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Optimization of the Technique for Obtaining Selenium Nanoparticles Stabilized with Cocamidopropyl Betaine

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Abstract—With the aim of optimizing the technique for the synthesis of selenium nanoparticles stabilized with cocamidopropyl betaine, a multifactorial experiment with three input parameters and three levels of variation was carried out. The selenous acid, cocamidopropyl betaine, and ascorbic acid concentrations were considered as input parameters. The output parameters were the average hydrodynamic radius of the particles (r_{av}) and ζ-potential. Photon correlation spectroscopy analysis revealed monomodal size distribution in all the samples. It was shown that the average hydrodynamic radius is most strongly influenced by the concentrations of selenous and ascorbic acids. The minimal size of the selenium nanoparticles ($r_{av} \leq 20$ nm) is achieved at selenous acid concentration of 0.05 to 0.15 M and at ascorbic acid concentrations of 0.0332 to 0.5 M. Acoustic and electroacoustic spectroscopy examination showed that the technique proposed allows formation of both positively (ζ-potential = +29.71 mV) and negatively (ζ-potential = –2.86 mV) charged nanoparticles. It was found that the ζ-potential of the selenium nanoparticles depends very heavily on the concentrations of the stabilizer and of selenous acid. For obtaining positively charged selenium nanoparticles the selenous acid concentration should not exceed 0.15 M and the cocamidopropyl betaine concentrations should be greater than 0.12 M. Negatively charged selenium nanoparticles are formed at selenous acid concentrations above 0.15 M and at cocamidopropyl betaine concentration under 0.12 M. The micelle structure for the positively charged and negatively charged selenium nanoparticles was proposed.

Keywords: selenium nanoparticles, optimization, photon correlation spectroscopy, acoustic and electroacoustic spectroscopy

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INTRODUCTION

Research interest in selenium, in particular, nanoselenium, increases every year due to the broad application prospects for this material possessing a number of properties that are useful for humans, plants, and animals [1–4]. Selenium nanoparticles are less toxic than elemental selenium [5] and show high biological activity [6]; they display antioxidant effects by increasing cellular defenses against oxidative stress [7]. Nanoselenium is actively used as a food additive [8, 9] and as a component of fertilizers for plants [10, 11] and also finds medicinal application in chemoradiotherapy [12–15] and targeted drug delivery [16, 17]. Active studies on the use of nanoselenium to combat various virus diseases, in particular, the COVID-19 virus, are underway now [18].

In view of the promise of wide applicability of nanoselenium, an important task consists in development and optimization of its preparation techniques. Synthesis of selenium relies on physical, chemical, and biological methods [19–22]. Among them, the most promising and popular are chemical methods based on reduction of selenium-containing compounds (e.g., sodium selenate, sodium selenite, selenous acid) to zero-valent nanoselenium with the aid of chemical reductants [23]. For example, selenium nanoparticles were obtained by

Table 1. Variation levels of the variables of the multifactorial experiment

Parameter	Parameter designation	Variation levels of the variable parameters		
$C(H_2SeO_3)$, M	*a*	0.0037	0.0295	0.2357
C(betaine), M	*b*	0.0055	0.0441	0.3551
C(ascorbic acid), M	*c*	0.0332	0.2712	2.1196

Table 2. Experiment planning matrix

Experiment no.	*a*, M	*b*, M	*c*, M
1	0.0037	0.0055	0.0332
2	0.0037	0.0441	0.2712
3	0.0037	0.3551	2.1196
4	0.0295	0.0055	0.2712
5	0.0295	0.0441	2.1196
6	0.0295	0.3551	0.0332
7	0.2357	0.0055	2.1196
8	0.2357	0.0441	0.0332
9	0.2357	0.3551	0.2712

Table 3. Experimental values of the output parameters

Sample no.	r_{av}, nm	ζ-potential, mV
1	16.3	+15.55
2	19.2	+17.29
3	243.2	+29.71
4	48.8	+26.16
5	176.0	+10.97
6	10.1	+12.71
7	362.9	+10.43
8	19.0	–2.86
9	175.1	+3.25

a "green chemistry" route using sodium selenate as a precursor and *Alternaria alternata* fungal culture filtrate as a reducing agent [24]. The average diameter of the obtained nanoparticles was estimated at 90±10 nm.

Importantly, significant effect produced by changes of the synthesis parameters such as concentration, temperature, agitation speed, type of stabilizer, etc. on the size, structure, and biological activity of selenium nanoparticles [25] suggests the need to optimize the synthesis routes for this material. Accordingly, the aim of this study was to optimize the procedure for the synthesis of selenium nanoparticles stabilized with cocamidopropyl betaine.

EXPERIMENTAL

Selenium nanoparticles stabilized with cocamidopropyl betaine (Matrix Oleochem Sdn Bhd, Egypt) were synthesized by the chemical reduction route in an aqueous medium. In the initial stage, weighed portions of the precursor, selenous acid (chemically pure grade, LenReaktiv, Russia), and stabilizer, cocamidopropyl betaine, were taken and dissolved in 100 mL of distilled water. Next, a solution of ascorbic acid (chemically pure grade, LenReaktiv, Russia) was prepared by dissolving the acid in 50 mL of distilled water. In the final stage of the synthesis, the ascorbic acid solution was all at once added to the solution containing the weighed portions of the precursor and the stabilizer with vigorous stirring, and the resulting sol was stirred for 5–10 min.

To optimize the technique for synthesizing selenium nanoparticles, a multifactorial experiment with three input parameters and three levels of variation was performed. The concentration of selenous acid $C(H_2SeO_3)$, the concentration of cocamidopropyl betaine C(betaine), and the concentration of ascorbic acid C(ascorbic acid) were considered as input parameters. The output parameters were the average hydrodynamic particle radius (r_{av}) and the ζ-potential. The levels of variation of the input parameters are presented in Table 1.

Based on Table 1, the matrix of the experiment was compiled (see Table 2).

The average hydrodynamic radius of the prepared selenium nanoparticles was determined by photon correlation spectroscopy on a Photocor Complex instrument setup. The results obtained were processed using the DynaLS software.

The ζ-potential of the selenium nanoparticles was determined by acoustic and electroacoustic spectroscopy using a DT-1202 analyzer.

The processing of the experimental data was carried out by the methods of regression, dispersion, and correlation analysis in the Statistica 12.0 software. Also, the experimental data were processed in the Statistica Neural Network software package [26].

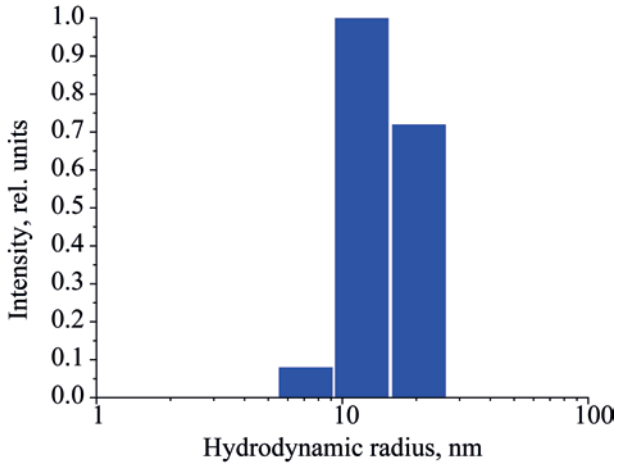

Fig. 1. Histogram of the hydrodynamic radius distribution for the selenium nanoparticles stabilized with cocamidopropyl betaine.

RESULTS AND DISCUSSION

In the initial stage, the output parameters, specifically the average hydrodynamic radius and the ζ-potential of the selenium nanoparticles, were determined (see Table 3). The histogram of the size distribution for the particles of sample no. 1 is shown in Fig. 1.

Analysis of the photon correlation spectroscopy data for the samples revealed monomodal size distribution for the particles of all the samples. It was found that the average hydrodynamic radius of the selenium nanoparticles formed in sample nos. 1, 2, 6, and 8 does not exceed 20 nm. The largest average hydrodynamic radius of the selenium particles is observed for sample no. 7 (r_{av} = 362.9 nm).

The acoustic and electroacoustic spectroscopy data revealed the formation of negatively charged selenium nanoparticles only in sample no. 8 (ζ-potential = –2.86 mV). In other cases formation of positively charged particles was observed, with the highest ζ-potential of +29.71 mV exhibited by sample no. 3.

Influence of the input parameters on the synthesis of the selenium nanoparticles was examined by the graphical analytical technique via plotting ternary surfaces, as shown in Figs. 2 and 3.

Analysis of the ternary surface presented in Fig. 2 reveals that the average hydrodynamic radius is most strongly affected by the concentrations of selenous

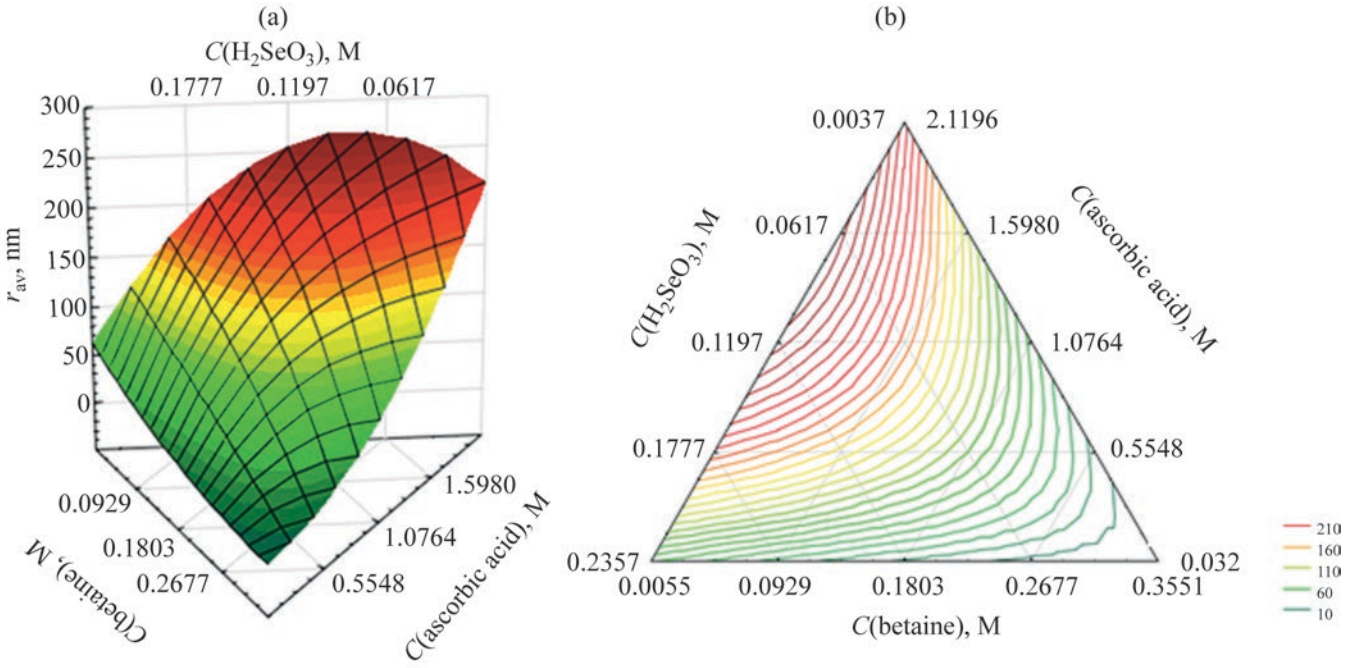

Fig. 2. Relationship between the average hydrodynamic radius of the selenium nanoparticles and the input parameters: (a) ternary surface and (b) ternary surface contour lines.

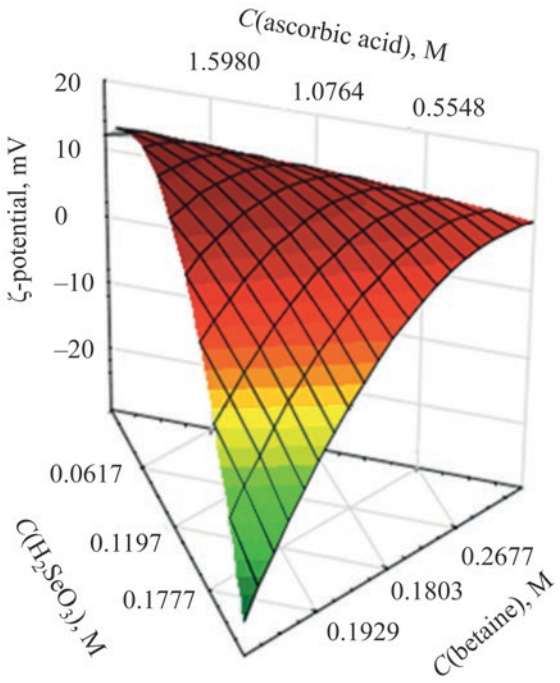

Fig. 3. Ternary surface demonstrating the relationship between the ζ-potential of the selenium nanoparticles and the input parameters.

and ascorbic acids. A minimal size of the selenium nanoparticles ($r_{av} \leq 20$ nm) is achieved at selenous acid concentrations of 0.05 to 0.15 M and ascorbic acid concentrations of 0.0332 to 0.5 M; a maximum size of the Se nanoparticles ($r_{av} \approx 250$ nm) is observed at the selenous acid concentrations of 0.06 to 0.11 M and ascorbic acid concentrations of 2.00 to 2.12 M. Importantly, the cocamidopropyl betaine concentration negligibly affects the average hydrodynamic radius of the particles.

The relationship between the ζ-potential of the selenium nanoparticles and the input parameters is demonstrated by the ternary surface shown in Fig. 3.

It was found that the ζ-potential of the selenium nanoparticles depends very heavily on the stabilizer concentration and the selenous acid concentration and that the ascorbic acid concentration negligibly affects the ζ-potential of the samples. At high selenous acid concentrations (>0.15 M) and low betaine concentrations (<0.12 M), a negative charge is generated on the selenium nanoparticles surface (ζ-potential < 0). In this case, according to the Paneth-Fajans rule, the potential-determining layer is formed due to adsorption of biselenite anions on the particle surface. The layer of counterions consists of cocamidopropyl betaine molecules oriented with their positively charged NH^+ groups toward the negatively charged surface of the selenium nanoparticles.

At low selenous acid concentrations (<0.15 M) and high stabilizer concentration (>0.12 M), a positive charge is generated on the selenium nanoparticles surface (ζ-potential > 0). In this case, the cocamidopropyl betaine molecule attaches to the surface of the Se nanoparticles with its hydrophobic tail, and its hydrophilic part faces the hydrophilic dispersion medium with the positively charged NH^+ groups. As a result, a positively charged potential-determining layer is formed on the surface of the selenium nanoparticles. The layer of counterions will be composed of the oxalate anions produced in the reaction system via oxidation of the ascorbic acid molecules.

CONCLUSIONS

The technique of the synthesis of selenium nanoparticles stabilized with cocamidopropyl betaine was optimized. It was found that obtaining selenium nanoparticles of less than 20 nm in size requires selenous acid concentration in the range from 0.05 to 0.15 M and the ascorbic acid concentration in the range from 0.0332 to 0.5 M. It was shown that the technique proposed allows formation of both positively and negatively charged nanoparticles. For obtaining positively charged selenium nanoparticles, the selenous acid concentration should not exceed 0.15 M, and the cocamidopropyl betaine concentration should be above 0.12 M. Negatively charged selenium nanoparticles are formed at selenous acid concentrations exceeding 0.15 M and at cocamidopropyl betaine concentrations under 0.12 M.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

1. El-Ramady, H., Faizy, S.E.D., Abdalla, N., Taha, H., Domokos-Szabolcsy, É., Fari, M., Elsakhawy, T., Omara, A.E.D., Shalaby, T., Bayoumi, Y., Shehata, S., Geilfus, C.M., and Brevik, E.C., *Soil Syst.*, 2020, vol. 4, no. 3, p. 57. https://doi.org/10.3390/soilsystems4030057

2. Kumar, A. and Prasad, K.S., *J. Biotechnol.*, 2021, vol. 325, pp. 152–163. https://doi.org/10.1016/j.jbiotec.2020.11.004

3. Molodtsov, P.A., Makarov, S.V., Dereve'nkov, I.A., and Makarova, A.S., *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, 2022, vol. 65, no. 4, pp. 56–61.
4. Poluboyarinov, P.A., Moiseeva, I.Ya., Mikulyak, N.I., Golubkina, N.A., and Kaplun, A.P., *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, 2022, vol. 65, no. 2, pp. 19–29.
5. Wang, H., Zhang, J., and Yu, H., *Free Radic. Biol. Med*., 2007, vol. 42, no. 10, pp. 1524–1533. https://doi.org/10.1016/j.freeradbiomed.2007.02.013
6. Peng, D., Zhang, J., Liu, Q., and Taylor, E.W., *J. Inorg. Biochem*., 2007, vol. 101, no. 10, pp. 1457–1463. https://doi.org/10.1016/j.jinorgbio.2007.06.021
7. Dawood, M.A., Zommara, M., Eweedah, N.M., Helal, A.I., and Aboel-Darag, M.A., *Environ. Sci. Pollut. Res*., 2020, pp. 1–10. https://doi.org/10.1007/s11356-020-07651-5
8. Zhang, J. and Spallholz, J.E., in General, *Applied and Systems Toxicology*, Ballantyne, B., Marrs, T.C., and Syversen, T.L.M., Eds., 3rd ed., vol. 1, Chichester: John Wiley and Sons, 2009. https://doi.org/10.1002/9780470744307.gat243
9. Surai, P.F. and Kochish, I.I., *Anim. Health. Res. Rev*., 2020, pp. 1–5. https://doi.org/10.1017/S1466252320000183
10. Hussein, H.A.A., Darwesh, O.M., Mekki, B.B., and El-Hallouty, S.M., *Biotechnol. Rep.*, 2019, vol. 24, p. e00377. https://doi.org/10.1016/j.btre.2019.e00377
11. Hussein, H.A.A., Darwesh, O.M., and Mekki, B.B., *Biocatal. Agric. Biotechnol*., 2019, vol. 18, p. 101080. https://doi.org/10.1016/j.bcab.2019.101080
12. Yu, B., Liu, T., Du, Y., Luo, Z., Zheng, W., and Chen, T., *Colloids Surf., B: Biointerface*, 2016, vol. 139, pp. 180–189. https://doi.org/10.1016/j.colsurfb.2015.11.063
13. Chen, F., Zhang, X.H., Hu, X.D., Liu, P.D., and Zhang, H.Q., *Artif. Cells Nanomed. Biotechnol*., 2018, vol. 46, no. 5, pp. 937–948. https://doi.org/10.1080/21691401.2017.1347941
14. Singh, R. and Lillard, J.W.Jr., *Exp. Mol. Pathol*., 2009, vol. 86, no. 3, pp. 215–223. https://doi.org/10.1016/j.yexmp.2008.12.004
15. Vekariya, K.K., Kaur, J., and Tikoo, K., *Nanomed: Nanotechnol., Biol., Med.*, 2012, vol. 8, no. 7, pp. 1125–1132. https://doi.org/10.1016/j.nano.2011.12.003
16. Guan, B., Yan, R., Li, R., and Zhang, X., *Int. J. Nanomed*., 2018, vol. 13, p. 7473. https://doi.org/10.2147/IJN.S181343
17. Veiseh, O., Gunn, J.W., and Zhang, M., *Adv. Drug Deliv. Rev*., 2010, vol. 62, no. 3, pp. 284–304. https://doi.org/10.1016/j.addr.2009.11.002
18. He, L., Zhao, J., Wang, L., Liu, Q., Fan, Y., Li, B., Yu, Y.L., Chen, C., and Li, Y.F., *Nano Today*, 2021, vol. 36, p. 101037. https://doi.org/10.1016/j.nantod.2020.101037
19. Hosnedlova, B., Kepinska, M., Skalickova, S., Fernandez, C., Ruttkay-Nedecky, B., Peng, Q., Baron, M., Melcova, M., Opatrilova, R., Zidkova, J., Bjørklund, G., Sochor, J., and Kizek, R., *Int. J. Nanomed*., 2018, vol. 13, p. 2107. https://doi.org/10.2147/IJN.S157541
20. El-Ramady, H.R., Domokos-Szabolcsy, É., Abdalla, N.A., Alshaal, T.A., Shalaby, T.A., Sztrik, A., Prokisch, J., and Fári, M., *Environ. Chem. Lett*., 2014, vol. 12, no. 4, pp. 495–510. https://doi.org/10.1007/s10311-014-0476-0
21. Makarov, S.V., Molodtsov, P.A., Dereven'kov, I.A., and Naidenko, E.V., *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, 2021, vol. 64, no. 11, pp. 65–70.
22. Mirzoeva, A.A. and Bakhtiyarly, I.B., *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, 2017, vol. 60, no. 3, pp. 67–71.
23. Siddiqui, S.A., Blinov, A.V., Serov, A.V., Gvozdenko, A.A., Kravtsov, A.A., Nagdalian, A.A., Raffa, V.V., Maglakelidze, D.G., Blinova, A.A., Kobina, A.V., Golik, A.B., and Ibrahim, S.A., *Coatings*, 2021, vol. 11, no. 7, p. 862. https://doi.org/10.3390/coatings11070862
24. Sarkar, J., Dey, P., Saha, S., and Acharya, K., *Micro Nano Lett*., 2011, vol. 6, no. 8, pp. 599–602. https://doi.org/10.1049/mnl.2011.0227
25. Zhang, S.Y., Zhang, J., Wang, H.Y., and Chen, H.Y., *Mater. Lett*., 2004, vol. 58, no. 21, pp. 2590–2594. https://doi.org/10.1016/j.matlet.2004.03.031
26. Blinov, A.V., Gvozdenko, A.A., Yasnaya, M.A., Golik, A.B., Blinova, A.A., Shevchenko, I.M., and Kramarenko, V.N., in *Fiziko-khimicheskie aspekty izucheniya klasterov, nanostruktur i nanomaterialov: mezhvuzovskii sbornik nauchnykh trudov* (Physicochemical Aspects of Study of Clusters, Nanostructures, and Nanomaterials: Intercoll. Coll. of Sci. Works), Samsonov, V.M. and Sdobnyakov, N.Yu., Eds., Tver: Tver. Gos. Univ., 2019, no. 11, pp. 298–306