International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 13, Issue 2, 2021

Review Article

OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES

NILESH PATIL[1*], RAJVEER BHASKAR, VISHAL VYAVHARE, RAHUL DHADGE, VAISHNAVI KHAIRE, YOGESH PATIL

Department of Quality Assurance at R. C. Patel Institute of Pharmaceutical Education and Research Shirpur (425405) Maharashtra India
*Email: pnilesh7275@gmail.com

Received: 05 Nov 2020, Revised and Accepted: 08 Jan 2021

ABSTRACT

In recent years, interest in the development of novel drug delivery systems using nanoparticles has gained more attention. The nanoparticles offer several advantages over other conventional drug delivery systems. Nanoparticles have gained importance in technological advancements due to their modifiable physical, chemical and biological properties with improved performance over their bulk foils. Nanoparticles can simply move in the body due to their small size and reach very complex organs through diverse routes. The high stability, controlled drug release makes nanoparticles the most suitable drug delivery system. Along with all these advantages, they offer variety in routes of administration. Both hydrophilic, as well as hydrophobic drugs, can be delivered in the form of nanoparticles. Nanoparticles have been used as a physical approach to modify and advance the pharmacokinetics and pharmacodynamics possessions of various types of drug molecules. Thesol-gel technique is a stress-free and very inexpensive process to formulate metal oxides and permits control over the doping process or adding of transition metals, as related to other research techniques. The study of different methods of synthesis of nanoparticles is essential to obtain desired nanoparticles with specific sizes and shapes. They are suitable candidates for various marketable and local applications, which include imaging, catalysis medical applications and environmental applications. This review mainly focuses on approaches used for the production of nanoparticles and different methods of synthesis of nanoparticles such as physical, chemical and biological method.

Keywords: Milling, Pulsed laser ablation, Co-precipitation, Sol-gel synthesis, Ion implantation

DOI: https://dx.doi.org/10.22159/ijcpr.2021v13i2.41556. Journal homepage: https://innovareacademics.in/journals/index.php/ijcpr

INTRODUCTION

A nanoparticle is usually defined as a particle of matter that is between 1 and 100 nm. Numerous terms have been used to define nanoparticulate drug delivery systems. In most cases, either polymer or lipid are used as carriers for the drug, and the delivery methods have particle dimension distribution from few nanometers to a few hundred nanometers. Novel and innovative polymers have been tried to advance nanoparticles for their claim as drug carriers [1].

Advantages of nanoparticles

Nanoparticles offer different advantages over other drug delivery systems that are listed in table 1[2, 3].

Table 1: Advantages of nanoparticles

Advantages of nanoparticles
▪ Enhancement of solubility and bioavailability
▪ Enhancement of pharmacological activity
▪ Sustained drug delivery
▪ Protection from degradation
▪ Enhancement of permeability
▪ Decreased side effects compared to conventional drug delivery
▪ Improved therapeutic effect

Factors affecting the synthesis of nanoparticles–

- Temperature
- Pressure
- Time
- Particle size and shape
- Cost of preparation
- Pore size [4, 5]

Synthesis approaches

A. Top-down approach

The top-down approach uses initial macroscopic structures. The methods begin with larger particles which are reduced to nanoparticles after a sequence of operations performed over them. Main shortcomings of these methods are that they involve large installations and hug capital is required for set up. The methods are quite expensive and not suitable for large-scale production. The method is suitable for laboratory experimentation. The approach is based upon the grinding of materials. These methods are not suitable for soft samples. A diagrammatic representation of this method is given in fig. 1[6, 7].

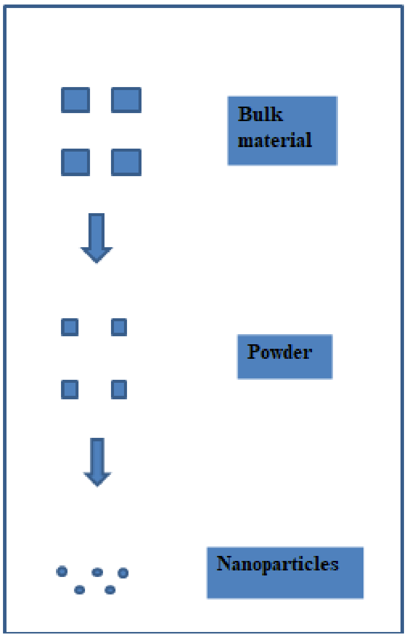

Fig. 1: Top-down approach

Methods in top-down approach:

1. Physical vapour deposition.

2. Chemical vapour deposition
3. Ion implantation
4. Electron beam lithography
5. X-ray lithography [8].

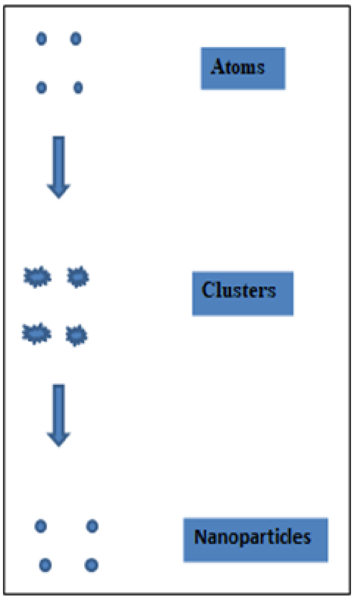

Fig. 2: Bottom-up approach

B. Bottom-up approach

Bottom-up approaches of production of nanomaterials comprise the miniaturization of materials constituents to the atomic level with the additional procedure leading to the development of nanostructures. Throughout the further progression, the physical forces working at nanoscale combined simple units into larger stable structures. The methodology is principally based on the principle of molecular recognition (self-assembly). Self-assembly means growing more and more things about one's kind from themselves. Many of these techniques are still under development or are just beginning to be used for the commercial production of nanoparticles. A diagrammatic representation of this approach is given in fig. 2 [9, 10].

Methods in a bottom-up approach:

1. Sol-gel synthesis
2. Colloidal precipitation
3. Hydrothermal synthesis
4. Organometallic chemical route
5. Electrodeposition [11].

Methods of synthesis of nanoparticles

There are three kinds of approaches for the production of nanoparticles. These methods are listed in table 2.

1. Physical Methods
2. Chemical Methods
3. Biological Methods

Table 2: Methods of synthesis of nanoparticles

Methods of synthesis		
A. Physical methods	**B. Chemical methods**	**C. Biological methods**
1. Mechanical Method	1. Sol-gel Method	1. Synthesis Using Microorganisms
2. Pulse Laser Ablation	2. Sonochemical Synthesis	2. Synthesis Using Plant Extracts
3. Pulsed Wire Discharge Method	3. Co-precipitation Method	3. Synthesis Using Algae
4. Chemical Vapor Deposition	4. Inert Gas Condensation Method	
5. Laser Pyrolysis	5. Hydrothermal Synthesis	
6. Ionized Cluster Beam Deposition		

Depending upon the need, the methods for synthesis of nanoparticles are selected. Every method has some advantages as well as disadvantages; the production method is selected based upon the availability of the facilities. Physical methods are suitable for small-scale production were as chemical methods are selected where the cost of production is a concern. Biological methods have different significance [12, 13].

Physical methods

Mechanical method

Ball milling

Ingenious approaches for the creation of nanoparticles. Forms of mills used are planetary, vibratory, rod, tumbler. The container contains hard balls made up of steel or carbide. Nanocrystalline Co, Cr, W, Ag-Fe, are synthesized using this method. The ratio of balls to materials is 2:1. The container is filled with inert gas or air and is rotated at high speed around the central axis. The materials are pressed between the walls of the container and balls. The speed and duration of milling play a significant role in synthesizing nanoparticles of optimum size [14, 15].

Melt mixing

Mixing molten streams of metals at high velocity with turbulence form nanoparticles. Nanoparticles get arrested in a glass. Glass–is an amorphous solid, deficient symmetric organization of atoms or molecules. Metals, when cooled at great cooling proportions, can form amorphous solids-metallic glasses. Ex: A melted stream of Cu-B and a heated stream of Ti forms nanoparticles of TiB_2 [16, 17].

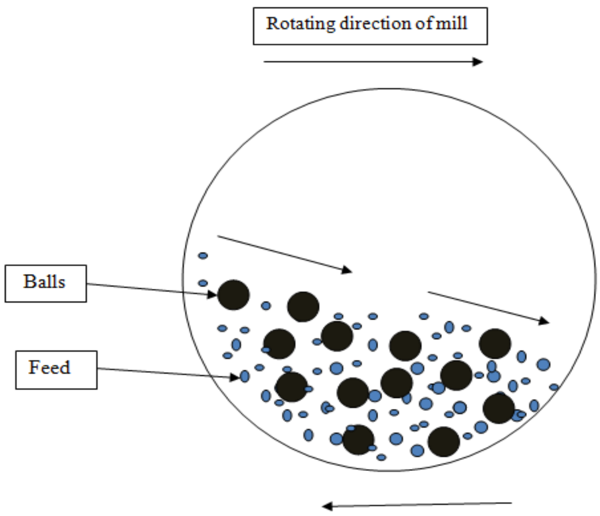

Fig. 3: Ball mill

Pulse laser ablation

The target sample is placed inside a vacuum chamber. The high-pulsed laser beam is focused on the sample and plasma is generated, which is formerly transformed into a colloidal solution of nanoparticles. The second-harmonic group type laser is frequently used to formulate nanoparticles. Elements affecting the final creation are the type of laser, some pulses, type of solvent, pulsing time [18-20].

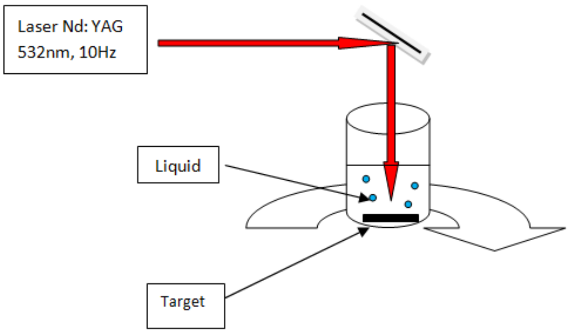

Fig. 4: Pulse laser ablation technique

Pulsed wire discharge method

The physical technique to prepare nanoparticles. Most widely used method for synthesis of metal nanoparticles. A metal wire is vaporized by a pulsated current to yield a vapour, which is then cool by ambient gas to procedure nanoparticles. This scheme has possibly a high fabricationspeed and high energy productivity. Ex. Nitride nanoparticles [21, 22].

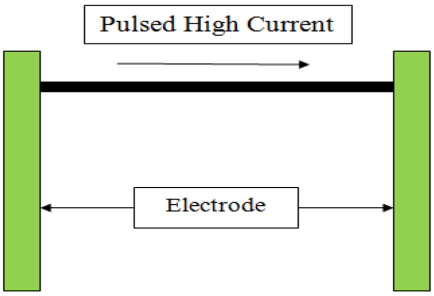

Fig. 5: Pulse wire discharge method

Chemical vapor deposition

A thin film of gaseous reactant is deposited on the substrate at around 300-1200 °C. A chemical reaction occurs between heated substrate and combining gas as an outcome thin film of product formed on the surface of the substrate. The applied pressure varies in the range of 100-10^5Pa. There are many variants of CVD like Metallo Organic CVD, Atomic Layer Epitaxy, Vapor Phase Epitaxy, Plasma Enhanced CVD. The advantages of this technique are stiff, uniform, robust and highly pure nanoparticles are manufactured. The by-products formed on the substrate have to be conveyed back to the gaseous phase eliminating them from the substrate. Cold wall and hot wall are two techniques by which substrates are heated. In the hot wall arrangement, the deposition can take place even on reactor walls. This is evaded in cold wall strategy. Gas pressure and the substrate temperature ultimately affects the growth rate and quality of film [23].

Laser pyrolysis

The process of synthesis of nanoparticles by using a laser is known as laser pyrolysis. An intense laser beam is focused to decompose the mixture of reactant gases in the existence of some inactive gas like helium or argon. The gas pressure shows a significant part in determining the particle sizes and their distribution [24].

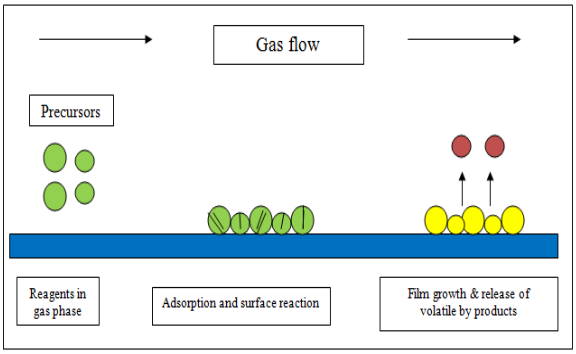

Fig. 6: Chemical vapour deposition

Ionised cluster beam deposition

The method was developed in 1985. The main aim of this method is to obtain high-quality single-crystalline thin films. The arrangement comprises a source of evaporation, a nozzle through which material can expand into the chamber, an electron beam to ionize the clusters, an arrangement to accelerate the clusters, and a substrate on which nanoparticle film can be deposited, all housed in a suitable vacuum chamber. After impact with an electron beam, collections get ionized. Due to applied hastening voltage, the clusters are focused near the substrate. It is likely to control the energy with which the clusters hit the substrate by monitoring the accelerating voltage. Steady clusters of certain materials would need significant energy to break their bonds and would rather favour remaining as small as clusters of particles. Hence the films of nanocrystalline material using an ionized cluster beam can be produced [25].

B. Chemical methods

Sol-gel method

It comprises the condensation, hydrolysis, and thermal decomposition of metal alkoxides or metal precursors in solution. A stable solution is formed, known as the sol. Upon hydrolysis or condensation, the gel is formed with increased viscosity. The particle size can be monitored by changing precursor concentration, temperature, and pH values. A mature step is mandatory to empower the development of solid mass it may take a few days in which the removal of the solvent, Ostwald ripening, and phase alteration could happen. The unstable reagents are detached to produce nanoparticles [26].

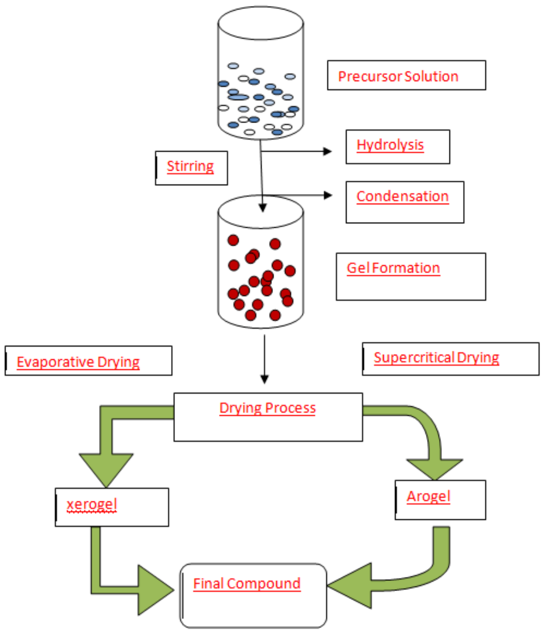

Fig. 7: Sol-gel method

Sonochemical synthesis

Pd-CuO nanohybrids have been effectively invented by the sonochemical fusion with copper salt in the existence of palladium and water. In the existence of palladium and water, switch metal salts could be altered into their oxides with the help of ultrasound energy. The palladium source is either pure metallic palladium Pd(0) or the palladium salts [27, 28].

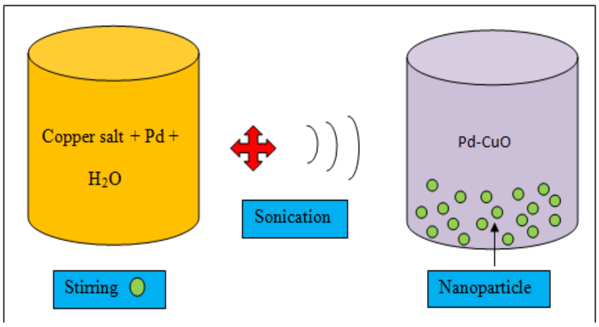

Fig. 8: Sonochemical synthesis

Co-precipitation method

It is a wet chemical process, also called a solvent displacement method. Polymer phase can be synthetic or natural; polymer solvents are ethanol, acetone, hexane, and nonsolvent polymer. Nanoparticles are produced by rapid diffusion of polymer-solvent into a nonsolvent polymer phase by mixing the polymer solution at last. Nanoparticles are produced by interfacial tension at two phases [29, 30].

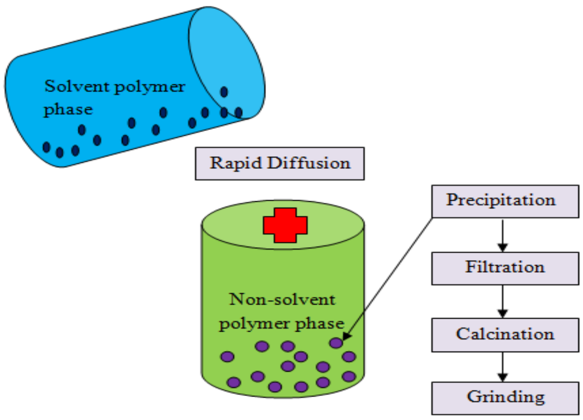

Fig. 9: Co-precipitation method

Inert gas condensation method

This process is broadly implemented for the creation of metal nanoparticles. The inactive gas compression technique, in which nanoparticles are produced via vanishing of metallic source in an inactive gas, had been widely used to yield fine nanoparticles. Metals are vaporized at a reasonable rate at an attainable temperature. Copper metal nanoparticles are synthesized by subjecting metal inside a chamber containing argon or helium or neon where the metal is vaporized. Once the atom is boil-off immediately loss its energy, by the cooling of the vaporized atom with inert gas. The gases cool by liquid nitrogen, to form nanoparticles in the series of 2-100 nm [31].

Hydrothermal synthesis

It is one of the most usually used methods for the preparation of nanoparticles. It is principally a chemical reaction-based approach. Hydrothermal synthesis involves a broad temperature range from room temperature to very high temperatures for the synthesis of nanoparticles. This method has a wide range of advantages over physical and biological methods. The nanomaterials generated through hydrothermal synthesis may be unstable at higher temperature ranges [32].

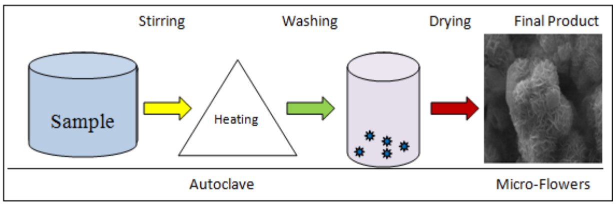

Fig. 10: Hydrothermal synthesis

C. Biological methods

Synthesis using microorganisms

In recent years synthesis of nanoparticles using microorganisms have gained more attention due to cost-effectiveness and eco-friendliness. There are two techniques by which nanoparticles can be synthesized from a microorganism, one is extracellular biosynthesis and another is intracellular biosynthesis. Certain microbes are capable of separating metal ions. *Pseudomonas stuzeri* Ag295 is frequently found in silver mines, accomplished by collecting silver inside or outside the cell walls. Different types of reductase enzymes exist in microorganisms thus can store and detoxify heavy metals. *Klebsiella pneumonia* can be used to produceCdS nanoparticles [33, 34].

Synthesis using plant extracts

Plant extracts show a vital character in the biosynthesis of nanoparticles. This process is also recognized as green synthesis or a greenprocess of manufacture of nanoparticles. Leaves of the geranium herb (*Pelargonium graveolens*) have been used to manufacture gold nanoparticles. 1 ml of 1 mmol aqueous solution of silver nitrate is added to 5 ml of the plant extract to synthesize silver nanoparticles. The same procedure is followed for synthesis from alcoholic extract, The plant extract, along with silver nitrate, is kept in a shaker at 150 rpm in the dark [35, 36].

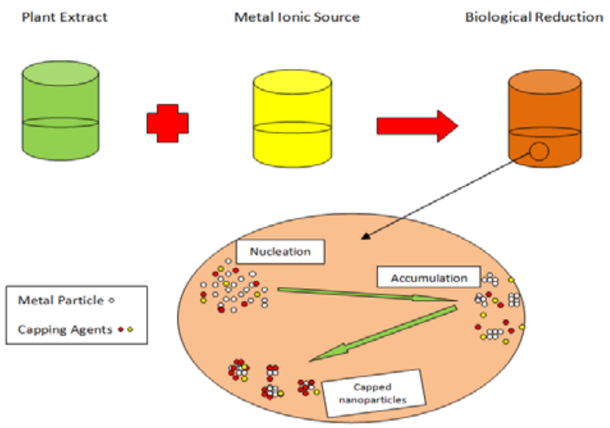

Fig. 11: Synthesis using plant extract

Synthesis using algae

Preparation of algae extract in Aqueous Solvent or an organic solvent by heat or boiling it for a definite period. Preparation of molar solution of ionic metallic complex. Incubation of algae solution and molar solution of ionic metallic complexes followed whichever by nonstop stirring or without stirring for a definite period under controlled conditions. Nanoparticles synthesis is dose dependant process and depends on the type of algae used. The biomolecules peptides, pigments and polysaccharides are accountable for the reduction of metals. Nanoparticles synthesis using algae takes a shorter duration than other biosynthesizing methods. To synthesize AgNPs of varying sizes and shapes certain seaweeds (*Sargassumwightii* and *Fucusvesiculosus*) can be used [37, 38].

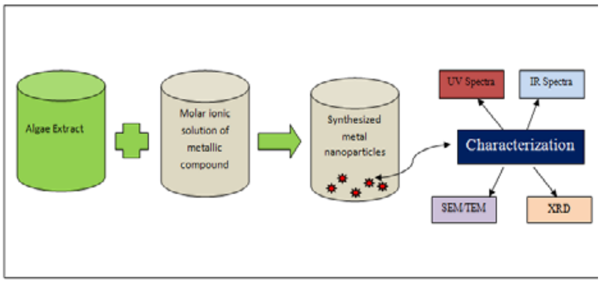

Fig. 12: Nanoparticles synthesis using algae

CONCLUSION

The top-down approach is quite expensive and not suitable for soft samples. The top-down method is not suitable for large-scale production but it is suitable for laboratory experimentation. The bottom-up approach is based on the principle of molecular recognition. Bottom-up methods involve atom by atom, molecule by molecule, or cluster by cluster manipulation for the synthesis of nanostructures. The study of different methods of synthesis of nanoparticles was done.

ACKNOWLEDGMENT

Authors thank the Principal, R. C. Patel Institute of Pharmaceutical Education and Research Shirpur 425405Dist-Dhule, Maharashtra (India)

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

The authors declare no conflict of interest, financial or otherwise.

REFERENCES

1. Pal SL, Jana U, Manna PK, Mohanta GP, Manavalan R. Nanoparticle: an overview of preparation and characterization. J Appl Pharm Sci 2011;1:228-34.
2. Hasany SF, Ahmed I, Rajan J, Rehman A. Systematic review of the preparation techniques of iron oxide magnetic nanoparticles. Nanosci Nanotechnol 2012;2:148-58.
3. Rajput N. Methods of preparation of nanoparticles-a review. Int J Adv Eng Technol 2015;7:1806.
4. Demazeau G. Solvothermal processes: definition, key factors governing the involved chemical reactions and new trends. Zeitschriftfür Naturforschung B 2010;65:999-1006.
5. Ma J, Liu X, Wu L, Zheng W. A solvothermal route to tellurium based thin films. Crystal Res Technol: J Exp Ind Crystallography 2008;43:1297-9.
6. Siwach OP, Sen P. Synthesis and study of fluorescence properties of Cu nanoparticles. J Nanoparticle Res 2008;10:107-14.
7. Muñoz JE, Cervantes J, Esparza R, Rosas G. Iron nanoparticles produced by high-energy ball milling. J Nanopart Res 2007;9:945-50.
8. Koch CC. Synthesis of nanostructured materials by mechanical milling: problems and opportunities. Nanostructured Materials 1997;9:13-22.
9. Doyle ME, Glass KA. Sodium reduction and its effect on food safety, food quality, and human health. Compr Rev Food Sci Food Saf 2010;9:44-56.
10. Rangarajan M, Vasanthakumari R, Vikram S. Superparamagnetic iron oxide nanoparticles from co-precipitation: composition, size, and magnetization. Nanosci Nanotechnol 2014;14:1-9.
11. Hou TH, Su CH, Liu WL. Parameters optimization of a nano-particle wet milling process using the Taguchi method, response surface method and genetic algorithm. Powder Technol 2007;173:153-62.
12. Krishnappa K, Pandiyan J, Paramanandham J, Elumalai K. Antibacterial and mosquitocidal potentials of selected Indian medicinal plants extracts and synthesized silver nanoparticles. Int J Zool Studies 2018;3:15-5.
13. Winterer M, Hahn H. Nanoceramics by chemical vapour synthesis. Zeitschriftfur Metallkunde 2003;94:1084-90.
14. Konrad A, Herr U, Tidecks R, Kummer F, Samwer K. Luminescence of bulk and nanocrystalline cubic yttria. J Appl Physics 2001;90:3516-23.
15. Andrievskii RA. The synthesis and properties of nanocrystalline refractory compounds. Russian Chem Rev 1994;63:411.
16. Rastogi A. A mini-review practice of formulations of nanoparticles. Int J Chem Synthesis Chem Reactions 2017;3:1-7.
17. Dikusar AI, Globa PG, Belevskii SS, Sidel'nikova SP. On limiting rate of dimensional electrodeposition at meso-and nanomaterial manufacturing by template synthesis. Surface Eng Appl Electrochem 2009;45:171-9.
18. Ponon NK, Appleby DJ, Arac E, King PJ, Ganti S, Kwa KS, *et al.* Effect of deposition conditions and post-deposition anneal on reactively sputtered titanium nitride thin films. Thin Solid Films 2015;578:31-7.
19. Patscheider J. Nanocomposite hard coatings for wear protection. MRS Bull 2003;28:180-3.
20. Guler U, Shalaev VM, Boltasseva A. Nanoparticle plasmonics: going practical with transition metal nitrides. Materials Today 2015;18:227-37.
21. Dong S, Chen X, Gu L, Zhang L, Zhou X, Liu Z, *et al.* A biocompatible titanium nitride nanorods derived nanostructured electrode for biosensing and bioelectrochemical energy conversion. Biosens Bioelectron X 2011;26:4088-94.
22. Boddolla S, Thodeti S. A review on characterization techniques of nanomaterials. Int J Eng Sci Mathematics 2018;7:169-75.
23. Dikusar AI, Globa PG, Belevskii SS, Sidel'nikova SP. On limiting rate of dimensional electrodeposition at meso-and nanomaterial manufacturing by template synthesis. Surface Eng Appl Electrochem 2009;45:171-9.
24. Behera S, Nayak PL. *In vitro* antibacterial activity of green synthesized silver nanoparticles using Jamun extract against multiple drug resistant bacteria. World J Nano Sci Technol 2013;2:62-5.
25. Karthikeyan B, Loganathan B. A close look of Au/Pt/Ag nanocomposites using SERS assisted with optical, electrochemical, spectral and theoretical methods. Phys E (Amsterdam Neth) 2013;49:105-10.
26. Li J, Wu Q, Wu J. Synthesis of nanoparticles via solvothermal and hydrothermal methods. Handbook of Nanoparticles; 2015. p. 1-28.
27. Sivasankaran S, Sankaranarayanan S, Ramakrishnan S. A novel sonochemical synthesis of metal oxides based Bhasmas. In: Materials Science Forum. Trans Tech Publications Ltd 2013;754:89-97.
28. Ziylan Yavas A, Mizukoshi Y, Maeda Y, Ince NH. Supporting of pristine TiO2 with noble metals to enhance the oxidation and mineralization of paracetamol by sonolysis and sonophotolysis. Appl Catal B 2015;172:7-17.
29. Das S, Srivasatava VC. Synthesis and characterization of ZnO–MgOnanocomposite by co-precipitation method. Smart Sci 2016;4:190-5.
30. Wang Y, Arandiyan H, Scott J, Bagheri A, Dai H, Amal R. Recent advances in ordered meso/macroporous metal oxides for heterogeneous catalysis: a review. J Materials Chem A 2017;5:8825-46.
31. Perez Tijerina E, Pinilla MG, Mejia Rosales S, Ortiz Mendez U, Torres A, Jose Yacaman M. Highly size-controlled synthesis of

Au/Pd nanoparticles by inert-gas condensation. Faraday Discussions 2008;138:353-62.

32. Banerjee AN, Krishna R, Das B. Size controlled deposition of Cu and Si nano-clusters by an ultra-high vacuum sputtering gas aggregation technique. Appl Physics A 2008;90:299-303.
33. Iravani S. Green synthesis of metal nanoparticles using plants. Green Chem 2011;13:2638-50.
34. Pandey S, Oza G, Mewada A, Sharon M. Green synthesis of highly stable gold nanoparticles using momordicacharantia as nano fabricator. Arch Appl Sci Res 2012;4:1135-41.
35. Manjula P, Boppella R, Manorama SV. A facile and green approach for the controlled synthesis of porous SnO2 nanospheres: application as an efficient photocatalyst and an excellent gas sensing material. ACS Appl Materials Interfaces 2012;4:6252-60.
36. Vidya C, Hiremath S, Chandraprabha MN, Antonyraj ML, Gopal IV, Jain A, *et al.* Green synthesis of ZnO nanoparticles by calotropisgigantea. Int J Curr Eng Technol 2013;1:118-20.
37. Yasmin A, Ramesh K, Rajeshkumar S. Optimization and stabilization of gold nanoparticles by using herbal plant extract with microwave heating. Nano Convergence 2014;1:1-7.
38. SP V, Udayabhanu U, HS L. Plant-mediated green synthesis of Ag nanoparticles using rauvolfiatetraphylla (L.) flower extracts: characterization, biological activities and screening of their catalytic activity in formylation reaction. ScientiaIranica 2019. DOI:10.24200/SCI.2019.51275.2093