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TECHNOLOGY OF PRODUCTION OF DRUG NANOPARTICLES FROM PLANT EXTRACTS BY GREEN SYNTHESIS METHODS

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Abstract

One of the innovative methods for obtaining drug nanoparticles is the green synthesis method of metal-based nanoparticles in extracts from medicinal plants. When nanoparticles are synthesised in extracts of medicinal plants, there is a high probability of the biologically active molecules (drugs) contained in the extract being attached to their surface. The attachment of specific drug-active molecules to the surface of nanoparticles creates the possibility of using them as nanomedicines. In synthesising nanoparticles in plant extracts, the biologically active molecules in them act as both reducing agents and stabilizers.In the presented research materials, a comparative technology of synthesis of silver (Ag) nanoparticles in extracts of some medicinal plants (*Melissa Lamiaceae, Rosmarinus officinalis, Achillea millefolium, Matricaria chamomilla*) by thermal and sonication methods was developed. By comparing the absorption spectra of Ag nanoparticles synthesized by both the thermal method and the sonication method, it was comparatively studied which method synthesized Ag nanoparticles better. It was found that the sizes of Ag nanoparticles vary depending on the dose of extracts in the synthesis by both methods. In the sonication method of nanoparticles, the sizes of nanoparticles depend on both the sonication time and the dose of extracts.

Keywords: *nanoparticles; green synthesis; medicinal plants; thermal synthesis****;*** *sonication synthesis*

1. Introduction

One of the most extensive fields of application of nanotechnology is medicine. The nanoparticles nanorobots, nanosensors and nanomedicines are widely used in medicine. The application of the nanoparticles is necessary for the achievement of their ecological clean forms. It was determined that the nanoparticles may form certain toxical effects being collected in the human organism, animals and as well as, in the plant. So, the effect of the nanoparticles to the biological systems and achievement of their non-toxic forms has been the object of several researches currently.

The silver nanoparticles (in 1-100 nm intervals) are the stable nano- particles in the colloidal disperse solution with electronic and antiseptic features. The silver nanoparticles are obtained from the reduction of Ag+ ions and are formed as particles with different measures. The stabilization of the silver nanoparticles and the regulation of their measures and forms depend on the nature of reducents, and the factors of

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environments such as pH, temperatures and thickness. The smallest size of the silver nanoparticles currently in 2-5 nm content. Their forms are spherical, triangle, cub, flower, with lays, triangular, polygonal, irregular, etc. The formation of the silver nanoparticles may be determined first of all with the change of the color of the solution. The change of color of the solution is happened due to the formation of surface plasmon effect on silver nanoparticles. Gold and silver nanoparticles have been found in the plants such as Cinnamomum camphora, Brassica juncea and Capsicum annum during the researches [1, 2]. It has been determined that, the plant lucerna may collect the silver from the liquid environment [3, 4]. The patterns of the plant lucerna have been cultivated in the environment rich with the silver ions and dried in the gas for 24 hours in 650°C being replaced inside the synthetic resin.

The TEM analysis shows that the silver atoms are collected as the result of the formation process of the nanoparticles. The nanoparticles Ag, Ni, Co, Zn and Cu are synthesized in the plant's *Brassica juncea* (Indian mustard), *Medi- cago sativa* (*Alpha alpha*), and *Helianthus annus* (Sunflower). As we mentioned, the hyperaccumulator plant differs from other plants in its feature of metal collecting in very high concentrations. Several active biomolecules, for example, the phenol acids (caffeine, theophylline) play a role in the synthesis of silver nanoparticles in plant extracts or homogenates. The green tea-C. the silver nanoparticles of various shapes, spherical, prismatic, trapezoidal and rod- shaped were obtained while using *Sinensis* leaves in the experience of Begum and his colleagues. According to their decision, the polyphenols and flavonoids are the molecules supplying the synthesis of the silver nanoparticles [5]. Kesarvani and his colleagues synthesized the silver nanoparticles in the interval of 16-40 nm using extracts of alfalfa (*Medicago sativa*), lemon grass (*Cymbo- pogon flexuosus*), and algae (*Pelargonium graveolens*). There are alkaloids, proteins, ferments, amino acids, alcohol compounds and polysaccharides in the extract of these plants, so, the synthesis of the silver nanoparticles become more efficient. The nanoparticles obtained are stable and mainly spheric [6]. Recently the results of the experiments of the scientists are more by archiving the synthesis of the silver nanoparticles in the plants. It is possible to come to a conclusion that, it is possible to obtain the silver nanoparticles in the different measure and forms through the extracts prepared from the different parts of the majority of plants. The characterization of the colloid solutions obtained through these extracts, the cleaning of the silver nanoparticles from these colloid solutions requires a special technology. The important works have begun in this field already [7, 8].

Recently the biological method for the synthesis of Ag nanoparticles with important priorities from an ecological viewpoint is deemed more acceptable. The synthesis of Ag nanoparticles biologically may be realized by using mainly bacteria, fungi and polypeptides, nucleic acids and at last, the different plant extracts [9, 10]. The most effective method of such biological methods is a synthesis of Ag nanoparticles by using plant extracts. It was determined that Ag nanoparticles synthesized through the plant extracts have different measures, forms and properties. The properties and measures of Ag nanoparticles depend on the type of plants, the amount, temperature, pH, the exposition period and at last the synthesis method of the extract. The main objective of the study was to work out a comparative technology for the synthesis of silver nanoparticles in extracts of some medicinal plants *(Melissa Lamiaceae, Rosmarinus officinalis, Achillea millefolium, Matricaria chamomilla)* using thermal and sonication methods.

2. Materials and methods

The synthesis of Ag nanoparticles has been realized by using these extracts as a reducing agent in the nitrate acid of the silver (AgNO3). The solution of the following matters have been considered in the research:

1. To prepare the extract from the dried leaves of the *Melissa Lamiaceae, Rosmarinus officinalis, Achillea millefolium, and Matricaria chamomilla;*
2. To synthesize the silver nanoparticles through the extract obtained from these plants;
3. To determine the dependence of the synthesis of silver nanoparticles in the plant by the concentration of the extract, the pH of the solution, the temperature and the concentration of silver salt;
4. To determine the UV-vis spectrum of the nanoparticles obtained during the synthesis of silver nanoparticles through the extracts of these plants;

In the thermal method, 50 ml of a 5.10^{-3}M solution of $AgNO_3$ salt was taken, and heated to a temperature of 70-80^{0}C in a heating magnetic stirrer, and the extracts of medicinal plants were added dropwise. After adding the extract, the heater was turned off and the solution was processed in a magnetic stirrer for 30 minutes. In the sonication method, 50 ml of a 5.10^{-3}M solution of $AgNO_3$ salt was taken in the same way, and extracts of medicinal plants in different doses were added to the solution in an ultrasonic device. For the synthesis of Ag nanoparticles in the thermal method, extracts of medicinal plants in different doses of 5,10,15,20 and 25 ml were added to the $AgNO_3$ solution. In the sonication method, the synthesis of Ag nanoparticles was investigated depending on both the sonication time and the dose of extracts. Experimentally, the optimal dose of the extract was determined for the synthesis of Ag nanoparticles in the thermal method, and the optimal dose of the extract and the optimal value of the sonication time in the sonication method. After the solutions of Ag nanoparticles synthesized in extracts of medicinal plants were kept at room temperature for 24 hours, their absorption spectra were recorded in a UV-vis spectrometer.

The chemical content of the *Melissa Lamiaceae*. Studies on the composition of *Melissa* have shown that it mainly contains flavonoids, terpenoids, phenolic acids, tannins and essential oils (0.33%) [11]. The leaves contain 5% of the active substances, resin, mucilage, ursolic and eleanolic acids and 150 mg of vitamin C, and the fruits contain 20% of fatty oil. The upper flowering part or leaves of the medicinal herb are used [12].

The chemical content of the *Rosmarinus officinalis*. The GC–MS analysis of essential oil of R. officinalis indicated three compounds: cineole, camphor and alpha-pinene [13]. Medicinal rosemary contains 1-2% essential oil and 85% tannins. The essential oil consists of 17-30% cineole, 30% pinene, borneol and other terpenes. Its leaves are used for medicinal purposes.

The chemical content of the *Achillea millefolium*. The composition of the *Achillea millefolium* is 0.12-0.5% essential oil (contains 1-10% azulene, axillein substance - glycoalkaloid, 2.8% tannin, asparagine, 1.8% oil). The essential oil contains cineole, pinene, eugenol, and borneol. The plant contains vitamin K. Flower baskets and young shoots are used in folk medicine [14, 15].

The chemical content of the *Matricaria chamomilla*. The composition of common chamomile contains up to 0.5% essential oil, sitosterol, choline, flavonoids, coumarins, glycosides, isovalerian and other organic acids. 10% hemazulene was found in the essential oil [16, 17].

Fig. 1. Medicinal plants which used in experiments

UV-Vis Spectroscopy. One of the methods used most of all for observance of the synthesis of the nanoparticles is UV-Vis absorption spectroscopy. UV-Vis spectroscopy is used to obtain the absorption spectra of the solid matter or complex solution. The electromagnetic spectra of the energy in the UV-Vis part belong to 1,5-6,2 eV of which the length of the wave is proper to 200-800 nm. The law Beer-Lambert expressed with the equality of A=Ɛbc stands based on the absorption spectra. A-absorption, Ɛ - the ability of absorption of the molecule and mix in the solution, the length of the tube where the b-pattern is located, and c is a concentration. The absorption spectrum was taken in UV-Vis spectrum (SPECORD 250 plus) by taking the extract and homogenates having the nanoparticles. The distilled water was taken as background to correct the UV-Vis spectra. The patterns were located in the quartz tubes (Fig. 2).

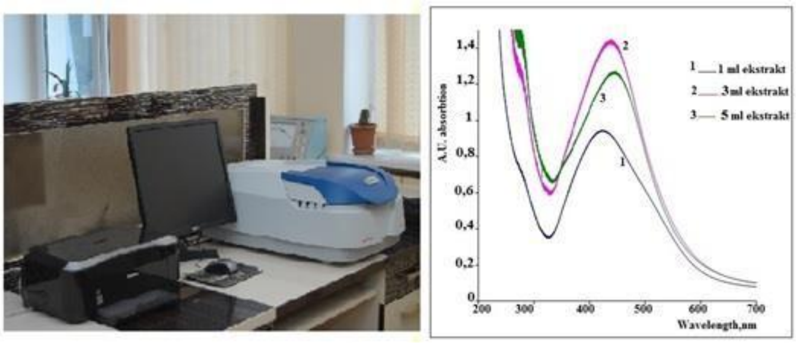

Fig. 2. UV-vis spectrum and absorption spectra of the pattern with the silver nanoparticles

3. Results and discussion

Green synthesis of Ag nanoparticles has been widely studied in many laboratories around the world. For this, extracts from leaves, stems, roots and fruits of various plants are used. Green synthesis of Ag nanoparticles is mainly carried out by thermal method. For this, a solution of AgNO3 salt in various concentrations is heated to a temperature of 80 C and extract obtained from plants in various doses is added dropwise and processed in a magnetic stirrer for 10-20 minutes. Then the resulting solution is kept at room temperature for 24 hours. Another method has been proposed in our experiments. This method is called synthesis by sonication in an ultrasound apparatus. As in the thermal method, extract obtained from plants is added dropwise to the $AgNO_3$ salt solution during sonication and sonicated for 10-20 minutes. To prevent heating of the solution during sonication, the container with the solution is covered with ice. The solution of Ag nanoparticles synthesized by sonication was kept at room temperature for 24 hours and then analyzed by UV-Vis spectrometer. When nanoparticles are synthesized from plant extracts, biologically active molecules (drugs) contained in the extracts play the role of both a reducing agent and a stabilizer in the formation of nanoparticles. These molecules, which play the role of stabilizers, can form a coating on the surface of nanoparticles or combine with their surface in a branched form. Thus, the active constituents (flavonoids, terpenoids, phenolic acids, tannins, and essential oil) contained in the *Melissa Lamiaceae* extract can cause the formation of functionalized silver nanoparticles, both as coatings and as individual molecules, during the synthesis process of silver nanoparticles. Fig. 3 shows the absorption spectra of Ag nanoparticles synthesized by ultrasonic and thermal methods in extracts of 4 medicinal plants.

The UV-vis spectra of the Ag nanoparticles solution synthesized in the extract obtained from the flowers of the *Matricaria chamomilla* plant show that the size of the nanoparticles obtained is in the range of 45-50 nm and the size of the nanoparticles obtained by the ultrasonic method does not differ from the size of the nanoparticles obtained by the thermal method. However, the amount of nanoparticles obtained by the thermal method is greater than that obtained by the ultrasonic method (Fig. 3A). The UV-Vis spectra of the Ag nanopar- ticles solution synthesized in the extract obtained from the leaves of the *Rosmarinus officinalis* plant show that the size of the nanoparticles obtained by the thermal method is smaller than that obtained by the ultrasonic method (40- 45 nm), but the amount of nanoparticles synthesized is the same (Fig. 3B).

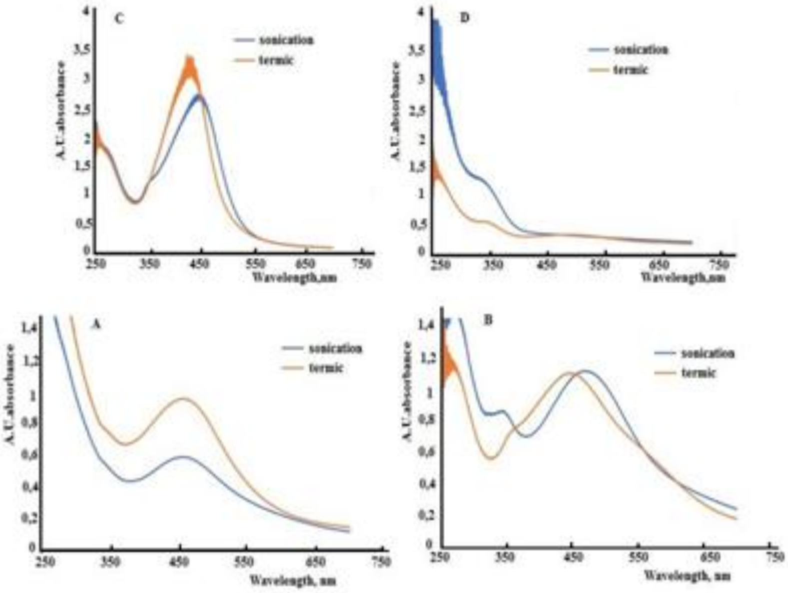

Fig. 3. Absorption spectra of Ag nanoparticles synthesized in extracts of medicinal plants by ultrasonic and thermal methods: A- *Matricaria chamomilla*, B- *Rosmarinus officinalis*, C- *Melissa Lamiaceae*, D- *Achillea millefolium*

The UV-Vis spectra of the Ag nanoparticles solution synthesized in the extract from the leaves of *Melissa Lamiaceae* show that the sizes of the nanoparticles synthesized by the thermal method are in the range of 20-30 nm, while the sizes of the nanoparticles synthesized by the ultrasonic method are in the range of 40-45 nm, and the amount of synthesized nanoparticles is relatively small (Fig. 3C). The UV-vis spectra of the Ag nanoparticles solution in the extract from the flowers of *Achillea millefolium* show that Ag nanoparticles are not synthesized in both synthesis methods, both thermal and ultrasonic (Fig. 3C). Thus, the results of the experiments show that the sizes and amounts of nanoparticles synthesized in the extracts of different medicinal plants vary depending on the synthesis method, and the smallest nanoparticles are synthesized in the extract from the leaves of *Melissa Lamiaceae*.

4. Conclusion

Since many characterization methods and techniques have been used for Ag nanoparticle synthesis still not suitable methods for the effective use and confirmation of the synthesized nanoparticles for the making of a drug. The main principle in the synthesis of the nanoparticles is that any given ions can be modified and transformed into neutral atoms, and these atoms merge into a nanoparticle. The main participants in this process are the reagents, that is the molecules with the ability of electron transfer. In addition, the majority of the stabilization molecules acting as stabilisers in this process are very important. The stabilizing molecules do not allow the neutral atoms to combine to form a multiatomic system. The sizes of the nanoparticles are determined by the stabilizers. From a future perspective, the phytochemical composition and pharmacological effects attributed to medicinal plants represent an opportu- nity to create new controlled release systems with the potential for targeted delivery. The potential of AgNPs for their use as drug carriers in cancer therapy, as biosensors for metabolites and pollutants, as catalysts etc. is quite high and requires intensive and integrated research activity for harnessing it.

References

[1] Afat Mammadova, Nariman Ismayilov, Roza Mammadova. The role of systemic bio-diagnostics in stabilizing and improving the ecological state in azerbaijan within the framework of sustainable development. Baku State University Journal of Life Scince & Biology, 2024,v1,(3),p.1-6 **https://doi.org/10.30546/300045.2024.1.3.6**

[2] Anderson C.W.N., Brooks R.R., Stewart R.B., Simcock R. Gold Bull. 1999; 32:48, 382, 347–352.

[3] Farzaliyeva NM, Hasanova LS, Mammadova AO, Muradov PZ. Characteristics of some plants growing on the motorway areas by ecolo-trof relations and prevalence random of mycobyota.//SYLWAN, 2018, No 9,v.162,p.70-78

[4] Begum N.A., Mondal S., Basu S., Laskar R.A., Mandal D. Biogenic synthesis of Au and Ag nanoparticles using aqueous solutions of black tea leaf extracts. Colloids Surf B Biointerfaces. 2009; 71:113–118.

[5] Bochořáková H., Paulová H., Slanina J., Musil P., Táborská E. Main flavonoids in the root of Scutellaria baicalensis cultivated in Europe and their comparative antiradical properties. Phytother Res. 2003; 17(6):640–644.

[6] Kesharwani J., Yoon K.Y., Hwang J., Rai M. Phytofabrication of silver nanoparticles by leaf extract of Datura metel: hypothetical mechanism involved in synthesis. J Bionanosci. 2009; 3:1–6.

[7] Ismat S. Ahmadova , Goncha M. Eyvazovaa , Taras S. Kavetskyy. Effect of metal-based nanoparticles on chlorophyll degradation in maize seedling leaves.Baku State University Journal of Life Scince & Biology, 2024,v1,(1),p.77-87

[8] Mohammad H, Malakouti Mohammad J, Dadpour Mohammad R, Stroeve Pieter, Mahmoudi Morteza Effects of Magnetite Nanoparticles on Soybean Chlorophyll. Environmental Science & Technology. 2013, 130906140819003. doi:10.1021/es402249b

[9] Ismailov NM, Mammadova AO. Assimilation potential of the territory of the Absheron industrial region in relation to technogenic atmospheric pollutants // Man and the Biosphere. (MaB, UNESCO). *Proceedings of the National Committee*.-2018, No. 13..-P.223-224. National Action Plan for Environmental Protection. -1998. -Baku.-67 p

[10] Tanaka A, Tsuji H. Effects of calcium on chlorophyll synthesis and stability plant extracts. Photochem Photobiol 4:193-200 in the early phase of greening in cucumber cotyledons. Plant Physiol. 1980, 65, p.121

[11] Zarei A., Ashtiyani S.C., Taheri S., Rasekh F. Comparison between effects of different doses of

Melissa officinalis and atorvastatin on the activity of liver enzymes in hypercholesterolemia rats. Avicenna J Phytomed. 2014; 4:15–23.

[12] Shakeri A., Sahebkar A., Javadi B. *Melissa officinalis* L.—A review of its traditional uses, phytochemistry, and pharmacology. J Ethnopharmacol. 2016; 188:204–228.

[13] Sharifi-Rad J., Ezzat S.M., El Bishbishy M.H.., Mnayer D., Sharopov F., Kılıç C.S., Neagu M., Constantin C., Sharifi-Rad M., Atanassova M., Nicola S.., Pignata G, Salehi B., Fokou P.V.T., Martins N. Rosmarinus plants: Key farm concepts towards food applications. Phytother Res. 2020; 34(7):1474–1518.

[14] Dias M.I., Barros L., Dueñas M., Pereira E., Carvalho A.M., Alves R.C., Oliveira M.B., Santos-Buelga C., Ferreira I.C. Chemical composition of wild and commercial Achillea millefolium L. and bioactivity of the methanolic extract, infusion, and decoction. Food Chem. 2013; 141(4):4152–4160.

[15] Mammadova AO.Environmental Challaenges and the fundamental importance of biomonitoring and bioindication as factors for optimizing biosocial ecosystems in the territory of Azerbaijan.// Acta Botanica Caucasica, 2022, №1. V 1,

[16] Samedov PA. et al. Biological indicators and their importance in diagnostics of saline soils of arid biocenoses of Azerbaijan. // Bulletin of the Ryazan State Agrotechnological University named after P.A. Kostychev. 2013. No. 4 (20). - P. 52-56.

[17] Dai YL., Li Y., Wang Q., Niu FJ., Li KW., Wang YY., Wang J., Zhou CZ., Gao LN. Chamomile: A review of its traditional uses, chemical constituents, pharmacological activities, and quality control studies. Molecules. 2022; 28(1):133.