

Chemical and Biological Approaches for the Synthesis of Iron Based Nanoparticles

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Abstract

Iron based nanoparticles are one of the most applicable and studied nanostructures in various sciences and technologies. These nanoparticles are also introduced to the pharmaceutical and biomedical sciences due to their unique physicochemical properties such as super paramagnetism, ease of synthesis, and biocompatibility. Several techniques are now developed and available for the preparation of iron based nanoparticles. Including chemical synthesis and biological synthesis which can be divided into microbial synthesis and plant mediated synthesis. Coprecipitation reaction is introduced as the main chemical method for the synthesis of magnetite nanoparticles as one of the most applied iron nanoparticle. The main approaches in biosynthesis of iron nanoparticles are also reviewed as microbial and plant mediated synthesis. In this mini review we are going to have an overview upon the main approaches for the synthesis of iron nanoparticles.

Keywords: Biological synthesis, Biosynthesis, Chemical synthesis, Iron nanoparticles, Iron nanostructures.

1. Introduction

Iron nanoparticles are one of the most applicable nanostructures in pharmaceutical sciences and biomedicine. These nanoparticles are unique due to their physicochemical properties, biocompatibility, easy of synthesis and functionalization (1-7). Iron nanoparticles can be used in tissue engineering, magnetic resonance imaging (MRI), DNA detection, DNA and cell separation, intracellular labeling, magnetic transfections, anti-proliferative hyperthermia therapy, and targeted drug delivery (8).

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Due to vast applications of iron nanoparticles in science and technology, various approaches have been developed for the synthesis of these nanoparticles. Chemical synthesis is one of the first approaches for the synthesis of iron nanoparticles. This production technique is the most defined and reproducible procedure with exact control over the synthesis process (9-12). But, this method employs harsh conditions such as protected atmosphere, high temperature and extreme pH (1, 2). Chemical synthesis protocols usually use organic solvents and toxic chemicals that may accumulate on the surface of the prepared nanoparticles and limit their medicinal and biomedical applications (1, 2).

In recent years, biological approaches have been introduced as a novel and environmental friendly technique to address chemical synthesis limitations (13-22). Biological compounds from living organisms are able to produce biocompatible nanoparticles in mild synthesis conditions without using toxic chemicals (22). Also, use of biological compounds reduces the synthesis costs and also is economic for scaling up. To dates, microorganisms and plants have been used for biosynthesis of nanoparticles (13, 21, 22). Main microorganisms are bacteria and fungi, which may be pathogenic to human (23-26). So, nowadays, algae have attracted significant interest to produce nanoparticles (13). Bioactive compounds from plants are also useful for the synthesis of iron based nanoparticles in a sustainable manner (22). This mini review is dealing with most common chemical and biological procedures for the production of iron nanoparticles.

2. Chemical synthesis

Magnetite (Fe_3O_4) nanoparticles are the most applicable iron nanoparticle in pharmaceutical sciences and biomedicine. These nanoparticles are used in drug delivery, magnetic resonance imaging (MRI), and hyperthermia therapy (27-37). Magnetite nanoparticles are commonly synthesised by coprecipitation reaction of ferric ions (usually from ferric chloride) and ferrous ions (usually from ferrous chloride or ferrous sulphate) as in Eq. (1). The synthesis reaction should be done in a protected atmosphere and in the absence of oxygen to protect prepared nanoparticles from oxidation (3, 4, 38, 39). Magnetite nanoparticles can be oxidised into more oxidation states of iron such as maghemite (Fe_2O_3), which is not more useful for mentioned applications. Iron nanoparticles are usually coated by using biocompatible coatings such as silica, amino silanes, amino acids, lipoamino acids, carbohydrates, and polyethylene glycol (3, 6, 7, 11, 20, 40, 41). Biocompatible coatings increase the biocompatibility of iron nanoparticles and also increase the chemical and colloidal stability of the nanoparticles (34, 39, 42-48). Coating of nanoparticles can be done in two main approaches, separate reactions and one-put reaction. In the separate reactions, naked nanoparticles are

synthesised and then are coated in a separate reaction. This approach is time and labour consuming including various steps of synthesis, separation and washing (4). But, in a one-put reaction both synthesis of nanoparticles and coating can be done in just one reaction. In this approach, coprecipitation of ferrous and ferric ions is done in the presence of coating materials (3, 4, 6, 7, 9-12, 38-41, 49-54). It has been shown that presence of a coating compound in the synthesis reaction has immense impacts on the physicochemical properties of prepared particles. The major impact is on the particles size and particle size distribution. Presence of a coating material in the synthesis reaction provides more uniform nanoparticles with narrower particle size distribution (3).



3. Biological synthesis

Iron nanoparticles can also be synthesised in biosynthesis reactions by using various living organisms such as plants, algae, and microbial cells such as bacteria, fungi, and microalgae (20-23). Microbial cells can produce intra or extra cellular iron nanoparticles. Magneto tactic bacteria are one the most studied iron nanoparticles producing bacteria. These bacteria are capable to produce magnetite nanoparticles in their cytoplasm. Magnetite nanoparticles which are produced by magneto tactic bacteria are surrounded by a phospholipid bilayer membrane and known as magnetosome. An array of magnetosomes is arranged in the cytoplasm of the magneto tactic bacteria and makes a biologic compass for the cell (55-57). Bacterial cells are also able to produce iron nanoparticles extracellularly. They can accumulate iron nanostructures in their exopolysaccharide and produce a metal shell around the cell (23-26). It has been shown that iron nanoparticles which are synthesised extracellularly are ferrihydrite (a hydrous ferric oxyhydroxide) (23-26). Macro and micro algae are also able to produce iron nanoparticles. It is interesting that all iron nanoparticles which are reported to be synthesised by using seaweeds are magnetite nanoparticles (58-61).

Cell culture problems such as culture equipment and costs are major problem with

application of microbial cell for biosynthesis purposes. Previous investigations have been shown that plants are full of bioactive compounds such as antioxidant, phenolic compounds, carbohydrates and proteins which are able to interact with metallic ions and convert them to nanoparticles (22). A diverse kind of iron nanoparticles such as iron complexes, iron oxides, iron oxide hydroxides, and zero valent iron nanoparticles have been reported to be produced by plant mediated synthesis (22). Since now, various parts of plants such as leaf extract, fruit extract, seed exudate, seed powder extract, peel extract, bran extract, bark extract and plant oil have been used for synthesis of nanoparticles (62-85). A divergent variety of iron salts such as $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, FeSO_4 , and $\text{Fe}(\text{NO}_3)_3$ can be used as iron precursor (21, 22, 75, 86).

4. Conclusion

Iron nanoparticles have retained most attention in various sciences and technologies due to their unique physicochemical and biological properties. Especially in pharmaceutical and biomedical sciences magnetite nanoparticles are one of the most studied and applied nanoparticles. These nanoparticles with special coatings are now commonly being synthesised by coprecipitation reaction. Also, these particles can be coated during synthesis reaction by one-put reaction techniques. Synthesis of nanoparticles is now developed toward green chemistry to reduce toxic wastes and non-sustainable protocols. Bioactive compound from biologic organisms such as bacteria, fungi, microalgae, algae, and plant are now being used instead of toxic chemicals to produce more safe and biocompatible nanoparticles.

Conflict of Interest

None declared.

5. References

- Ebrahimi N, Rasoul-Amini S, Ebrahimezhad A, Ghasemi Y, Gholami A, Seradj H. Comparative Study on Characteristics and Cytotoxicity of Bifunctional Magnetic-Silver Nanostructures: Synthesized Using Three Different Reducing Agents. *Acta Metall Sin Engl.* 2016;29:326-34.
- Ebrahimi N, Rasoul-Amini S, Niazi A, Erfani N, Moghadam A, Ebrahimezhad A, et al. Cytotoxic and Apoptotic Effects of Three Types of Silver-Iron Oxide Binary Hybrid Nanoparticles. *Curr Pharm Biotechnol.* 2016;17:1049-57.
- Ebrahimezhad A, Ghasemi Y, Rasoul-Amini S, Barar J, Davaran S. Impact of amino-acid coating on the synthesis and characteristics of iron-oxide nanoparticles (IONS). *Bull Korean Chem Soc.* 2012;33:3957-62.
- Ebrahimezhad A, Ghasemi Y, Rasoul-Amini S, Barar J, Davaran S. Preparation of novel magnetic fluorescent nanoparticles using amino acids. *Colloids Surf B.* 2013;102:534-9.
- Ebrahimezhad A, Rasoul-Amini S, Davaran S, Barar J, Ghasemi Y. Impacts of iron oxide nanoparticles on the invasion power of *Listeria monocytogenes*. *Curr Nanosci.* 2014;10:382-8.
- Gholami A, Rasoul-Amini S, Ebrahimezhad A, Abootalebi N, Niroumand U, Ebrahimi N, et al. Magnetic properties and antimicrobial effect of amino and lipoamino acid coated iron oxide nanoparticles. *Minerva Biotechnol.* 2016;28:177-86.
- Gholami A, Rasoul-amini S, Ebrahimezhad A, Seradj SH, Ghasemi Y. Lipoamino Acid Coated Superparamagnetic Iron Oxide Nanoparticles Concentration and Time Dependently Enhanced Growth of Human Hepatocarcinoma Cell Line (Hep-G2). *J Nanomater.* 2015;2015:1-9.
- Pankhurst QA, Connolly J, Jones S, Dobson J. Applications of magnetic nanoparticles in biomedicine. *J Phys D: Appl Phys.* 2003;36:R167.
- Ranmadugala D, Ebrahimezhad A, Manley-Harris M, Ghasemi Y, Berenjian A. Iron oxide nanoparticles in modern microbiology and biotechnology. *Crit Rev Microbiol.* 2017:1-15
- Ranmadugala D, Ebrahimezhad A, Manley-Harris M, Ghasemi Y, Berenjian A. The effect of iron oxide nanoparticles on *Bacillus subtilis* biofilm, growth and viability. *Process Biochem.* 2017;62:231-40.
- Ranmadugala D, Ebrahimezhad A, Manley-Harris M, Ghasemi Y, Berenjian A. Impact of 3-Aminopropyltriethoxysilane-Coated Iron Oxide Nanoparticles on Menaquinone-7 Production Us-

ing *B. subtilis*. *Nanomater*. 2017;7:350.

12. Ranmadugala D, Ebrahiminezhad A, Manley-Harris M, Ghasemi Y, Berenjian A. Magnetic immobilization of bacteria using iron oxide nanoparticles. *Biotechnol Lett*. 2017:1-12.

13. Ebrahiminezhad A, Bagheri M, Taghizadeh S, Berenjian A, Ghasemi Y. Biomimetic synthesis of silver nanoparticles using microalgal secretory carbohydrates as a novel anticancer and antimicrobial. *Adv Nat Sci*. 2016;7.

14. Ebrahiminezhad A, Barzegar Y, Ghasemi Y, Berenjian A. Green synthesis and characterization of silver nanoparticles using *Alcea rosea* flower extract as a new generation of antimicrobials. *Chem Ind Chem Eng Q*. 2016;2016:31-7.

15. Ebrahiminezhad A, Berenjian A, Ghasemi Y. Template free synthesis of natural carbohydrates functionalised fluorescent silver nanoclusters. *IET Nanobiotechnol*. 2016;2016:1-4.

16. Ebrahiminezhad A, Taghizadeh S, Berenjian A, Heidaryan Naeini F, Ghasemi Y. Green Synthesis of Silver Nanoparticles Capped with Natural Carbohydrates Using *Ephedra intermedia*. *Nanosci Nanotechnol Asia*. 2016;6:1-9.

17. Ebrahiminezhad A, Taghizadeh S, Berenjian A, Rahi A, Ghasemi Y. Synthesis and characterization of silver nanoparticles with natural carbohydrate capping using *Zataria multiflora*. *Adv Mater Lett*. 2016;7:122-7.

18. Ebrahiminezhad A, Taghizadeh S, Ghasemi Y. Green synthesis of silver nanoparticles using Mediterranean Cypress (*Cupressus sempervirens*) leaf extract. *Am J Biochem Biotechnol*. 2017;13:1-6.

19. Ebrahiminezhad A, Taghizadeh S, Ghasemi Y, Berenjian A. Green synthesized nanoclusters of ultra-small zero valent iron nanoparticles as a novel dye removing material. *Sci Total Environ*. 2017. pii: S0048-9697(17)32779-1.

20. Ebrahiminezhad A, Zare M, Kiyampour S, Berenjian A, Niknezhad SV, Ghasemi Y. Biosynthesis of xanthan gum coated iron nanoparticles by using *Xanthomonas campestris*. *IET Nanobiotechnol*. 2017.

21. Ebrahiminezhad A, Zare-Hoseinabadi A, Berenjian A, Ghasemi Y. Green synthesis and characterization of zero-valent iron nanoparticles using stinging nettle (*Urtica dioica*) leaf extract. *Green Processing and Synthesis*. 2017;6:469-75.

22. Ebrahiminezhad A, Zare-Hoseinabadi A,

Sarmah AK, Taghizadeh S, Ghasemi Y, Berenjian A. Plant-Mediated Synthesis and Applications of Iron Nanoparticles. *Mol Biotechnol*. 2017:1-15.

23. Kianpour S, Ebrahiminezhad A, Mohkam M, Tamaddon AM, Dehshahri A, Heidari R, et al. Physicochemical and biological characteristics of the nanostructured polysaccharide-iron hydrogel produced by microorganism *Klebsiella oxytoca*. *J Basic Microbiol*. 2016:132-40.

24. Baldi F, Marchetto D, Battistel D, Daniele S, Faleri C, De Castro C, et al. Iron-binding characterization and polysaccharide production by *Klebsiella oxytoca* strain isolated from mine acid drainage. *J Appl Microbiol*. 2009;107:1241-50.

25. Baldi F, Marchetto D, Paganelli S, Piccolo O. Bio-generated metal binding polysaccharides as catalysts for synthetic applications and organic pollutant transformations. *N Biotechnol*. 2011;29:74-8.

26. Baldi F, Minacci A, Pepi M, Scozzafava A. Gel sequestration of heavy metals by *Klebsiella oxytoca* isolated from iron mat. *FEMS Microbiol Ecol*. 2001;36:169-74.

27. Hergt R, Dutz S, Müller R, Zeisberger M. Magnetic particle hyperthermia: nanoparticle magnetism and materials development for cancer therapy. *J Phys: Condens Matter*. 2006;18:S2919.

28. Johannsen M, Gneveckow U, Eckelt L, Feussner A, Waldöfner N, Scholz R, et al. Clinical hyperthermia of prostate cancer using magnetic nanoparticles: presentation of a new interstitial technique. *Int J Hyperthermia*. 2005;21:637-47.

29. Kim M-H, Yamayoshi I, Mathew S, Lin H, Nayfach J, Simon SI. Magnetic nanoparticle targeted hyperthermia of cutaneous *Staphylococcus aureus* infection. *Ann Biomed Eng*. 2013;41:598-609.

30. Kobayashi T. Cancer hyperthermia using magnetic nanoparticles. *Biotechnol J*. 2011;6:1342-7.

31. Nguyen T-K, Duong HT, Selvanayagam R, Boyer C, Barraud N. Iron oxide nanoparticle-mediated hyperthermia stimulates dispersal in bacterial biofilms and enhances antibiotic efficacy. *Sci Rep*. 2015;5.

32. Rodrigues D, Bañobre-López M, Espiña B, Rivas J, Azeredo J. Effect of magnetic hyperthermia on the structure of biofilm and cellular viability of a food spoilage bacterium. *Biofouling*. 2013;29:1225-32.

33. Akbarzadeh A, Mikaeili H, Zarghami N, Mohammad R, Barkhordari A, Davaran S. Preparation and in vitro evaluation of doxorubicin-loaded Fe₃O₄ magnetic nanoparticles modified with biocompatible copolymers. *Int J Nanomedicine*. 2012;2012:511-26.
34. Saltan N, Kutlu HM, Hur D, Iscan A, Say R. Interaction of cancer cells with magnetic nanoparticles modified by methacrylamido-folic acid. *Int J Nanomedicine*. 2011;6:477-84.
35. F Hasany S, H Abdurahman N, R Sunarti A, Jose R. Magnetic Iron Oxide Nanoparticles: Chemical Synthesis and Applications Review. *Curr Nanosci*. 2013;9:561-75.
36. Islam S, Kusumoto Y, Abdulla-Al-Mamun M, Manaka H, Horie Y. Synthesis, Characterization and Application of Dumbbell-shaped Magnetic (Fe₃O₄ and-Fe₂O₃) Nanoparticles Against HeLa (Cancer) Cells. *Curr Nanosci*. 2012;8:811-8.
37. Chertok B, Moffat BA, David AE, Yu F, Bergemann C, Ross BD, et al. Iron oxide nanoparticles as a drug delivery vehicle for MRI monitored magnetic targeting of brain tumors. *Biomaterials*. 2008;29:487-96.
38. Ebrahiminezhad A, Davaran S, Rasoul-Amini S, Barar J, Moghadam M, Ghasemi Y. Synthesis, characterization and anti-Listeria monocytogenes effect of amino acid coated magnetite nanoparticles. *Curr Nanosci*. 2012;8:868-74.
39. Ebrahiminezhad A, Rasoul-Amini S, Kouhpayeh A, Davaran S, Barar J, Ghasemi Y. Impacts of amine functionalized iron oxide nanoparticles on HepG2 cell line. *Curr Nanosci*. 2015;11:113-9.
40. Ebrahiminezhad A, Varma V, Yang S, Berenjian A. Magnetic immobilization of *Bacillus subtilis* natto cells for menaquinone-7 fermentation. *Appl Microbiol Biotechnol*. 2016;100:173-80.
41. Ebrahiminezhad A, Varma V, Yang S, Ghasemi Y, Berenjian A. Synthesis and Application of Amine Functionalized Iron Oxide Nanoparticles on Menaquinone-7 Fermentation: A Step towards Process Intensification. *Nanomaterials*. 2015;6:1-9.
42. Davda J, Labhsetwar V. Characterization of nanoparticle uptake by endothelial cells. *Int J Pharm*. 2002;233(1-2):51-9.
43. Goya GF, Marcos-Campos I, Fernandez-Pacheco R, Saez B, Godino J, Asin L, et al. Dendritic cell uptake of iron-based magnetic nanoparticles. *Cell Biol Int*. 2008;32:1001-5.
44. Jing H, Wang J, Yang P, Ke X, Xia G, Chen B. Magnetic Fe₃O₄ nanoparticles and chemotherapy agents interact synergistically to induce apoptosis in lymphoma cells. *Int J Nanomedicine*. 2010;5:999.
45. Kim JS, Yoon TJ, Yu KN, Noh MS, Woo M, Kim BG, et al. Cellular uptake of magnetic nanoparticle is mediated through energydependent endocytosis in A549 cells. *J Vet Sci*. 2006;7:321-6.
46. Lai YR, Chiang PC, Blom JD, Li N, Shevlin K, Brayman TG, et al. Comparison of in vitro nanoparticles uptake in various cell lines and in vivo pulmonary cellular transport in intratracheally dosed rat model. *Nanoscale Res Lett*. 2008;3:321-9.
47. Patlolla A, Berry A, Land D, Tchounwou P. Determining cytotoxicity of nano iron oxide in HepG2 cell line using MTT assay. Sixth International Symposium on Recent Advances in Environmental Health Research; September 13-16; Marriott Hotel, Jackson, Mississippi. USA.2009. p. 53.
48. Thorek DLJ, Tsourkas A. Size, charge and concentration dependent uptake of iron oxide particles by non-phagocytic cells. *Biomaterials*. 2008;29:3583-90.
49. Durmus Z, Kavas H, Toprak MS, Baykal A, Altincekic TG, Aslan A, et al. l-lysine coated iron oxide nanoparticles: Synthesis, structural and conductivity characterization. *J Alloys Compd*. 2009;484:371-6.
50. Park JY, Choi ES, Baek MJ, Lee GH. Colloidal stability of amino acid coated magnetite nanoparticles in physiological fluid. *Mater Lett*. 2009;63:379-81.
51. Patel D, Chang Y, Lee GH. Amino acid functionalized magnetite nanoparticles in saline solution. *Curr Appl Phys*. 2009;9:S32-S4.
52. Theerdhala S, Bahadur D, Vitta S, Perkas N, Zhong Z, Gedanken A. Sonochemical stabilization of ultrafine colloidal biocompatible magnetite nanoparticles using amino acid, l-arginine, for possible bio applications. *Ultrason Sonochem*. 2010;17:730-7.
53. Viota JL, Arroyo FJ, Delgado AV, Horno J. Electrokinetic characterization of magnetite nanoparticles functionalized with amino acids. *J*

Colloid Interface Sci. 2010;344:144-9.

54. Wang Z, Zhu H, Wang X, Yang F, Yang X. One-pot green synthesis of biocompatible arginine-stabilized magnetic nanoparticles. *Nanotechnology.* 2009;20:465-606.

55. Lefevre CT, Bernadac A, Yu-Zhang K, Pradel N, Wu LF. Isolation and characterization of a magnetotactic bacterial culture from the Mediterranean Sea. *Environ Microbiol.* 2009;11:1646-57.

56. Li WB, Yu LJ, Zhou PP, Min Z. Isolation of magnetotactic bacterium WM-1 from freshwater sediment and phylogenetic characterization. *Arch Microbiol.* 2007;188:97-102.

57. Zhu KL, Pan HM, Li JH, Yu-Zhang K, Zhang SD, Zhang WY, et al. Isolation and characterization of a marine magnetotactic spirillum axenic culture QH-2 from an intertidal zone of the China Sea. *Res Microbiol.* 2010 May;161:276-83.

58. El-Kassas HY, Aly-Eldeen MA, Gharib SM. Green synthesis of iron oxide (Fe₃O₄) nanoparticles using two selected brown seaweeds: characterization and application for lead bioremediation. *Acta Oceanologica Sinica.* 2016;35:89-98.

59. Mahdavi M, Namvar F, Ahmad MB, Mohamad R. Green biosynthesis and characterization of magnetic iron oxide (Fe₃O₄) nanoparticles using seaweed (*Sargassum muticum*) aqueous extract. *Molecules.* 2013;18:5954-64.

60. Silva V, Andrade P, Silva M, Valladares LDLS, Aguiar JA. Synthesis and characterization of Fe₃O₄ nanoparticles coated with fucan polysaccharides. *J Magn Magn Mater.* 2013;343:138-43.

61. Yew YP, Shameli K, Miyake M, Kuwano N, Khairudin NBBA, Mohamad SEB, et al. Green synthesis of magnetite (Fe₃O₄) nanoparticles using seaweed (*Kappaphycus alvarezii*) extract. *Nanoscale Res Lett.* 2016;11:1-7.

62. Basavegowda N, Idhayadhulla A, Lee YR. Preparation of Au and Ag nanoparticles using *Artemisia annua* and their in vitro antibacterial and tyrosinase inhibitory activities. *Mater Sci Eng, C.* 2014;43:58-64.

63. Cruz D, Falé PL, Mourato A, Vaz PD, Luisa Serralheiro M, Lino ARL. Preparation and physicochemical characterization of Ag nanoparticles biosynthesized by *Lippia citriodora* (Lemon Verbena). *Colloids Surf B.* 2010;81:67-73.

64. Doughman SD, Krupanidhi S, Sanjeevi CB. Omega-3 fatty acids for nutrition and medi-

cine: considering microalgae oil as a vegetarian source of EPA and DHA. *Curr Diabetes Rev.* 2007;3:198-203.

65. Dubey SP, Lahtinen M, Särkkä H, Sillanpää M. Bioprospective of *Sorbus aucuparia* leaf extract in development of silver and gold nanocolloids. *Colloids Surf B.* 2010;80:26-33.

66. Dubey SP, Lahtinen M, Sillanpää M. Green synthesis and characterizations of silver and gold nanoparticles using leaf extract of *Rosa rugosa*. *Colloids Surf Physicochem Eng Aspects.* 2010;364:34-41.

67. Dubey SP, Lahtinen M, Sillanpää M. Tansy fruit mediated greener synthesis of silver and gold nanoparticles. *Process Biochem.* 2010;45:1065-71.

68. Ghaffari-Moghaddam M, Hadi-Dabanlou R. Plant mediated green synthesis and antibacterial activity of silver nanoparticles using *Crataegus douglasii* fruit extract. *J Ind Eng Chem.* 2014;20:739-44.

69. Goodarzi V, Zamani H, Bajuli L, Moradshahi A. Evaluation of antioxidant potential and reduction capacity of some plant extracts in silver nanoparticle synthesis. *Molecular Biology Research Communications.* 2014;3:165-74.

70. He Y, Du Z, Lv H, Jia Q, Tang Z, Zheng X, et al. Green synthesis of silver nanoparticles by *Chrysanthemum morifolium* Ramat. extract and their application in clinical ultrasound gel. *Int J Nanomedicine.* 2013;8:1809-15.

71. Jean-Denis JB, Pezet R, Tabacchi R. Rapid analysis of stilbenes and derivatives from downy mildew-infected grapevine leaves by liquid chromatography-atmospheric pressure photoionisation mass spectrometry. *J Chromatogr.* 2006;1112:263-8.

72. Lukman AI, Gong B, Marjo CE, Roessner U, Harris AT. Facile synthesis, stabilization, and anti-bacterial performance of discrete Ag nanoparticles using *Medicago sativa* seed exudates. *J Colloid Interface Sci.* 2011;353:433-44.

73. Mo Y-y, Tang Y-k, Wang S-y, Ling J-m, Zhang H-b, Luo D-y. Green synthesis of silver nanoparticles using eucalyptus leaf extract. *Mater Lett.* 2015;144:165-7.

74. Nadagouda MN, Varma RS. Green synthesis of silver and palladium nanoparticles at room temperature using coffee and tea extract. *Green Chem.* 2008;10:859-62.

75. Njagi EC, Huang H, Stafford L, Genuino H, Galindo HM, Collins JB, et al. Biosynthesis of iron and silver nanoparticles at room temperature using aqueous sorghum bran extracts. *Langmuir*. 2010;27:264-71.
76. Okafor F, Janen A, Kukhtareva T, Edwards V, Curley M. Green Synthesis of Silver Nanoparticles, Their Characterization, Application and Antibacterial Activity. *Int J Env Res Public Health*. 2013;10:5221-38.
77. Rajasekharreddy P, Rani PU. Biofabrication of Ag nanoparticles using *Sterculia foetida* L. seed extract and their toxic potential against mosquito vectors and HeLa cancer cells. *Mater Sci Eng, C*. 2014;39:203-12.
78. Reddy NJ, Nagoor Vali D, 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.
79. 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 Surf B*. 2009;73:332-8.
80. Sathishkumar M, Sneha K, Yun Y-S. Immobilization of silver nanoparticles synthesized using Curcuma longa tuber powder and extract on cotton cloth for bactericidal activity. *Bioresour Technol*. 2010;101:7958-65.
81. Šileikaitė A, Prosyčėvas I, Puišo J, Juraitis A, Guobienė A. Analysis of silver nanoparticles produced by chemical reduction of silver salt solution. *Mater Sci-Medzg*. 2006;12:287-91.
82. Song JY, Jang H-K, Kim BS. Biological synthesis of gold nanoparticles using *Magnolia kobus* and *Diopyros kaki* leaf extracts. *Process Biochem*. 2009;44:1133-8.
83. Sun Q, Cai X, Li J, Zheng M, Chen Z, Yu C-P. Green synthesis of silver nanoparticles using tea leaf extract and evaluation of their stability and antibacterial activity. *Colloids Surf Physicochem Eng Aspects*. 2014;444:226-31.
84. Vivekanandhan S, Schreiber M, Mason C, Mohanty AK, Misra M. Maple leaf (*Acer* sp.) extract mediated green process for the functionalization of ZnO powders with silver nanoparticles. *Colloids Surf B*. 2014;113:169-75.
85. Yilmaz M, Turkdemir H, Kilic MA, Bayram E, Cicek A, Mete A, et al. Biosynthesis of silver nanoparticles using leaves of *Stevia rebaudiana*. *Mater Chem Phys*. 2011;130:1195-202.
86. Machado S, Pacheco J, Nouws H, Albergaria JT, Delerue-Matos C. Characterization of green zero-valent iron nanoparticles produced with tree leaf extracts. *Sci Total Environ*. 2015;533:76-81.

