloramphenicol weighed sample was placed into the weighing bottle with a cap and weighed five times.

The mass of the chloramphenicol weighed sample (m_s) was calculated according to Eq. (2):

$$m_s = (n_{b+s} - n_b) \cdot 1mg, \tag{2}$$

where n_{b+s} is the scale reading while weighing the capped weighing bottle and the chloramphenicol weighed sample, mg; n_b is the scale reading while weighing the weighing bottle with a cap and without chloramphenicol, mg.

The mass concentration of chloramphenicol in the C solution (mg/dm^3) was calculated using Eq. (3):

$$C = \frac{1000 \cdot (m_s - m_r)}{V}, \tag{3}$$

where m_s is the mass of the chloramphenicol weighed sample taken to prepare the IHRM, g; m_r is the mass of the chloramphenicol non-dissolved residue, g; V is the volume of the ethanol taken to prepare the IHRM, cm^3.

The mass of the non-dissolved IHRM residue in the weighing bottle was determined using Eq. (2) and following the procedure described above.

The quantitative evaluation of the standard uncertainty of the IHRM certified value relates to the determination of the chloramphenicol weighed sample mass and the volume of ethanol used to prepare the IHRM.

According to the type specification, the systematic weighing error of the laboratory analytical balance (Ohaus Explorer Pro, model EP114C, accuracy class I, 0.1 mg resolution[8]) is 0.75 mg. The additive component of the systematic error was eliminated with the error compensation by sign method. This method implies taking measurements in such a way that the measurement error would enter the data with one sign first and with the opposite sign next time. In accordance with this premise, to determine the mass of the chloramphenicol weighed sample and the non-dissolved residue, two weighings of each were performed: clean laboratory ware was weighed during the first weighing and laboratory ware with the chloramphenicol weighed sample or the non-dissolved residue during the second one. The chloramphenicol weighed sample mass was determined as the difference between the two above-mentioned weighings. As a result, the additive component of the systematic error was eliminated. The non-eliminated (multiplicative) component of the systematic error was taken equal to the resolution of the balance, i.e. 0.1 mg. Thus, the expanded uncertainty of the B type connected with the technical characteristics of the balance was taken equal to the non-eliminated component of the systematic error. Due to

[8] Electronic balance (number in the state register 16,313–08). https://fgis.gost.ru/fundmetrology/registry/4/items/315230.

this, the standard uncertainty of the B type was estimated according to Eq. (4):

$$u_B = \frac{d}{1,96}, \tag{4}$$

where d is the resolution of the used balance, i.e. 0.1 mg.

The standard uncertainty of the A type associated with weighing the chloramphenicol weighed sample was evaluated according to Eq. (5):

$$u_A = \sqrt{\frac{\sum_{i=1}^{n}(m_m - m_{am})^2}{n(n-1)}}, \tag{5}$$

where m_m is the results of mass measurements of the chloramphenicol weighed sample, mg; m_{am} is the arithmetic mean value of the chloramphenicol weighed sample mass obtained from the n measurements, mg; n is the number of mass measurements of the weighed chloramphenicol sample.

The standard uncertainty (u_V) associated with the ethanol volume was evaluated using the data from the calibration certificate of the utilized dispensing pipette and calculated according to Eq. (6):

$$u_V = \sqrt{u_A^2 + u_B^2}, \tag{6}$$

where u_A is the type A standard uncertainty taken equal to the maximum permissible mean-square deviation of the random component of relative error, cm^3; u_B is the B type standard uncertainty taken equal to the maximum permissible systematic component of the basic relative error, cm^3.

According to the type specification of the adjustable volume dispensing pipette covering ranges of 1000 to 10,000 mcl[6], the maximum permissible mean-square deviation of the random component of relative error is 1.0%; the maximum permissible systematic component of the basic relative error is ± 1.0%. The values of the A and B types of the standard uncertainty are taken equal to the maximum permissible mean-square deviation of the random component of relative error and the maximum permissible systematic component of the basic relative error in measuring the ethanol volume, respectively.

The combined standard uncertainty of the IHRM certified value in function of the technique used to estimate the certified value of the IHRM (u_t) was evaluated using the equation:

$$u_t = 100 \cdot \sqrt{\left(\frac{1,41 \cdot u_B}{m_s - m_r}\right)^2 + \left(\frac{u_V}{V}\right)^2}, \tag{7}$$

where u_t is the combined standard uncertainty of chloramphenicol mass concentration in the IHRM, %; u_B is the standard uncertainty of mass measurement during weighing, mg; m_s is the mass of the weighed chloramphenicol sample taken for the preparation of the IHRM, mg; m_r is the mass of the non-dissolved chloramphenicol residue, mg; u_V is the standard uncertainty of volume measurement dependent on the dispensing pipette, cm^3; V is the added volume of the ethanol taken to prepare the suspension, cm^3.

The combined standard uncertainty of the certified value (u) was taken equal to the standard uncertainty in function of the technique employed to determine the IHRM certified value:

$$u = u_t, \tag{8}$$

where u_t is the standard uncertainty in function of the technique used to estimate the certified value of the IHRM, %. The expanded uncertainty (with the coverage factor k = 2) of the IHRM certified value was evaluated in accordance with Eq. (9):

$$U_E = 1,96 \cdot u. \tag{9}$$

The calculation results of the combined standard and expanded uncertainties are shown in Table 1.

Stability testing of the materials for both IHRMs was not performed as the established validity period for the IHRMs being developed is much shorter than the established expiry validity period for the source materials. The shelf life of the IHRM for reduced glutathione is six months, while the expiry date of the IHRM material is three years. The shelf life of the IHRM for chloramphenicol is one month, while the expiry date of the IHRM material (chloramphenicol) is four years.

Table 1 Uncertainty characterization of the IHRM for chloramphenicol

Characterization of the IHRM uncertainty	Calculation data, %
Standard uncertainty dependent on the technique of determining the IHRM certified value	2.0
Combined standard uncertainty	2.0
Expanded uncertainty of the certified value with the coverage factor k = 2	4.0

Table 2 Metrological characterization of the developed IHRMs

In-house reference material	Name of the characteristic being certified	Certified value	Expanded uncertainty of the certified value with k = 2, %
Reduced glutathione	Mass fraction, %	98.5	± 0.3
Chloramphenicol	Mass concentration, g/dm^3	10.0	± 4.0

Results and Discussion

Reduced Glutathione

An IHRM for glutathione mass fraction has been developed to reproduce the mass concentration of reduced glutathione. The metrological characteristics of the IHRM for reduced glutathione are the mass fraction of reduced glutathione in the composition of the IHRM and the value of the expanded uncertainty of the certified value with the coverage factor k = 2 (Table 2). The IHRM is a powder with an analyte mass fraction equal to 98.5%; it is intended for the preparation of preset concentration working solutions immediately before use. Deionized water is utilized as a solvent. The IHRM is intended for verification, calibration, and graduation of measuring instruments as well as controlling metrological characteristics during their testing. The IHRM can also be used to control the accuracy of measurement results and to certify measurement procedures used at the enterprise. Additionally, the IHRM is intended for detecting reduced glutathione mass concentration in water and other liquid and biological media with an optical nanosensor system based on fluorescence.

In the first place, the developed IHRM is designed for plotting calibration curves while detecting reduced glutathione in unknown samples as there is a direct correlation between reduced glutathione concentration and the fluorescence intensity of quantum dots in the nanosensor systems developed in VNIIOFI. For instance, the calibration graph given in Fig. 2 was constructed for measuring reduced glutathione concentration in human blood plasma samples with a system based on the effect of quantum dots excitation energy transfer. The designed system provides a means for determining reduced glutathione in the range of 0 to 100 μmol/dm^3, which corresponds to the physiological concentration of glutathione in blood plasma.

Chloramphenicol

An IHRM was developed to reproduce chloramphenicol mass concentration. The reference material has the following metrological characteristics: the mass concentration of chloramphenicol in ethanol and the value of the expanded uncertainty of the certified value with the coverage factor k = 2 (Table 2). The IHRM is an ethanol

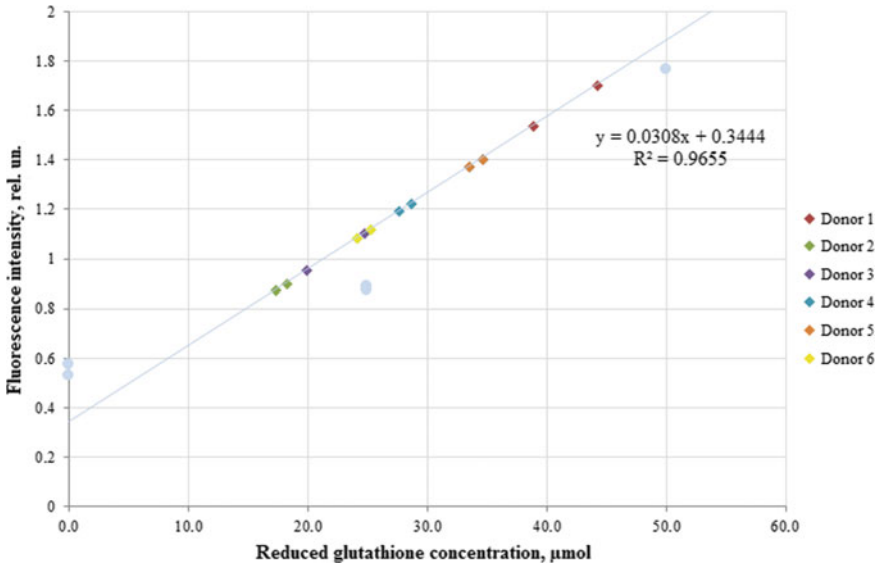

Fig. 2 Calibration graph and the values of reduced glutathione concentration in plasma determined with a nanosensor system based on the effect of quantum dots excitation energy transfer

solution of chloramphenicol with a mass concentration of 10.0 g/dm^3. The IHRM is assumed to be diluted to prepare working solutions of preset concentrations immediately before use. The IHRM purposes are as follows: verification, calibration, and graduation of measuring instruments as well as controlling metrological characteristics during their testing. The IHRM can also be utilized to control the accuracy of measurement results and to certify measurement procedures followed at the enterprise. Additionally, the IHRM is intended for determining chloramphenicol mass concentration in water and liquid and biological media including foodstuffs, food raw material, environmental media.

Figure 3 shows an example of a calibration graph constructed for measuring chloramphenicol mass concentration using the DLS method and a nanosensor system based on competition assay developed by VNIIOFI.

Conclusion

The present paper focused on the feasibility of developing in-house reference materials intended for metrological support of the procedures for measuring chloramphenicol and reduced glutathione with optical nanosensor systems, for detecting the antibiotic chloramphenicol (whose trade name is laevomycetin), for the detection and quantification of reduced glutathione, a marker for ischemic stroke and several other diseases. The certified value of the IHRM for chloramphenicol is traceable to

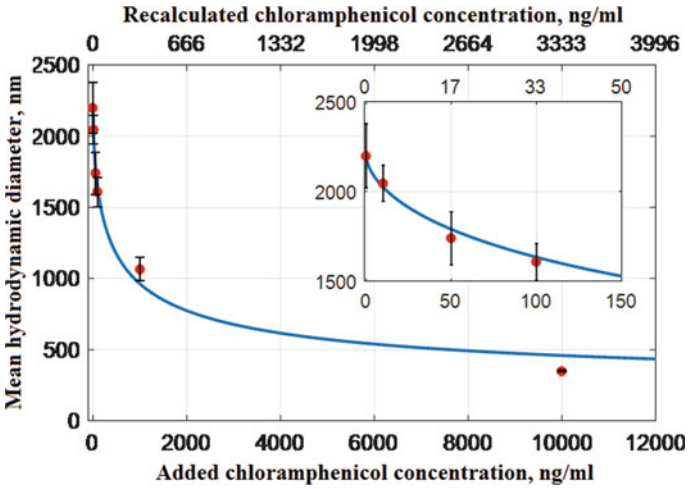

Fig. 3 Size dependence of functionalized gold nanoparticles on chloramphenicol concentration in aqueous solution

state primary reference materials SPRM 3–2020 and SPRM 216–2018. The certified value of the IHRM for reduced glutathione is traceable to the certified reference material for reduced glutathione of the USA pharmacopoeia.

The developed IHRMs for chloramphenicol and reduced glutathione can be further certified as certified reference materials and used for verification, calibration, and graduation of compact detection devices of the "point of care diagnostics" type designed for express tests right on the sampling site.

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Author Contributions A.A. Yushina: literature review; preparation of technical specification; data collection and processing; experimental data analysis.

M.K. Alenichev: concept advancement; data collection and processing; preparation of documents for reference material testing for the purpose of type approval.

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References

1. Alenichev MK, Yushina AA, Drozhennikova EB, Filimonov IS, Levin AD, Baranova OA, Chekanov AV (2019) Fluorescent nanosensors based on colloidal quantum dots for the determination of reduced glutathione. Meas Tech 62(9):16–21. https://doi.org/10.1007/s11018-019-01695-x
2. Yaraki MT, Tan YN (2020) Recent Advances in metallic nanobiosensors development: colorimetric, dynamic light scattering and fluorescence detection. Sensors Int 100049. https://doi.org/10.1016/J.SINTL.2020.100049
3. Javidi M, Housaindokht MR, Verdian A, Razavizadeh BM (2018) Detection of chloramphenicol using a novel apta-sensing platform based on aptamer terminal-lock in milk samples. Anal Chim Acta 1039:116–123. https://doi.org/10.1016/j.aca.2018.07.041
4. Mi Y, Lei X, Han H, Liang J, Liu L (2018) A sensitive label-free FRET probe for glutathione based on CdSe/ZnS quantum dots and MnO2 nanosheets. Anal Methods 10(34):4170–4177. https://doi.org/10.1039/C8AY01532E
5. Ambrin G, Kausar H, Ahmad A (2020) Designing and construction of genetically encoded FRET-based nanosensor for qualitative analysis of digoxin. J Biotechnol 323:322–330. https://doi.org/10.1016/j.jbiotec.2020.09.008
6. Liu J, Bao C, Zhong X, Zhao C, Zhu L (2010) Highly selective detection of glutathione using a quantum-dot-based OFF–ON fluorescent probe. Chem Commun 46(17):2971–2973. https://doi.org/10.1039/b924299f
7. Yu L, Li L, Ding Y, Lu Y (2016) A fluorescent switch sensor for glutathione detection based on Mn-doped CdTe quantum dots-methyl viologen nanohybrids. J Fluoresc 26(2):651–660. https://doi.org/10.1007/s10895-015-1751-6
8. Wu D, Li G, Chen X, Qiu N, Shi X, Gl C et al (2017) Fluorometric determination and imaging of glutathione based on a thiol-triggered inner filter effect on the fluorescence of carbon dots. Microchim Acta 184(7):1923–1931. https://doi.org/10.1007/s00604-017-2187-2
9. Rezaei B, Shahshahanipour M, Ensafi AA (2017) In situ production of silver nanoparticles for high sensitive detection of ascorbic acid via inner filter effect. Mater Sci Eng C 71:663–668. https://doi.org/10.1016/j.msec.2016.10.046
10. Zheng T, Bott S, Huo Q (2016) Techniques for accurate sizing of gold nanoparticles using dynamic light scattering with particular application to chemical and biological sensing based on aggregate formation. ACS Appl Mater Interfaces 8(33):21585–21594. https://doi.org/10.1021/acsami.6b06903
11. Mustafaoglu N, Kiziltepe T, Bilgicer B (2017) Site-specific conjugation of an antibody on a gold nanoparticle surface for one-step diagnosis of prostate specific antigen with dynamic light scattering. Nanoscale 9(25):8684–8694. https://doi.org/10.1039/C7NR03096G
12. Zheng T, Finn C, Parrett CJ, Dhume K, Hwang JH, Sidhom D (2017) A rapid blood test to determine the active status and duration of acute viral infection. ACS Infect Dis 3(11):866–873. https://doi.org/10.1021/acsinfecdis.7b00137
13. Levin AD, Ringaci A, Alenichev MK, Drozhzhennikova EB, Shevchenko KG, Cherkasov VR, Nikitin MP, Nikitin PI (2020) Dynamic light scattering biosensing based on analyte-induced inhibition of nanoparticle aggregation. Anal Bioanal Chem 412:3423–3431. https://doi.org/10.1007/s00216-020-02605-9
14. Ulanova TS, Karnazhitskaya TD, Pshenichnikova YeO, Nakhieva EA (2013) The development of a method for chloramphenicol determination in meat products. Health Risk Anal (4):82–90. https://doi.org/10.21668/health.risk/2013.4.11
15. Alanazi AM, Mostafa GAE, Al-Badr AA (2015) Glutathione. In: Profiles of drug substances, excipients and related methodology (40):43–158
16. GOST ISO Guide 35-2015 (2016) Reference materials. General and statistical principles for certification. Standartinform Publ, Moscow, 61p (In Rus)
17. GOST ISO/IEC 17025-2019 (2019) General requirements for the competence of testing and calibration laboratories. Standartinform Publ, Moscow, 25p (In Rus)

18. State Pharmacopoeia of the Russian Federation. Edition XIV, Volume III, Medicines of synthetic and mineral origin. Federal Electronic Medical Library. http://femb.ru/femb/pharmacopea.php
19. GOST 5962-2013 (2014) Rectified ethyl alcohol from food raw materials. Technical conditions. Standartinform Publ, Moscow, 9p (In Rus)
20. RMG 93-2015 State system for ensuring the uniformity of measurements. Estimation of metrological characteristics of reference materials. https://beta.docs.cntd.ru/document/1200138923 (In Rus.)
21. GOST OIML R 76-1-2011 (2013) State system for ensuring the uniformity of measurements. Non-automatic weighing instruments. Part 1 Metrological and technical requirements tests. Standartinform Publ, Moscow, 140p (In Rus)
22. (2012) State system for ensuring the uniformity of measurements. Weights of classes E1, E2, F1, F2, M1, M1-2, M2, M2-3 and M3. Part 1 Metrological and technical requirements. Standartinform Publ, Moscow, 102p (In Rus)

Anna A. Yushina Engineer of the Laboratory of Analytical Spectroscopy and Nanoparticles Metrology, the All-Russian Scientific Research Institute for Optical and Physical Measurements.

Mikhail K. Alenichev Researcher of the Laboratory of Analytical Spectroscopy and Nanoparticles Metrology, the All-Russian Scientific Research Institute for Optical and Physical Measurements.