Vol.64: e21210069, 2021
https://doi.org/10.1590/1678-4324-2021210069
ISSN 1678-4324 Online Edition

Article - Biological and Applied Sciences

Green Synthesized Silver Nanostructure Using *Rhus coriaria* Fruit Extract Inhibits the Growth of Malignant MCF-7 Cell Line

Mahta Charghadchi[1]
https://orcid.org/0000-0002-5002-1489

Zahra Gharari[2]
https://orcid.org/0000-0002-8404-3555

Somayeh Sadighian[1,3]
https://orcid.org/0000-0002-0706-8513

Alireza Yazdinezhad[1*]
https://orcid.org/0000-0002-6776-1395

Ali Sharafi[4,5*]
https://orcid.org/0000-0002-6012-1424

[1]Zanjan University of Medical Sciences, School of Pharmacy, Zanjan, Iran; [2]Alzahra University, Faculty of Biological Sciences, Department of Biotechnology, Tehran, Iran; [3]Zanjan University of Medical Sciences, School of Pharmacy, Department of Pharmaceutical Biomaterials, Zanjan, Iran; [4]Zanjan University of Medical Sciences, Zanjan Pharmaceutical Biotechnology Research Center, Zanjan, Iran; [5]Zanjan University of Medical Sciences, School of Pharmacy, Department of Pharmaceutical Biotechnology, Zanjan, Iran.

Editor-in-Chief: Alexandre Rasi Aoki
Associate Editor: Daniel Fernandes

Received: 2021.02.27; Accepted: 2021.06.27.

*Correspondence: yazdinezhad@zums.ac.ir (A.Y.); alisharafi@zums.ac.ir; Tel.: +98-24-33473635 (A.S.).

HIGHLIGHTS

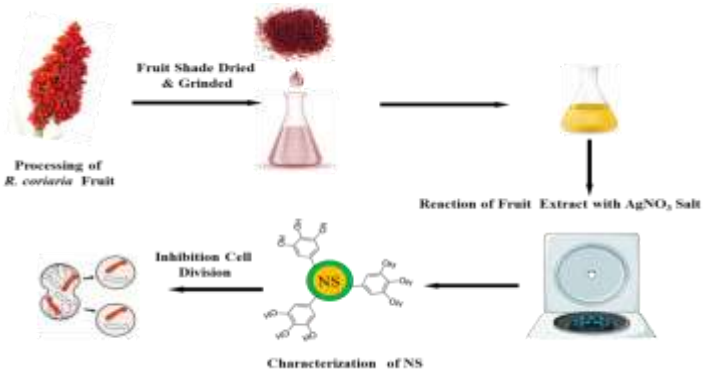
- Green synthesis of silver nanostructures (Ag-NSs) using *Rhus coriaria* fruit extract.
- Characterization of green synthesized Ag-NSs using UV-Vis, TEM, XRD and Zeta potential methods.
- Significant anti-proliferative activity of Ag-NSs against MCF-7 breast cancer cells.

Abstract: *Rhus coriaria*, popularly known as sumac, has been used as a spice powder in the Middle East for centuries. It contains a broad range of naturally occurring compounds such as flavonoids, proteins, anthocyanins and volatile oils. It showed a putative importance in treatment of different disorders including cancers. In the current study, *R. coriaria* fruit extract was used for green synthesis of silver nanostructures (Ag-NSs) and their anticancer activity was tested against human breast cancer cells (MCF-7). The aqueous fruit extract was prepared. The synthesis of Ag-NSs under different conditions was optimized. The optimal reaction medium comprised 1:2 concentration of fruit extract and 3 mM concentration of silver nitrate solution. The green-synthesized Ag-NSs were confirmed by using UV-Visible spectroscopy at a range 300-700 nm, transmission electron microscopy (TEM), X-ray diffraction (XRD) and zeta potential measurements. The anti-

proliferative activity of Ag-NSs was confirmed with inhibitory activity on MCF-7 cell line growth. The results showed that the IC_{50} values at 24 and 48h were 14.27 and 13.4 µg/ml, respectively. In conclusion the results of this study provide a simple, rapid, non-toxic and eco-friendly protocol for green-synthesis of Ag-NSs, which could be used as an alternative and interesting approach for safe and simple synthesis of Ag nanoparticles for biomedical uses.

Keywords: Cytotoxicity; Green synthesis; Nanostructures; *Rhus coriaria*; Silver.

GRAPHICAL ABSTRACT



INTRODUCTION

Despite many advances in disease control and treatment, cancer, still remains one of the global human health challenges. The most common treatment for cancer is chemotherapy. An important point in the treatment of cancer with chemotherapy is the acquired resistance of the tumor to chemical drugs. Due to the high rate of mutation and genetic instability of cancerous cells and also the rapid changes in their genetics, these cells become resistant to drugs. In order to overcome the drug resistance of cancers cells, more research on the discovery of new treatment strategies is required [1]. Meanwhile, nanotechnology has created a promising context in the field of cancer treatment [2]. In recent years, the anti-cancer and anti-angiogenic effects of silver nanoparticles have been reported. It revealed that silver nanoparticles can be considered as a potential anti-cancer agent [3]. On the other hand, the organic solvents required for synthesis of nanoparticles are toxic and they have devastating environmental effects. Hence there is a great trend to use eco-friendly, nontoxic, and safe methods for the synthesis of silver nanoparticles [4].

The biological approach, called green-synthesis or phyto-synthesis of nano-particles, has played a significant role in pharmaceutical, medical and textile industries. Green synthesis of metal or metal oxide nanoparticles utilizes bacteria [5], algae, fungi [6-8], yeast and plant extracts as both reducing and natural capping agent for the production of nanoparticles [9]. Plant secondary metabolites such as terpenoids, polyphenols, phenolic acids and flavonoids are responsible to react with nanoparticles to produce their reduced and stabilized forms [10]. Recently, several studies were carried out for green synthesis of silver-based nanoparticles from various plants parts like bark extract of *Cinnamon zeylanicum* [11], fruit of *Piper longum* [12], root extract of *Scutellaria baicalensis* [13], seeds and leave extract of *Citrullus colocynthis* [14], leave extract of *Pongamia pinnata* [15], petal extract of *Rosa indica* [16], etc. for the antioxidant, antibacterial, anti-inflammatory and cytotoxic effects.

Green synthesis of metallic nanoparticles (NPs) from plants and other biological sources showed the considerable environmental and economic superiorities over current physical and chemical methods [17]. Increased risk of carcinogenesis following exposure to nano-materials containing hazardous chemical agents raises some concerns about their environmental toxicity and safety issues. The increased levels of free radicals, the mitochondrial malfunction, the overexpression of inflammatory factors, such as NF-kB and STATs, and the increased levels of intracellular calcium which occurs due to exposure to nanoparticles (NPs) are primarily responsible for the genotoxicity of metal NPs [18].

Elm-Leaved Sumac (*Rhus coriaria* L.), belongs to the *Anacardiaceae* family, widely distributed from the Canary Islands to the Mediterranean coast, North Africa, Iran and Afghanistan. It has been used for treatment of various diseases including anorexia, hemorrhage, diarrhea and hyperglycemia in traditional medicine [19]. From all parts of this plant especially its fruits, many biological active compounds have been isolated such as hydrolysable tannins, phenolic acids, flavonoids, anthocyanins and organic acids [20]. Methanolic extracts of Sumac has antifungal, antibacterial activities [21], hypoglycemic and antioxidant properties [22] and many

others activities. Also, *R. coriaria* fruit has anticancer activity against human uterus cervix cancer [23], colon cancer [24] and breast cancer cells *in vitro* [25]. According to GLOBOCAN 2018 data, breast cancer led to more than 2 million new cases and nearly 627,000 deaths in 2018 worldwide [26]. The disease occurs as a result of damage to a cell's DNA and mutations in the genes responsible for regulating the growth of cells [27]. Basing on the above mentioned data and also the several toxic side effects of drugs used in chemotherapy on non-tumor tissues [28], the aim of the current study was to use the safe green synthesize method through the production of Ag nanostructures from *R. coriaria* fruit extract to determine its anticancer potency against growth of malignant MCF-7 cell line. To our knowledge this is the first report for anticancer activity of the green synthesized silver nanostructures using *R. coriaria* fruit extract.

MATERIAL AND METHODS

Collection and Identification of Plant Material

The whole plant of *R. coriaria* was collected from Tarom County, Zanjan Province, Iran at the end of month September 2019 during the fruiting season. After taxonomic identification of the plant by Dr. Alireza Yazdinezhad (Department of Pharmacognosy, School of Pharmacy, Zanjan), it was air dried under shade at room temperature. The air dried leaves sample was powdered and kept in the refrigerator at 4°C until extraction.

Preparation of Plant Extract Using Maceration Method

Powdered plant material (10 g) was taken in an Erlenmeyer flask and extracted with ddH_2O (125 ml) in a mechanical shaker at room temperature (25 °C) and constant stirring rate at 200 rpm for 30 minutes. The obtained plant extract was centrifuged at 6000 rpm for 10 minute and then the solid residues were filtered using Whatman No. 1 filter. The extract was maintained at -20 °C until further studies.

Green Synthesis and characterization of $AgNO_3$ Using *R. coriaria* Fruit Extract

In order to find the optimum conditions for green synthesis Ag-NS using *R. coriaria* fruit extract, the concentration ratio of fruit extract and $AgNO_3$ was optimized with the increase in concentration of fruit extract (1.6, 2.6 and 4 mL) in 8 mL of 3 mM $AgNO_3$ solution (ratio- 1: 5, 1: 3 and 1: 2). In addition, the effect of different incubation times (0, 2 and 24 h) were evaluated. The reaction mixtures were stirred at 150 rpm for 30 min and then were incubated under dark condition for 0, 2h and 24 h, respectively to minimize photo-activation of $AgNO_3$. After 24 h incubation dark-brown color $AgNO_3$-NS pellets were obtained which indicates the formation of AgNSs. In the next step, the reaction mixtures were centrifuged at 6000 rpm for 15 min to pellet the synthesized $AgNO_3$-NS. The pellets were washed three times with ddH_2O and then the equal volumes of the suspensions (1mL) were taken and transferred inside the tubes. The absorbance of the resulting solutions was measured with a spectrophotometer (Shimadzu UV-VIS 2550, Japan) at a range 300–700 nm at a resolution of 1 nm. Control was maintained by using ddH_2O. Presence of a peak in the range of 450–600 nm indicated synthesis of $AgNO_3$-NS. The obtained $AgNO_3$-NS pellet by *R. coriaria* fruit extract with dark-brown color (AgNSs) was dried overnight in an oven setup to 60 °C. AgNSs synthesized with the use of *R. coriaria* fruit extract was also characterized by using transmission electron microscopy (TEM), X-ray diffraction (XRD) and zeta potential measurement techniques. The TEM technique was carried out to recognize the morphology, shape and the size of nanoparticles. The very small amount of silver nanoparticles was placed on a Formvar coated grid (Sigma-Aldrich), and then the extra solution was removed by using a blotting paper. After drying, samples were analyzed using Zeiss EM 900 TEM at an operating voltage of 80 kV. The XRD patterns of the samples were determined using the X-ray diffractometer (XRD Philips PW1730) under constant conditions of 40 kV voltage, in 2θ angels ranging of 10–80. In order to measure the particle electrostatic charge, zeta potential measurements carried out using Zeta sizer-nano instrument (Malvern Instruments Ltd., UK). For this aim, 100 µL of the AgNSs solution was diluted with 1.5 mL of water and analyzed at a wavelength of 633 nm and a detection angle of 90◦ at 25◦C.

Anti-cancer Activity

The cytotoxicity assay of the Ag-NS was determined using the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay against human mammary cancer cells (MCF-7 cell line) and human foreskin fibroblast cells (HFF-2 cell line) - as a normal cell line. MCF-7 and HFF-2 were obtained from Pasteur Institute (Tehran, Iran). The cells were maintained at 37 °C in a humidified atmosphere containing 50 µg mL^{-1}

CO_2. The aqueous extract of plant and Ag-NS solution were diluted to obtain concentration range of 1.25–160 µg mL^{-1}. MCF-7 and HFF-2 cell lines were cultured in DMEM and RPMI-1640 with 10% (v/v) FBS and 100Uml^{-1} penicillin/streptomycin, respectively. For MTT assay, cells (1×10^5 cells/ well) were plated overnight onto flat-bottomed 96-well culture plates, then, cell lines were treated with plant extract and silver nanostructure solutions. Then, the wells were incubated in the presence samples for 24 and 48 h at 37°C [29]. After removing the supernatant, the cells were incubated with 20 µL MTT solution (5 mg mL^{-1}) for 4 h; afterward, the MTT solution was replaced by 100 µL DMSO to solubilize the resulting formazan precipitate. After 15 min shaking at room temperature, the absorbance at 570 nm using multi scan plate reader was used to measure the cells viability. The wells without tested compounds were determined as blanks. The cytotoxicity activity of aqueous plant extract (50 and 100 µg mL^{-1}) was used as positive control. The concentration required for a 50% inhibition of cellular growth of MCF-7 and HFF-2 cells by the tested samples was determined as the IC_{50} value and calculated using the following formula:

$$\text{Viability (\%)} = (\text{A sample})/ (\text{A control})*100 \quad (1)$$

RESULTS AND DISCUSSION

Visual observation and UV-Vis spectroscopy

Different parameters including concentration of *R. coriaria* fruit extract and incubation time were optimized, which are important factors affecting the yields of silver nanoparticles. Silver nanoparticles were synthesized at different concentrations of fruit extract i.e., 1.6, 2.6 and 4 mL with constant concentration (8 ml) of 3 mM silver nitrate. On addition of different concentrations (1.6, 2.6 and 4 mL) of fruit extracts to aqueous silver nitrate solution keeping its concentration 3 mL (3 mM) constant, the color of the solution changed from colorless to yellowish brown and finally to colloidal brown indicating formation of silver nanoparticles (Figure 1) [30]. UV-Vis spectroscopy has been used to confirm the formation of silver nanoparticles. In the present study, UV spectra of Plasmon resonance band observed between 415-450 nm similar to those reported in literature [31]. By using UV-Visible spectrum the maximum absorbance peak for 1:5, 1:3 and 1:2 ratio of plant extract: Ag-NS was observed at 417, 417 and 420 nm, respectively (Figure 2). Similarly, Krithiga and coauthors reported that the maximum absorbance peak for *Clitoria ternatea* was detected at 420 nm [32].

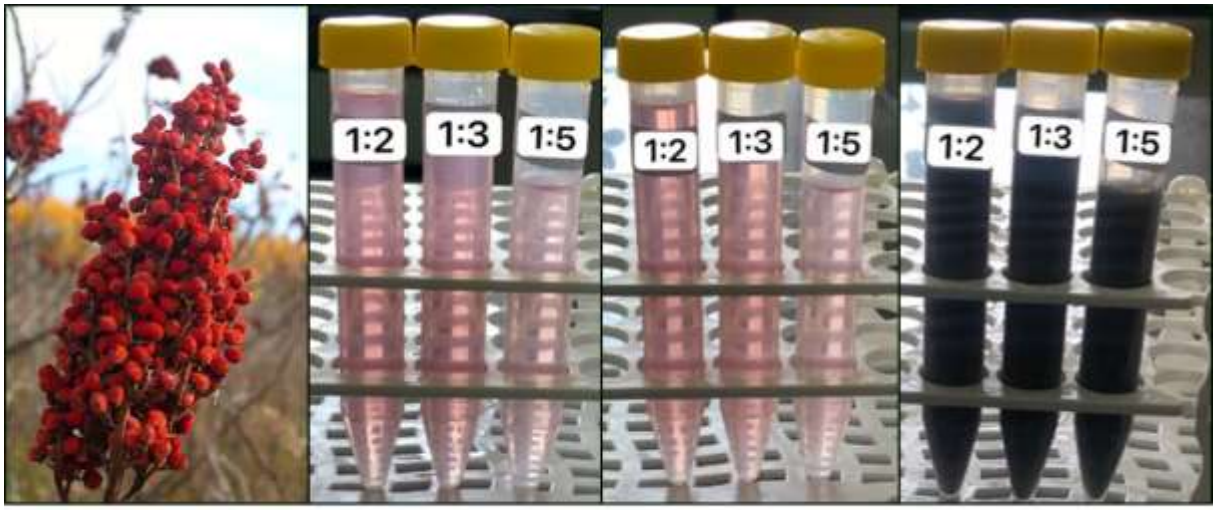


Figure 1. (a) *R. coriaria* fruit in nature; Digital optical images of green synthesized Ag-NS with different ratios of *R. coriaria* fruit extract: Ag solution (1:2, 1:3 and 1:5) at different incubation times (b) after 0 h; (c) after 2h; (d) after 24 h.

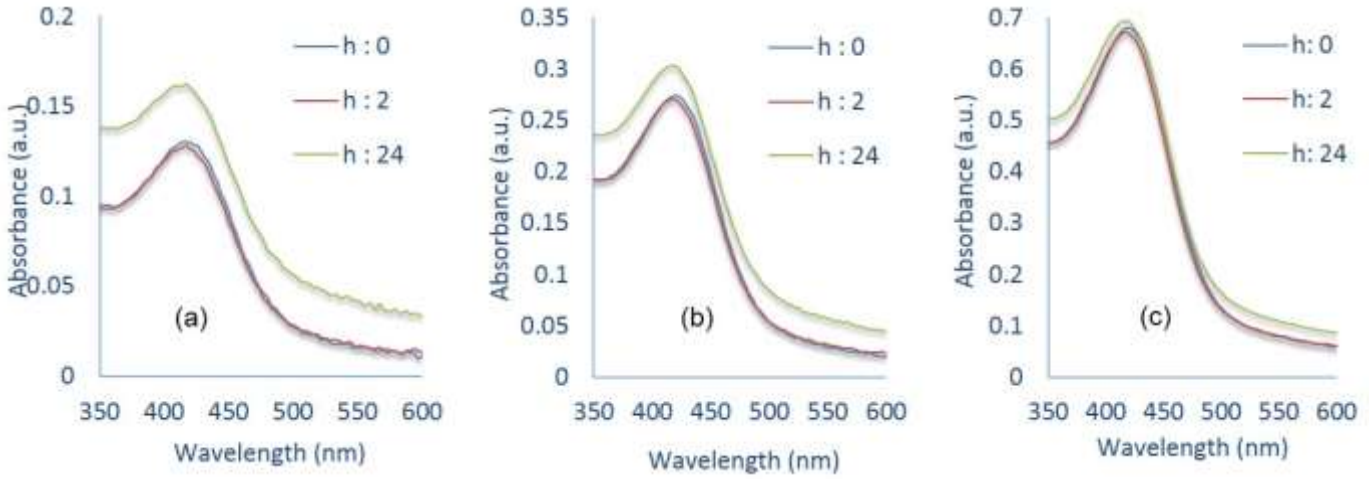


Figure 2. UV-Visible spectroscopy analysis of synthesized Ag-NSs. (a) 1: 5 ratio of plant extract: $AgNO_3$-NS; (b) 1: 3 ratio of plant extract: Ag-NS; (c) 1: 2 ratio of plant extract: Ag-NS.

TEM analysis

TEM was employed to identify the morphological and structural features of green synthesized silver nanoparticles. Figure 3 presents TEM image of the sample obtained in this study. It confirmed that silver nanoparticles are predominantly spherical in shape, well-dispersed and with a narrow particle size distribution. The particle size of obtained silver nanoparticles was between 10 to 25 nm (Figure 3). The observed result was in accordance with the results of Krithiga and coauthors, where the X-Ray Diffraction (XRD) studies reveal that the average size of silver nanoparticles synthesized by *Clitoria ternatea* is 20 nm [32].

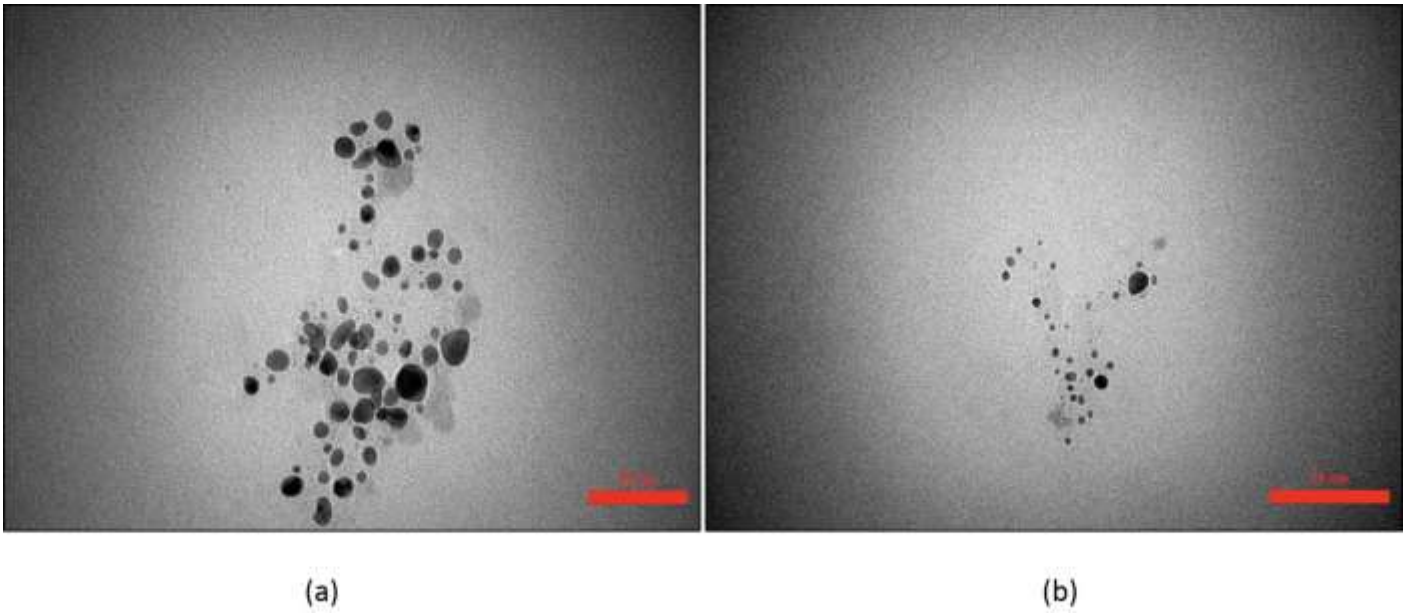


Figure 3. TEM micrograph of silver nanoparticles synthesized by using *R. coriaria* fruit extract. (a) 50 nm; (b) 75 nm.

Characterization of magnetic nanoparticles

XRD analysis: X-ray diffraction (XRD) is an effective method to study the entity of intercalation in composites. XRD patterns of silver nanoparticles (AgNPs) are shown in Figure 4. Diffraction peaks of silver nanoparticles at 2θ of 38.2º, 44.4º, 64.5º and 74º corresponded to (111), (200), (220) and (311) lattice planes of AgNPs which was consistent with the database of silver nanoparticles. In all curves, diffraction peaks can be indexed to face-centered cubic structure of nanoparticles. The average crystallite size was calculated using the Debye–Sherrer equation. The crystalline estimated size was about 11 nm [33].

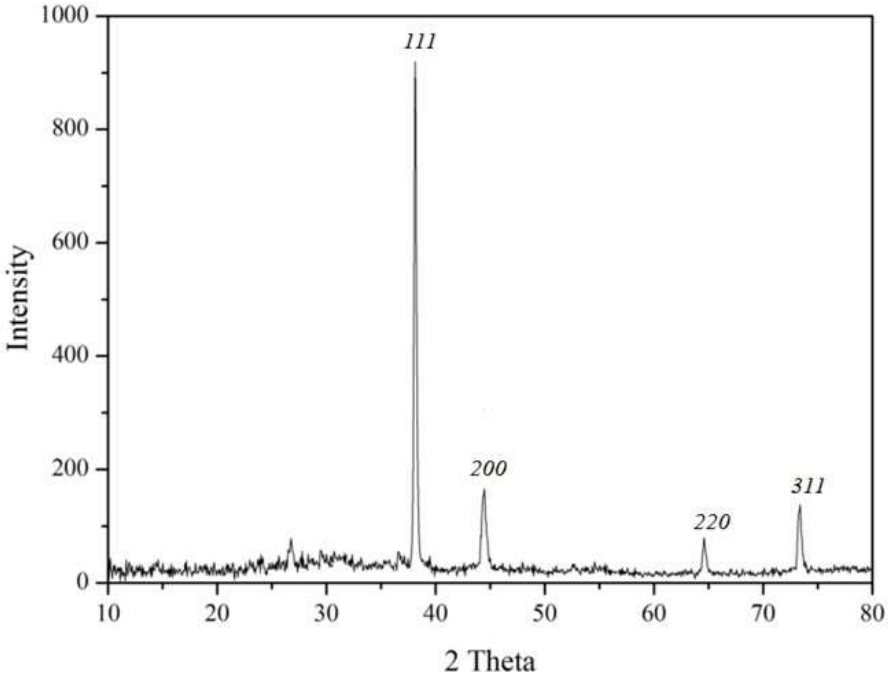


Figure 4. XRD pattern of silver nanoparticles.

Zeta potential measurement

Zeta potential values give information about the surface charges of AgNSs, which is characteristic of their colloidal stability. As shown in Figure 5, the *zeta* potential values of silver nanoparticles were −4.67 mV, indicating the stability of the green-synthesized silver particles which warped with anionic plant bio-molecules and resulted in an average particle size of approximately 10–25 nm. *Zeta* potential values was primarily by the acidity and size of AgNSs [34]. According to Dubey and coauthors, the lower *zeta* potential value indicates the acidic pH of solution [35].

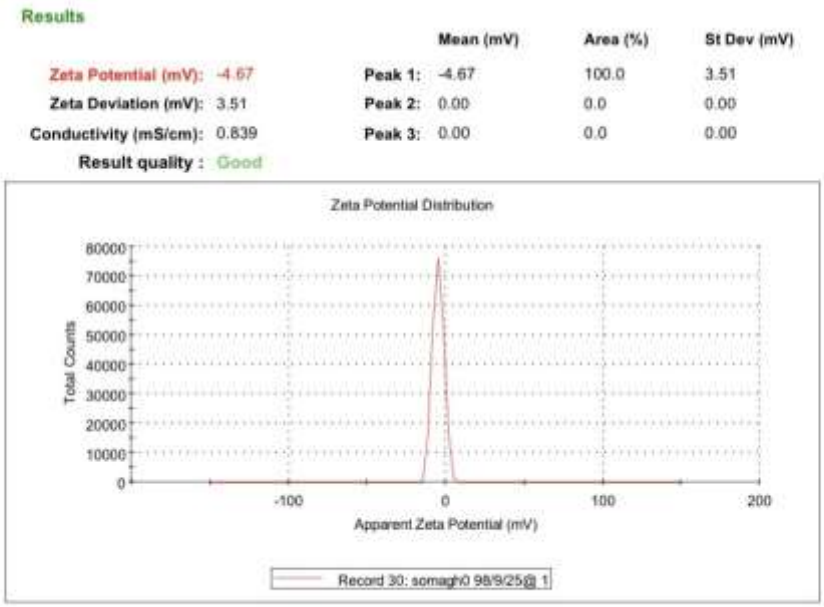


Figure 5. *Zeta* potential distribution of *R. coriaria* fruit extract-AgNPs shows negative results in mV.

Anti-proliferative assessment of Ag-NSs on MCF7 and HFF2 cells by MTT assay

In order to examine the growth-inhibitory activity of green synthesized AgNSs using *R. coriaria* fruit extract, malignant breast cancer cells (MCF-7 Cells) and HFF-2 normal cells were incubated with various concentrations of Ag-NSs (1.25-160 µg mL^{-1}) and plant extract (160 µg mL^{-1}) for 24 and 48 h and then MTT

assay was performed. MTT assay is a colorimetric *in vitro* method for assessing cellular metabolic activity, proliferation and cytotoxicity. In cell viability assays, MTT test generally is used to measure the cytotoxicity of plant extracts or other biologically active compounds against cancerous cell lines.

The results obtained by MTT test on MCF7 and HFF2 cells are summarized in Figures 6a and 6b. The MTT assay demonstrated that green synthesized AgNSs using *R. coriaria* fruit extract has an inhibitory effect on MCF-7 cell growth and decreases cell viability in a dose-dependent manner. The maximum decrease in cell viability of MCF7 and HFF2 cells was measured as 12.5% and 19.2 % each at 160 µg mL^{-1} AgNSs, respectively. As shown in Figure 6a, silver nanoparticles exhibited a marked inhibition of proliferation on MCF-7 cells with half maximal inhibitory concentration (IC_{50}) values of 14.27 and 13.4 µg mL^{-1} at 24 and 48 h, respectively and on HFF2 at 24 and 48 h with IC_{50} values of 62.7 and 81.73 µg mL^{-1} (Figure 6b). According to screening analyses silver nanoparticles had significantly effectiveness on inhibiting of biological/biochemical functions of malignant MCF-7 cell line than that of normal HFF2 cells.

There are many research projects showing the influence of silver nanoparticles features including size distribution, morphology, surface charge density, and surface chemistry, and also capping agents on various biological activities of mammalian and microbial cells such as cellular metabolism, proliferation, differentiation, reprogramming, gene transfer, and many other processes, which among the all these cases, the morphology of the nanomaterial plays a vital role [36,37].

Several studies have shown that green synthesized silver nanoparticles could inhibit tumor initiation and also tumor progression [38-41]. Jang and coauthors was reported that green synthesized silver nanoparticles from aqueous extract of *Lonicera hypoglauca* flower is a reducing and capping agents being significantly toxic to MCF-7 cells by the induction of apoptosis [38]. Khateef and coauthors demonstrated that green-synthesized silver nanoparticles using fresh *Buchanania axillaris* leaves' aqueous-*n*-butanolic extract, also has significant anti-cancer action on viability of the MCF-7 cancer cells and distinguishable alterations in their morphology as compared to the controls [39].

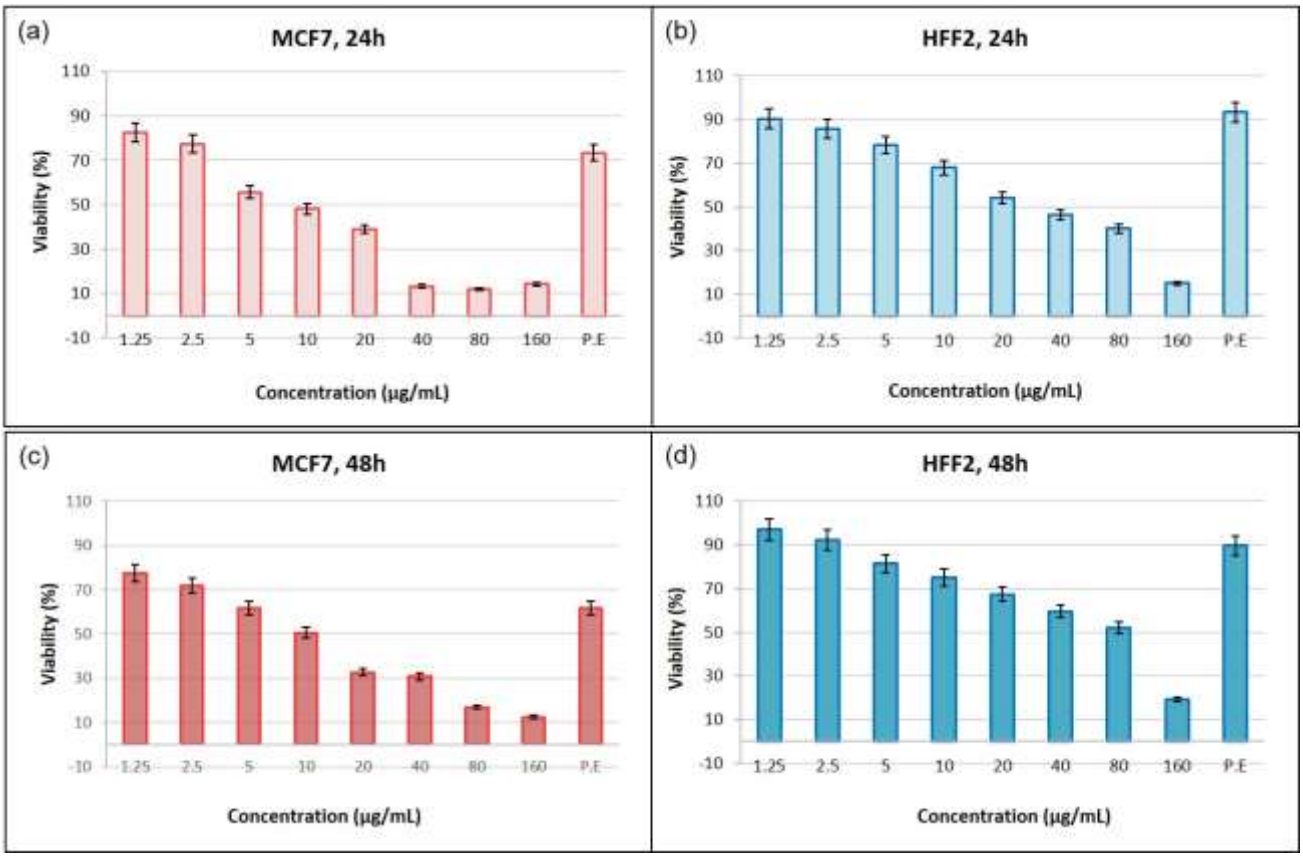


Figure 6. Anticancer activity of green synthesized AgNSs against (a) MCF7; (b) HFF2 cell lines.

It has been reported that silver nanoparticles derived from the cyanobacterium *Oscillatoria limnetica* could exhibit strong anti-proliferative activities against both human breast (MCF-7) and colon cancer (HCT-116) cell lines as well as antimicrobial activity against multidrug-resistant bacteria (*Escherichia coli* and

Bacillus cereus) [40]. Erdogan and coauthors conducted that synthesized silver nanoparticles from the leaf extracts of *Cynara scolymus*, showed a broad-spectrum of anti-cancer activity with PDT therapy by reduction in cell migration and expression of Bax, suppression of Bcl-2 and eventually promotion of ROS generation, which occurs by modulating mitochondrial apoptosis induction in MCF7 breast cancer cells [41].

CONCLUSION

To conclude, the current study established a facile eco-friendly protocol to synthesis AgNSs using *R. coriaria* fruit extract. UV-Visible, TEM and zeta potential measurements were confirmed the formation of green synthesized silver nanoparticles. The efficiency of biosynthesized AgNSs as anticancer treatment was approved by significant anti-cancer activity against malignant MCF-7 breast cancer cells, which indicate their potential as promising alternative for damaging cancerous cells. However, to improve the biological applications of biosynthesized AgNSs, more and a detailed study is necessary.

Funding: This research was funded by Zanjan University of Medical Sciences, grant number A-12-307-32.
Acknowledgments: This study has been supported financially by Zanjan University of Medical Sciences, Zanjan, Iran, under a Pharm. D. thesis proposal (No. A-12-307-32).
Conflicts of Interest: The authors declare no conflicts of interest.

REFERENCES

1. Baharara J, Hosseini N, Farzin TR. Extremely low frequency electromagnetic field sensitizes cisplatin-resistant human ovarian adenocarcinoma cells via P53 activation. Cytotechnology 2016;68:1403-13.
2. Castiglioni S, Caspani C, Cazzaniga A, Maier JA. Short-and long-term effects of silver nanoparticles on human microvascular endothelial cells. World J. Biol. Chem. 2014;5:457.
3. Satapathy SR, Mohapatra P, Preet R, Das D, Sarkar B, Choudhuri T, et al. Silver-based nanoparticles induce apoptosis in human colon cancer cells mediated through p53. Nanomedicine 2013;8:1307-22.
4. Jeyaraj M, Sathishkumar G, Sivanandhan G, MubarakAli D, Rajesh M, Arun R, et al. Biogenic silver nanoparticles for cancer treatment: an experimental report. Colloids and surfaces B: Biointerfaces 2013;106:86-92.
5. Hulkoti NI, Taranath T. Biosynthesis of nanoparticles using microbes—a review. Colloids and Surfaces B: Biointerfaces 2014;121:474-83.
6. Barabadi H, Honary S, Mohammadi MA, Ahmadpour E, Rahimi MT, Alizadeh A, et al. Green chemical synthesis of gold nanoparticles by using Penicillium aculeatum and their scolicidal activity against hydatid cyst protoscolices of Echinococcus granulosus. Environ. Sci. Pollut. Res. 2017;24:5800-10.
7. Ghomi ARG, Mohammadi-Khanaposhti M, Vahidi H, Kobarfard F, Reza MAS, Barabadi H. Fungus-mediated extracellular biosynthesis and characterization of zirconium nanoparticles using standard penicillium species and their preliminary bactericidal potential: a novel biological approach to nanoparticle synthesis. Iran J Pharm Res**:** IJPR 2019;18:2101.
8. Barabadi H, Tajani B, Moradi M, Kamali KD, Meena R, Honary S, et al. Penicillium family as emerging nanofactory for biosynthesis of green nanomaterials: a journey into the world of microorganisms. J. Clust. Sci. 2019;30:843-56.
9. Nasrollahzadeh M, Mahmoudi-Gom Yek S, Motahharifar N, Ghafori Gorab M. Recent developments in the plant-mediated green synthesis of Ag-based nanoparticles for environmental and catalytic applications. The Chemical Record 2019;19:2436-79.
10. Izadiyan Z, Shameli K, Miyake M, Hara H, Mohamad SEB, Kalantari K, et al. Cytotoxicity assay of plant-mediated synthesized iron oxide nanoparticles using Juglans regia green husk extract. Arab. J. Chem. 2020;13:2011-23.
11. Sathishkumar M, Sneha K, Won S, Cho C-W, Kim S, Yun Y-S. Cinnamon zeylanicum bark extract and powder mediated green synthesis of nano-crystalline silver particles and its bactericidal activity. Colloids and Surfaces B: Biointerfaces 2009;73:332-8.
12. Reddy NJ, Vali DN, Rani M, Rani SS. Evaluation of antioxidant, antibacterial and cytotoxic effects of green synthesized silver nanoparticles by Piper longum fruit. Mater. Sci. Eng. C 2014;34:115-22.
13. Chen L, Huo Y, Han YX, Li JF, Ali H, Batjikh I, et al. Biosynthesis of gold and silver nanoparticles from Scutellaria baicalensis roots and in vitro applications. Applied Physics A 2020;126:1-12.
14. Shawkey AM, Rabeh MA, Abdulall AK, Abdellatif AO. Green nanotechnology: anticancer activity of silver nanoparticles using Citrullus colocynthis aqueous extracts. Adv. Life Sci. Technol. 2013;13:60-70.
15. Khatua A, Priyadarshini E, Rajamani P, Patel A, Kumar J, Naik A, et al. Phytosynthesis, characterization and fungicidal potential of emerging gold nanoparticles using Pongamia pinnata leave extract: a novel approach in nanoparticle synthesis. J. Clust. Sci. 2020;31:125-31.
16. Manikandan R, Manikandan B, Raman T, Arunagirinathan K, Prabhu NM, Basu MJ, et al. Biosynthesis of silver nanoparticles using ethanolic petals extract of Rosa indica and characterization of its antibacterial, anticancer and anti-inflammatory activities. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2015;138:120-9.

17. Barabadi H, Najafi M, Samadian H, Azarnezhad A, Vahidi H, Mahjoub MA, et al. A systematic review of the genotoxicity and antigenotoxicity of biologically synthesized metallic nanomaterials: are green nanoparticles safe enough for clinical marketing? Medicina 2019;55:439.
18. Mortezaee K, Najafi M, Samadian H, Barabadi H, Azarnezhad A, Ahmadi A. Redox interactions and genotoxicity of metal-based nanoparticles: A comprehensive review. Chemico-biological interactions 2019;312:108814.
19. Shabbir A. Rhus coriaria linn, a plant of medicinal, nutritional and industrial importance: a review. J Anim Plant Sci 2012;22:505-12.
20. Jakobek L, Seruga M, Novak I, Medvidovic-Kosanovic M. Flavonols, phenolic acids and antioxidant activity of some red fruits. Deutsche Lebensmittel Rundschau 2007;103:369-77.
21. Saxena G, McCutcheon A, Farmer S, Towers G, Hancock R. Antimicrobial constituents of Rhus glabra. J. ethnopharmacol. 1994;42:95-9.
22. Nasar-Abbas S, Halkman AK. Antimicrobial effect of water extract of sumac (*Rhus coriaria* L.) on the growth of some food borne bacteria including pathogens. Int. J. Food Microbiol. 2004;97:63-9.
23. Abdallah S, Abu-Reidah I, Mousa A, Abdel-Latif T. *Rhus coriaria* (sumac) extract reduces migration capacity of uterus cervix cancer cells. Rev. Bras. Farmacogn. 2019;29:591-6.
24. Munusamy S, Eid AH. Aqueous extract of Rhus coriaria decreases proliferation and promotes apoptosis in human colon cancer cells in vitro. Wiley Online Library; 2013.
25. El Hasasna H, Saleh A, Al Samri H, Athamneh K, Attoub S, Arafat K, et al. Rhus coriaria suppresses angiogenesis, metastasis and tumor growth of breast cancer through inhibition of STAT3, NFκB and nitric oxide pathways. Scientific reports 2016;6:1-15.
26. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: Cancer J. Clin. 2018;68:394-424.
27. Davis JD, Lin S-Y. DNA damage and breast cancer. World J Clin. Oncol. 2011;2:329.
28. Li S, Yuan S, Zhao Q, Wang B, Wang X, Li K. Quercetin enhances chemotherapeutic effect of doxorubicin against human breast cancer cells while reducing toxic side effects of it. Biomed. Pharmacother. 2018;100:441-7.
29. Gharari Z, Aghajanzadeh M, Sharafi A. Scutellaria orientalis subsp. Bornmuelleri: phytochemical composition and biological activities. Natural product research 2021:1-6.
30. Ahmed S, Saifullah, Ahmad M, Swami BL, Ikram S. Green synthesis of silver nanoparticles using Azadirachta indica aqueous leaf extract. J. Radiat . Res. Appl. Sci. 2016;9:1-7.
31. Chahardooli M, Khodadadi E, Khodadadi E. Green synthesis of silver nanoparticles using oak leaf and fruit extracts (Quercus) and its antibacterial activity against plant pathogenic bacteria. Int J Biosci 2014;4:97-103.
32. Krithiga N, Rajalakshmi A, Jayachitra A. Green synthesis of silver nanoparticles using leaf extracts of Clitoria ternatea and Solanum nigrum and study of its antibacterial effect against common nosocomial pathogens. J. Nanosci. 2015;2015.
33. Yadav P, Manjunath H, Selvaraj R. Antibacterial and dye degradation potential of zero-valent silver nanoparticles synthesised using the leaf extract of Spondias dulcis. IET nanobiotechnology 2019;13:84-9.
34. Medina-Ramirez I, Bashir S, Luo Z, Liu JL. Green synthesis and characterization of polymer-stabilized silver nanoparticles. Colloids and Surfaces B: Biointerfaces 2009;73:185-91.
35. Dubey SP, Lahtinen M, Sillanpää M. Tansy fruit mediated greener synthesis of silver and gold nanoparticles. Process Biochemistry 2010;45:1065-71.
36. Barabadi H, Kamali KD, Shoushtari FJ, Tajani B, Mahjoub MA, Alizadeh A, et al. Emerging theranostic silver and gold nanomaterials to combat prostate cancer: a systematic review. J. Clust. Sci. 2019;30:1375-82.
37. Barabadi H, Vahidi H, Kamali KD, Hosseini O, Mahjoub MA, Rashedi M, et al. Emerging theranostic gold nanomaterials to combat lung cancer: a systematic review. J. Clust. Sci. 2020;31:323-30.
38. Jang SJ, Yang IJ, Tettey CO, Kim KM, Shin HM. In-vitro anticancer activity of green synthesized silver nanoparticles on MCF-7 human breast cancer cells. Mater. Sci. Eng.: C 2016;68:430-5.
39. Khateef R, Khadri H, Almatroudi A, Alsuhaibani SA, Mobeen SA, Khan RA. Potential in-vitro anti-breast cancer activity of green-synthesized silver nanoparticles preparation against human MCF-7 cell-lines. Advances in Natural Sciences: Nanoscience and Nanotechnology 2019;10:045012.
40. Hamouda RA, Hussein MH, Abo-Elmagd RA, Bawazir SS. Synthesis and biological characterization of silver nanoparticles derived from the cyanobacterium Oscillatoria limnetica. Scientific reports 2019;9:1-17.
41. Erdogan O, Abbak M, Demirbolat GM, Birtekocak F, Aksel M, Pasa S, et al. Green synthesis of silver nanoparticles via Cynara scolymus leaf extracts: The characterization, anticancer potential with photodynamic therapy in MCF7 cells. PLoS One 2019;14:e0216496.