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Nanoparticles: An Overview of Preparation

Swati Tyagi[1*] and Vinay Kumar Pandey[2]

[1]Department of Biotechnology, Meerut Institute of Engineering and Technology, Meerut, Uttar Pradesh, India
[2]Department of Botany, Lucknow University, Lucknow, Uttar Pradesh, India

Review Article

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***For Correspondence**

*Corresponding author: Swati Tyagi, Department of Biotechnology, Meerut Institute of Engineering and Technology, Meerut, Uttar Pradesh, India.

E-mail: swatityagi99@gmail.com

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ABSTRACT

Nanoparticles ranging below several 10 nm such as metals, semiconductors and metal oxides are of great interest for a wide variety of applications in the field of information, energy, environmental and medical technologies due to their unique size, composition and structure. In this review article synthesis method of nanosized particles is briefly described including their application in today's world. The preparation and synthesis of nanoparticles is carried out by different methods such as polymerization, preformed polymers or ionic gelation etc. These methods can be useful in certain methods such as drugs can be entrapped in the polymer matrix, encapsulated in a nanoparticle core, surrounded by a shell- like polymer membrane, chemically conjugated to the polymer, or either it may be bound to the particle's surface by adsorption.

INTRODUCTION

A technology that measures, manipulate or incorporate materials with a critical dimensions between 1-100 nm in size [1,2], also whose application exploits properties distinct from bulk macroscopic systems from which they arise is referred as Nanotechnology that deals with nano-meter sized objects. Nanotechnology will be developed at several levels of materials, devices and a system including development at nanomaterial level is the most advanced at present, both in scientific knowledge and in commercial applications through nanoparticles.

Nanoparticles are nanosized colloidal structures manufactured from biocompatible and biodegradable polymers that ranges in size from 10 to 1000 nm composed of synthetic or semisynthetic polymers [3,4]. Such polymeric nanoparticles can modify the activity of drugs, delay and control of drug release, and increase the drug adhesivity. On the basis of preparation methods, nanostructures can be obtained from Nanospheres of solid core spherical particulates which are nanometric in size containing drug embedded within the matrix or take up onto the surface of nanomaterials membrane, while in Nanocapsules drugs are embedded to a cavity surrounded by a unique polymer membrane.

Significantly, technological advancement of nanometer-sized particles is expanding by the variety of chemical compositions with advancement in their sturctures and applications. In field of synthesis of different types of nanoparticles, polymeric nanoparticles [5-10] (PNP's) playing an important role in field of electronics [11], photonics, conducting materials, sensors, medicine, biotechnology, therapeutics, pollution control and environmental technology, drug delivery [12-15] as nanoparticles are known for delivery of drugs, proteins and DNA to their target cells and organs that plays a vital role in medication and treatment of various diseases [16]. The nature, size and optical properties of nanoparticles make them easier to enter, translocate and damage living microorganisms or the target cell as nanoparticles can penetrate physiological barriers and travel within the circulatory systems of a host.

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TECHNIQUES OF PREPARATION

The appropriate method for the preparation of nanoparticles depends on the characteristics of polymer and the drug that is to be used in Nano preparations therefore in order to achieve the properties of interest the mode of preparation plays a vital role. Different techniques employed in preparation [17-20] and synthesis of nanoparticles is discussed below:

Solvent Evaporation

Solvent evaporation **(Figure 1)** was the first method that was developed for the preparation of nanoparticles, in this technique the polymer solutions [21] were prepared in volatile solvents and emulsions [22] were formulated by employing dichloromethane and chloroform, but now it is replaced with ethyl acetate that shows a much better toxicological profile to obtain polymeric particles less than 500 nm in size. During the preparation, emulsion is converted into a nanoparticle suspension on evaporation of the solvent, after that the solution is allowed to diffuse through the continuous phase of the emulsion to carry out conventional mode of methods i.e. single emulsions e.g., oil-in-water (o/w) and double emulsions [22] e.g., (water-in-oil)-in-water, (w/o)/w. Such type of methods utilize high-speed homogenization or ultrasonication, followed by evaporation of the solvent [23,24], either by continuous magnetic stirring at room temperature or under reduced pressure resulting in the formation of solidified nanosized particle collected by ultracentrifugation followed by washing to remove surfactants and at last the product is lyophilized.

Single emulsion and Double emulsion has been widely used for pharmaceutical applications [25] to obtain clinically applicable drug delivery systems, encapsulation of various hydrophilic and hydrophobic anticancer drugs, anti-inflammatory drugs, antibiotic drugs, proteins and amino acids and their applications in theranostics. In solvent evaporation technique [26], efforts are being made in clinics to develop more specific, individualized therapies for various diseases, and to combine diagnostic and therapeutic capabilities into a single agent.

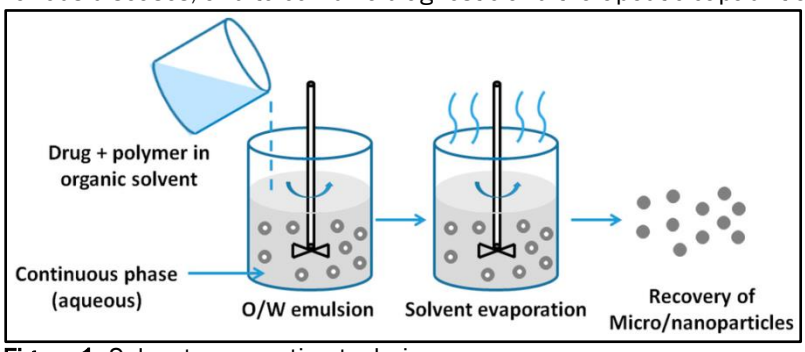

Figure 1: Solvent evaporation technique.

Nanoprecipitation

Nanoprecipitation **(Figure 2)** is a facile, mild, and low energy input process to carry out polymeric nanoparticles synthesis [27] which is also termed as solvent displacement [28,29] method. The process of preparing involves preformed polymer of organic solution (acetone, ethanol, or methanol) and then in the presence or absence of surfactant [30] the organic solvent is allowed to diffuse generally using polymer Poly-Lactic Acid (PLA).

The polymer PLA of intermediate polarity is allowed to dissolved in a water-miscible solvent, resulting in formation of nanospheres [1,2] and the solution is injected into an aqueous solution containing stabilizer as a surfactant as to result the formation of nanoparticles due to interaction between the water and the organic solvent. The nanoparticles synthesised through the process are of submicron size (<210 nm) with of low polydispersity. Biodegradable nanocarriers [31-35] such as lipid or polymer based nanoparticles that were designed to enhance the efficacy of nanoparticles and reduce the toxic effects of drugs [36] that results from therapeutic delivery of drugs for treatment of diseases. The Nanoprecipitation, without using surfactant of hydrophobic compounds in a non-solvent solutions leads to scattering of nanoparticles with effect of nanosized particles and such process is termed as “Ouzo” effect.

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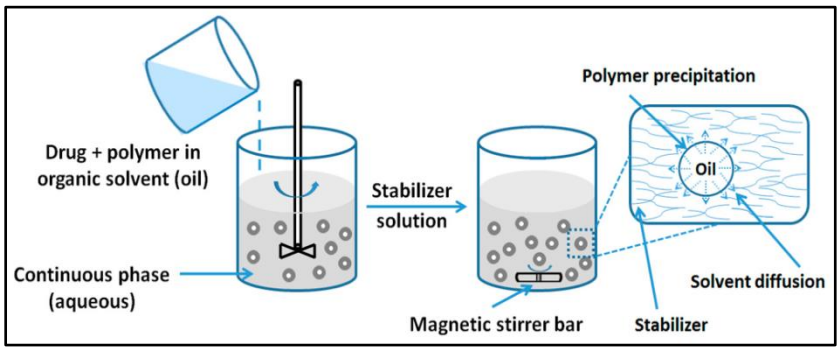

Figure 2: Nanoprecipitation technique.

Emulsification Diffusion

Emulsification or solvent diffusion (ESD) technique **(Figure 3)** is the modification of solvent evaporation method which utilizes water miscible solvent [37-40] and a small amount of water immiscible organic solvent due to the spontaneous diffusion of immiscible solvents that generate turbulence [41] between the two phases results the formation of nanosized particles. The formation of nanoparticles depends only on the diffusion of the solvent of the dispersed phase [42,43] and the formation of nanospheres or nanocapsules [46], according to the oil-to-polymer ratio in which an aqueous solution containing stabilizer [44] successfully leads to solvent diffusion to the external phase[45] of the solution for nanoparticle formation.

ESD presents many advantages such as high encapsulation efficiencies [47], no homogenization required, high batch-to-batch reproducibility [48], ease of scale-up, simplicity, narrow size distribution [49,50]. As drug loaded nanoparticles can be prepared by ESD technique [52], thus hydrophobic or hydrophilic drugs [51] can be used for medical and electronical importance. Similarly, several other nanoparticles such as mesotetra porphyrin-loaded PLGA (p-THPP) nanoparticles [52-57], doxorubicin-loaded PLGA nanoparticles, plasmid DNA-loaded PLA nanoparticles, coumarin-loaded PLA nanoparticles, indocyanine [58-60] can also be used for a number of applications.

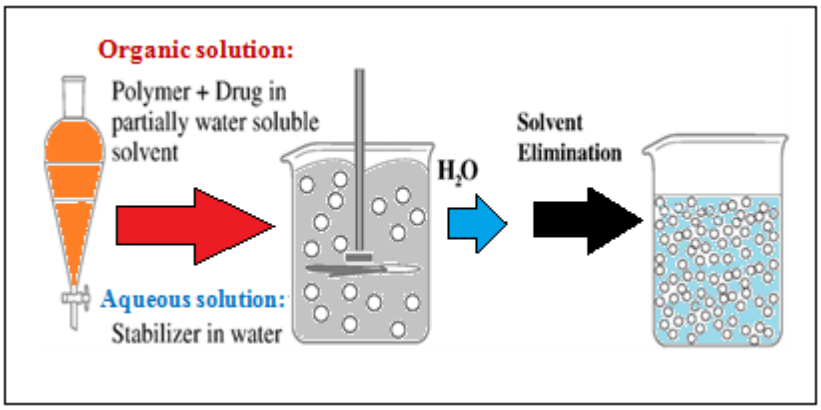

Figure 3: Emulsification diffusion technique.

Salting Out

The salting out **(Figure 4)** is modification of emulsification solvent diffusion technique [61-65] in which water miscible solvent is separated from aqueous solution through salting out process where, initially polymer and drug are dissolved in a solvent such as acetone, then it emulsifies into an aqueous gel consisting a salting-out agent in it as electrolytes such as magnesium chloride, calcium chloride, and magnesium acetate, or non- electrolytes such as sucrose. Importance of technique depends upon the type of salting out agent used, as it play an important property of encapsulating efficiency [66] of the drugs because the solvent and the salting out agent [67,68] are then eliminated by cross-flow filtration.

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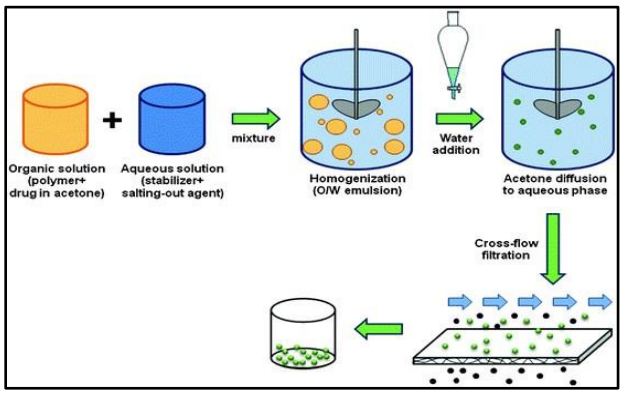

Figure 4: Salting out technique.

Dialysis

Dialysis is a simple and effective method for the preparation of small, narrow-distributed nanoparticles synthesis [69,70] in which polymer is dissolved in an organic solvent and placed inside a dialysis tube with proper molecular weight cut off and the displacement of solvent inside the membrane is followed by the progressive aggregation of polymer [71] due to a loss of solubility and the formation of homogeneous suspensions [72] of nanoparticles. The mechanism of dialysis [73] **(Figure 5)** is similar to Nanoprecipitation [74] whereas, it is based on the use of a physical barrier, specifically dialysis membrane [75] or common semi permeable membranes that allow the passive transport of solvents to slow down the mixing of the polymer solution with a non-solvent; the dialysis membrane [76,77] contains the solution of the polymer.

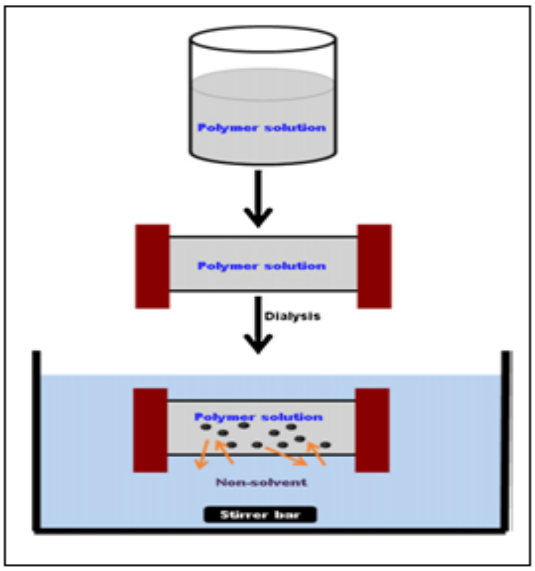

Figure 5: Dialysis or osmosis based method for nanoparticles preparation.

Supercritical Fluid Technology (SCF)

Supercritical fluid **(Figure 6)** is defined as a solvent at a temperature above its critical temperature, at which the single phase regardless of pressure moreover; the technology has been used as an alternative to prepare biodegradable [78] micro and nanoparticles because supercritical fluids [79] are environmentally safe. Supercritical CO_2 is most widely used as supercritical fluid because of its mild conditions, non-toxicity, non-flammability where this fluid along with dense gas technology [80] are expected to offer an interesting and effective technique of particle production [81], avoiding most of the drawbacks of the traditional methods **(Figure 6).** This technique is environmentally friendly, suitable for mass production and is more expensive.

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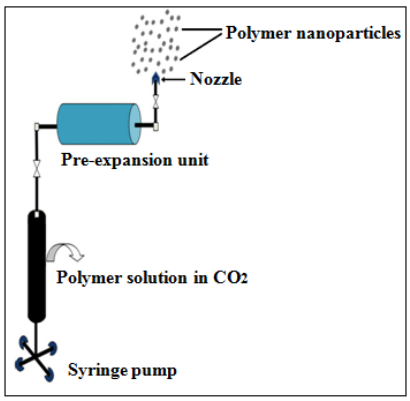

Figure 6: Experimental set up for Nanoparticles preparation of Supercritical fluid solution.

To attain the desired properties for a particular application of nanoparticles, suitable polymer nanoparticles must be designed, which can be done during the polymerization of monomers [82] and processes for the production of NPs through the polymerization of monomers are discussed below

Polymerization in Emulsion

The term Emulsion is defined as a mixing of two or more totally or partially immiscible liquids obtained in the presence or absence of a surface active agent [83] basically depending on the type of dispersed phase and of the dispersion medium. Emulsion technique is one of the fastest methods for nanoparticle preparation [84] and this major emulsion polymerization technique is classified into two categories, based on the use of an organic or aqueous continuous phase. The major emulsion polymerization method includes conventional emulsion polymerization, surfactant-free emulsion polymerization, as well as mini- (or nanoemulsions) and microemulsions [85] polymerizations which differ from the kinetically and thermo-dynamically different emulsion behaviours.

The continuous organic phase [86,87] technique involves the dispersion of monomer into an emulsion or inverse microemulsion, or into a material in which the monomer is not soluble (nonsolvent) as a result, polyacrylamide nanospheres [88] were produced by this method. In the aqueous continuous phase the monomer is dissolved in a continuous phase that is usually an aqueous solution, and the surfactants or emulsifiers are not needed thus, the polymerization [89,90] process can be initiated by different mechanisms resulting the synthesis of nanoparticle of submicron size.

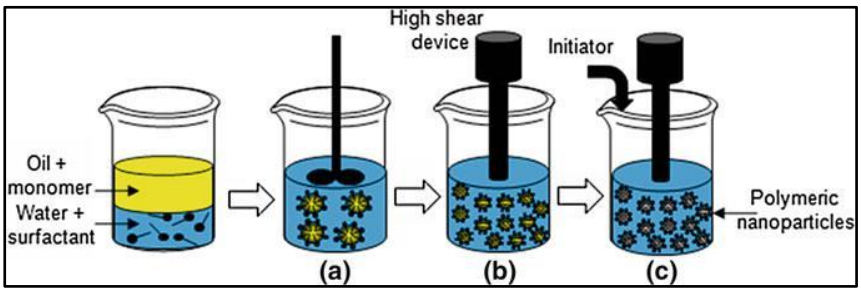

Figure 7: Miniemulsion Polymerization Method. **(a)** Pre-emulsification **(b)** Nanoemulsification using a high shear device **(c)** Formation of polymeric nanoparticles upon addition of initiator.

Miniemulsion polymerization **(Figure 7)** is generation of Nanoemulsions [91,92] using high-energy methods and employing low molecular mass compound as co-stabilizer prior initiating polymerization by formulation the synthesis in water, monomer mixture, co-stabilizer, surfactant, and initiator. The successful synthesis of NP's is achieved by low water solubility of reactants and the slower polymerization kinetics than emulsification. Microemulsion [93] is a thermodynamically and spontaneous stable system prepared with a high quantity of surfactant and characterized by an interfacial tension at the oil/water interface close to zero that depicts, the main difference between microemulsion and miniemulsion polymerization method. Nanoparticles synthesized through microemulsion results in smaller particle size (<80 nm) than in miniemulision processes.

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Interfacial Polymerization

Interfacial polymerization **(Figure 8)** is characterized by the polycondensation of monomers [94] at the droplet interface leading to the generation of mainly nanocapsules [95] instead of nanospheres as the method involves step polymerization of two reactive monomers or agents, which are dissolved respectively in two phases (i.e., continuous and dispersed phase), and the reaction takes place at the interface of the two liquids. Finally, nanometer-sized hollow polymer particles were synthesized by employing interfacial cross-linking reactions as polyaddition and polycondensation or radical polymerization [96] effective formulation of nanocapsules through polymerization of monomers.

Oil-containing nanocapsules [97] were obtained by the polymerization of monomers at the oil/water interface of a very fine oil-in-water micro- emulsion alternatively, water-containing nanocapsules can be obtained by the interfacial polymerization of monomers in water-in-oil micro-emulsions. In this method the organic solvent, which was completely miscible with water, served as a monomer vehicle and the interfacial polymerization of the monomer [98] was believed to occur at the surface of the oil droplets that formed during emulsification results in formation of Oil-containing nanocapsules whereas the polymer formed locally at the water-oil interface and precipitated to produce the nanocapsule shell [99] produce water-containing nanocapsules.

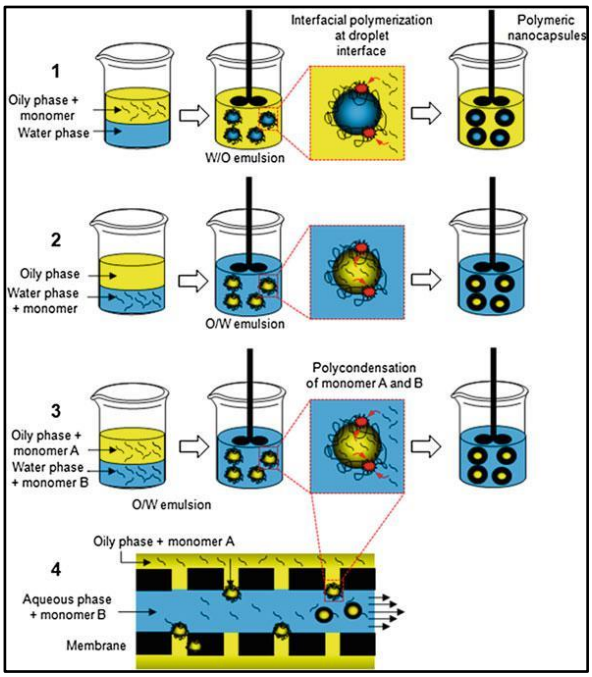

Figure 8: Different strategies of Interfacial Polymerization. (1) Monomer introduction onto oily phase (2) Monomer in aqueous phase (3) Monomers introduction in the oily and aqueous phase (4) Polymerization using a membrane reactor device.

Controlled/Living radical polymerization(C/LRP)

The principal methods of controlled/living radical polymerization [100,101] are nitroxide-mediated polymerization (NMP), atom transfer radical polymerization (ATRP), and reversible addition and fragmentation transfer chain polymerization (RAFT) that relies only on pure reactions as to ignore terminations aroused due to impurities. Several kinds of polymeric nanoparticles [102] have been synthesized by this technique such as polybutyl acrylate, polystyrene, or polymethyl methacrylate and even block copolymers.

The controlled/living radical polymerization has emerged as a new field in the recent past years helped by the industrial production of hydrophilic polymeric nanoparticles [100] that were designed specifically for biomedical applications and for environmental concern with the development of ‘‘green chemistry’’. This technique also have some drawbacks due to the lack of control over the molar mass, molar mass distribution, end functionalities and macromolecular architecture, which are due to unavoidable fast radical–radical termination reactions during the preparation of nanoparticles.

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Living and Controlled radical polymerization differ differently as Living radical polymerization developed by Ostu, et al. in 1982, where they referred organic disulfide initiator with chain transfer and termination as initiator-transfer agent terminator (iniferter) and Controlled radical polymerization developed by Michael Szwarc in 1956 empolyes living anionic polymerization of styrene with an alkali metal for further preparation of nanoparticles.

Ionic Gelation or Coacervation Of Hydrophilic Polymers

In ionic gelation technique, **Figure 9** also known as ion induced gelation in which PNPs are prepared by using biodegradable hydrophilic polymers such as chitosan, gelatin and sodium alginate in which ionic gelation refers to the material undergoing transition from liquid to gel due to ionic interaction conditions at room temperature. Chitosan, a natural linear biopolyaminosaccharide that is used for the synthesis of nanosized particles under which involves the mixture of two aqueous phases, one is polymer chitosan, and the other is a poly anion sodium tripolyphosphate. Finally, the positively charged amino group of chitosan interacts with negative charged groups of tripolyphosphate to form Coacervates resulting in the formation of nanosized particles by employing emulsion cross-linking technique. These microparticles formed due to electrostatic interaction between two aqueous phases can be characterized using FTIR (Fourier Transform Infrared) spectrum.

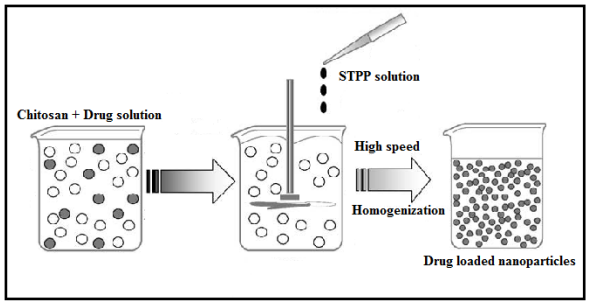

Figure 9: Ionic gelation method.

CONCLUSION

The main goal of this review article was to reflect techniques for the preparation and synthesis of organic & bioorganic NP's. Nanoparticles present a highly attractive platform for a diverse array of biological application as it was observed that the preparation of nanoparticles is a state-of-art technology that emerges in recent past years.

The technique for the preparation of NP's are more challenging as an important challenge is to obtain materials with well-defined structures and morphologies including wide range of physical, chemical, biological, physiological factors and conditions that must be taken into account for successful preparation and biofunctionalization of nanoparticles for a given biomedical application. A better fundamental acknowledgement about the processes, mechanism & techniques for NP's preparation should be the subject of an intensive research in next decades because nanoparticles have therapeutic potential at both research and clinical levels.

REFERENCES

1. Kreuter J. Nanoparticles In: Kreuter J (ed) Colloidal drug delivery systems. Marcel Dekker Inc, New York. 1994;219–342.
2. Couvreur P. Polyalkylcyanoacrylates as colloidal drug carriers. Crit Rev Ther Drug Carr Syst. 1988;5:1–20.
3. Kumaresh S. Biodegradable polymeric nanoparticles as drug delivery devices. J. Control. Release. 2001;70 1–20.
4. Mohanraj VJ and Y Chen. Nanoparticles – A Review. Trop J Pharm Res. 5;561-573.
5. Hadziioannou G and Malliaras GG. Semiconducting polymers. Wiley-VCH Publisher, Weinheim. 2000.
6. Couvreur P and Vauthier C. Nanotechnology: intelligent design to treat complex disease. Pharm Res. 2006;23:1417–1450.
7. Pinto Reis C, et al. Nanoencapsulation I Methods for preparation of drug-loaded polymeric nanoparticles. Nanomed Nanotechnol Biol Med. 2006;2: 8–21.

8. Pinto Reis C, et al. Nanoencapsulation II. Biomedical applications and current status of peptide and protein nanoparticulate delivery systems. Nanomed Nanotechnol Biol Med. 2006;2:53–65.
9. Rao JP and Geckeler KE. Polymer nanoparticles: preparation techniques and size-control parameters. Prog Polym Sci. 2011;36:887–913.
10. Pecher J and Mecking S. Nanoparticles of conjugated polymers. Chem Rev. 2010;110: 6260–6279.
11. Anton N, et al. Design and production of nanoparticles formulated from nano-emulsion templates–A review. J Controlled Release. 2008;128:185–199.
12. Vauthier C and Bouchemal K. Methods for the preparation and manufacture of polymeric nanoparticles. Pharm Res. 200926:1025–1058.
13. Landfester K, et al. From polymeric particles to multifunctional nanocapsules for biomedical applications using the miniemulsion process. J Polym Sci A Polym Chem. 2010;48:493–515.
14. Allemann E, et al. Drug-loaded nanoparticles—Preparation methods and drug targeting issues. Eur J Pharm Biopharm. 1993;39:173–191.
15. Quintanar-Guerrero D, et al. Preparation techniques and mechanisms of formation of biodegradable nanoparticles from preformed polymers. Drug Dev Ind Pharm. 1998;24:1113–1128.
16. De Jaeghere F, et al. Nanoparticles, In: Mathiowitz E (ed) Encyclopedia of controlled drug delivery, vol 2. Wiley-VCH, New York. 1999;641–664.
17. Couvreur P, et al. Nanocapsule technology: a review. Crit Rev Ther Drug. 2001;19:99–134.
18. Tuncel D and Demir HV. Conjugated polymer nanoparticles. Nanoscale. 2010;2:484–494.
19. Gangopadhyay R. Conducting Polymer Nanostructures, In: Nalwa H S (ed) Encyclopedia of nanoscience and nanotechnology. American Scientific Publishers, Stevenson Ranch. 2004;2:105–131.
20. Wallace GG and Innis PC. Inherently conducting polymer nanostructures. J Nanosci Nanotechnol. 2002;2:441–451.
21. Koushik OS, et al. Nano Drug Delivery Systems to Overcome Cancer Drug Resistance - A Review. J Nanomed Nanotechnol. 2016;7: 378.
22. Salager JL. Pharmaceutical emulsions and suspensions, formulation concepts for the emulsion maker. Marcel Dekker Inc, New York. 2000;19–72.
23. Hwi Jin Ko. Recent Update of Nanobiosensors Using Olfactory Sensing Elements and Nanomaterials. Biosens J. 2015;4: 129.
24. Zaman H. Addressing Solubility through Nano Based Drug Delivery Systems. J Nanomed Nanotechnol. 2016;7: 376.
25. Kashif Maroof, et al. Scope of Nanotechnology in Drug Delivery. J Bioequiv Availab. 2016; doi: 10.4172/jbb.1000257.
26. Shi J, et al. Nanotechnology in drug delivery and tissue engineering: From discovery to applications. Nano. Lett. 2010;10:3223–3230.
27. Mironov V, et al. Nanotechnology in vascular tissue engineering: from nanoscaffolding towards rapid vessel biofabrication. Trends Biotechnol. 2008;26:338–344.
28. Suprava Pate, et al. Nanotechnology in Healthcare: Applications and Challenges. Med Chem. 2015;5:528.
29. The Royal Society and The Royal Academy of Engineering. Nanoscience and nanotechnologies: opportunities and uncertainties. London, UK:2004.

30. Luis E Trujillo, et al. Nanotechnology Applications for Food and Bioprocessing Industries. Biol Med. 2015;8:289.
31. Kim BS. et al. Nanolayer: Delivering Multiple Therapeutics from Hierarchically Assembled Surface Coatings. Langmuir. 2009;25:14086–14092.
32. Tasleem Arif, et al. Therapeutic and Diagnostic Applications of Nanotechnology in Dermatology and Cosmetics. J Nanomedine Biotherapeutic Discov. 2015; 5:134.
33. Jiji Abraham, et al. Carbon Nanotube-thermally Reduced Graphene Hybrid/Styrene Butadiene Rubber Nano Composites: Mechanical, Morphological and Dielectric Studies. 2015;4: 3.
34. Iijima S. Helical microtubules of graphitic carbon. Nature. 1991;354:56–58.
35. Kreuter J. Nanoparticles. In: Kreuter J, editor. Colloidal Drug Delivery Systems. M. Dekker; New York. 1994;219–342.
36. Moghimi SM, et al. Long-circulating and target-specific nanoparticles: theory to practice. Pharmacol Rev. 2001;53: 283–318.
37. Panyam J, et al. Solid-state solubility influences encapsulation and release of hydrophobic drugs from PLGA/PLA nanoparticles. J Pharm Sci. 2004;93: 1804–1814.
38. Panyam J, et al. Solid-state solubility influences encapsulation and release of hydrophobic drugs from PLGA/PLA nanoparticles. J Pharm Sci. 2004;93: 1804–1814.
39. Ramsay, DA. Intensities and shapes of infrared absorption bands of substances in the liquid phase. J Am Chem Soc. 1952;74:72–80.
40. Asane, G. et al. Polymers for mucoadhesive drug delivery system: a current status. Drug Dev. Ind. Pharm. 2008;34:1246–1266.
41. Alaqad K and Saleh TA. Gold and Silver Nanoparticles: Synthesis Methods, Characterization Routes and Applications towards Drugs. J Environ Anal Toxicol. 2016;6: 384.
42. Vicky VM et al. Introduction to metallic nanoparticles. J Pharm Bioallied Sci. 2010;2:282–289.
43. Tawfik AS. Nanomaterials for Pharmaceuticals Determination. Bioenergetics. 2016;doi: 10.4172/2167-7662.1000226.
44. Robert JH et al. Low-Dimensional Nanoparticle Clustering in Polymer Micelles and Their Transverse Relaxivity Rates. ACS Nano. 2013;7:5824–5833.
45. Sreeraj G et al. Effective Drug Delivery System of Biopolymers Based On Nanomaterials and Hydrogels - A Review. Drug Des. 2016;5:2.
46. Carlos RA et al. Reliable Tools for Quantifying the Morphogical Properties at the Nanoscale. Biol Med. 2016;8:281.
47. Alivisatos P. The use of nanocrystals in biological detection. Nat. Biotechnol. 2004;22:47–52.
48. Kong J et al. Nanotube molecular wires as chemical sensors. Science. 2000;287:622–625.
49. Kong J and Dai H. Full and modulated chemical grating of individual carbon nanotubes by organic amine compounds. J. Phys. Chem. 2001;105:2890–2893.
50. Cui Y et al.. Nanowire nanosensors for highly sensitive and Selective detection of biological and chemical species. Science. 2001;293:1289–1292.
51. Tolani SB et al. Towards biosensors based on conducting polymer nanowires. Anal. Bioanal. Chem. 2009;393:1225–1231.

52. Wang ZL. Characterizing the structure and properties of individual wire-like nanoentities. Adv Mater. 2000;12:1295.
53. Duan X et al. Indium phosphide nanowires as building blocks for nanoscale electronic and optoelectronic devices. Nature. 2001;409:66.
54. Cui Y and Lieber CM. Functional nanoscale electronic devices assembled using silicon nanowire building blocks. Science. 2001;291:851.
55. Huang Y et al. Logic gates and computation from assembled nanowire building blocks. Science. 2001;294:1313.
56. Xia Y et al. One-dimensional nanostructures: synthesis, characterization, and applications. Adv Mater. 2003;15:353.
57. Jibowu T. The Formation of Doxorubicin Loaded Targeted Nanoparticles using Nanoprecipitation, Double Emulsion and Single Emulsion for Cancer Treatment. J Nanomed Nanotechnol. 2016;7: 379.
58. Novoselov KS et al. Electric field effect in atomically thin carbon films. Science. 2004;306:666–669.
59. Winkin N et al. Nanomaterial-modified Flexible Micro-electrode Array by Electrophoretic Deposition of Carbon Nanotubes. Biochip Tissue Chip. 2016;6:115.
60. Zhao Q et al. Electrochemical sensors based on carbon nanotubes. Electroanalysis. 2002;14:1609–1613.
61. Weaver CL et al. Electrically controlled drug delivery from graphene oxide nanocomposite films. ACS nano. 2014;8:1834–1843.
62. Lone B. Adsorption of Cytosineon Single-walled Carbon Nanotubes. J Nanomed Nanotechnol. 2016;7:354.
63. Soleimani H et al. Synthesis of Carbon Nanotubes for Oil-water Interfacial Tension Reduction. Oil Gas Res. 2015;1:104.
64. Dumsile W Nyembe et al. Effects of Ingested Multi-Walled Carbon Nanotubes in Poecilia reticulata: Localization and Physiological Responses. J Environ Anal Toxicol. 2016;6:368.
65. Soto K et al. Cytotoxic effects of aggregated nanomaterials. Acta Biomater. 2007;3:351–358.
66. Sreelakshmy V et al. Green Synthesis of Silver Nanoparticles from Glycyrrhiza glabra Root Extract for the Treatment of Gastric Ulcer. J Dev Drugs. 2016;5:152.
67. Sindhwani S et al. Three-Dimensional Optical Mapping of Nanoparticle Distribution in Intact Tissues. Science Advances. 2016;1:10.
68. Sameh SA. Carboxyfullerenes: Nanomolecules that Work. J Nanomedine Biotherapeutic Discov. 2012;2:e110.
69. Valter B and Claudio N. Fabrication of Supports for Carbon Fullerenes Hard Disk Unit. J Nanomed Nanotechnol. 2014;5:230.0
70. Kepley C. Fullerenes in Medicine; Will it ever Occur. J Nanomed Nanotechnol. 2012;3:e111.
71. Kazue M et al. Antimicrobial Photodynamic Therapy with Functionalized Fullerenes: Quantitative Structure-activity Relationships. J Nanomed Nanotechnol. 2011;2:109.
72. Imtiyaz RP and Athar AH. Dendrimers as an Efficient Catalyst for the Oxidation of Multi Substituted Alcohols. J Fertil Pestic. 2016;7:160.
73. Khalid A and Tawfik AS. Gold and Silver Nanoparticles: Synthesis Methods, Characterization Routes and Applications towards Drugs. J Environ Anal Toxicol. 2016;6:384.

74. Liron L et al. Ultrasound-Mediated Surface Engineering of Theranostic Magnetic Nanoparticles: An Effective One-Pot Functionalization Process Using Mixed Polymers for siRNA Delivery. J Nanomed Nanotechnol. 2016,7: 385.
75. Mohammad N and Hossein M. Polymeric Nanostructures as Colloidal Drug Delivery Systems: Thermosensitive Hydrogels Containing Self-Assembled Micelles. J Nanomed Nanotechnol. 2015; 6:301.
76. Lee CC et al. A single dose of doxorubicin-functionalized bow-tie dendrimer cures mice bearing C-26 colon carcinomas. Proc Natl Acad Sci. 2006;103:16649–16654.
77. Vashist SK. Dendrimers: Prospects for Bioanalytical Sciences. J Nanomed Nanotechnol. 2013; 4:e131.
78. Ahmed AH. Targeting of Somatostatin Receptors using Quantum Dots Nanoparticles Decorated with Octreotide. J Nanomedic Nanotechnol. 2015;S6-005.
79. Demir E. Genotoxicology of Quantum Dots Used in Medical and Pharmaceutical Sciences. Hereditary Genet. 2015;4:151.
80. Nikalje AP. Nanotechnology and its Applications in Medicine. Med chem. 2015;5:081-089.
81. Ingale AG et al. Chaudhari AN. Biogenic Synthesis of Nanoparticles and Potential Applications: An Eco-Friendly Approach. J Nanomed Nanotechol. 2013;4:165.
82. Ghashghaei S and Emtiazi G. Production of Hydroxyapatite Nanoparticles Using Tricalcium-Phosphate by Alkanindiges illinoisensis. J Nanomater Mol Nanotechnol. 2013;2:5.
83. Hartung GA and Mansoori GA. In vivo General Trends, Filtration and Toxicity of Nanoparticles. J Nanomater Mol Nanotechnol. 2013;2:3.
84. Brigger I et al. Nanoparticles in cancer therapy and diagnosis. Adv Drug Deliv Rev. 2012;64:24–36.
85. Salager JL. Microemulsions, handbook of detergents—part A: properties. Marcel Dekker Inc. 1999;253–302.
86. Muhammad SN et al. Design and Fabrication of Biomass Extruder of 50 mm Diameter Briquette Size. Innov Ener Res. 2015;5:128.
87. Stejskal J. Colloidal dispersions of conducting polymers. J Polym Mater. 2001;18:225–258
88. Vincent B. Electrically conducting polymer colloids and composites. Polym Adv Technol. 1995;6:356–361.
89. Armes SP. Electrically conducting polymer colloids. Polym News. 1995;20:233–237.
90. Aldissi M and Armes SP. Colloidal dispersions of conducting polymers. Prog Org Coat. 1991;19:21–58.
91. Armes SP and Vincent B. Post-doping of sterically-stabilized polyacetylene latexes. Synth Met 1988;25:171–179.
92. Groenendaal L et al. Poly(3,4-ethylenedioxythiophene) and its derivatives: past, present, and future. Adv Mater. 2000;12:481–494.
93. Huyal IO et al. Quantum efficiency enhancement in film by making nanoparticles of polyfluorene. Opt Express. 12008;6:13391–13397.
94. Ozel IO et al. Non-radiative resonance energy transfer in bi-polymer nanoparticles of fluorescent conjugated polymers. Opt Express. 2010;18:670–684.
95. Grigalevicius S et al. Excitation energy transfer from semi-conducting polymer nanoparticles to surface-bound fluorescent dyes. Macromol Rapid Commun. 2006;27:200–202.
96. Pecher J and Mecking S. Nanoparticles from step-growth coordination polymerization. Macromolecules. 2007;40:7733–7735.

97. Müller RH et al. Solid lipid nanoparticles (SLN) for controlled drug delivery—A review of the state of the art. Eur J Pharm Biopharm. 2000;50:161–177.
98. Pragati S et al. Solid lipid nanoparticles: a promising drug delivery technology. Int J Pharm Sci Nanotechnol. 2009;2:509–516.
99. Freitas C and Müller RH. Correlation between long-term stability of solid lipid nanoparticles (SLN(TM)) and crystallinity of the lipid phase. Eur J Pharm Biopharm. 1999;47:125–132.
100. Olbrich C et al. Lipid-drug-conjugate (LDC) nanoparticles as novel carrier system for the hydrophilic antitrypanosomal drug diminazenediaceturate. J Drug Targeting. 2000;10:387–396.
101. Lee SH et al. Nano spray drying: a novel method for preparing protein nanoparticles for protein therapy. Int J Pharm. 2011;403:192–200.
102. York P. Strategies for particle design using supercritical fluid technologies. Pharm Sci Technol Today. 1999;2:430–440.
103. Salager JL et al. Formulation des micro-émulsions par la méthode HLD, Techniques De L'Ingénieur, Génie Des Procédés. 2001;J2: 1–20.
104. Li X et al. Nanoparticles by spray drying using innovative new technology: the Büchi Nano spray dryer B-90. J Controlled Release. 2010;147:304–3.