ISSN: 0976-822X

Available online on www.ijcpr.com

International Journal of Current Pharmaceutical Review and Research 2021; 13(4); 10-24
Review Article

# HISTORY & PREPARATIONS OF NANOPARTICLES

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**Received: 5-10-2021 / Revised: 07-11-2021 / Accepted: 02-12-2021**
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**Conflict of interest: Nil**

**Abstract**

A nanoparticle (or nanopowder, or nanocluster, or nanocrystal) is a microscopic particle containing at least one dimension less than 100 Nm.4 Nanoparticles are particles between 1 and 100 nanometers (nm) in size, with the surrounding interfacial layer. Integral parts of nanoscale subject matter, all its properties are profoundly influenced by the interfacial layer. Usually, the interfacial layer is made up of ions, inorganic and organic molecules. Organic molecules that cover inorganic nanoparticles are known as stabilizers, ligands of capping and surface or passivating agents. In nanotechnology, a particle is characterized as a small object that acts in terms of its transport and properties as a whole. Particles are additionally graded according to their diameter. Nanotechnology refers to the production and use of materials whose nanoscale components exist and, by definition, are up to 100 nm in size. Nanotechnology investigates both electrical, optical, and magnetic activity, and molecular and submolecular structural behavior. It has the ability to revolutionize a range of methods and procedures in medical and biotechnology to make them compact, simpler, safer, and easier to administer.

**Keyword**: Nanotechnology, Bactericidal, Thermal conductivity, optical devices etc.



## INTRODUCTION

To understand the growth of nanotechnology, to highlight some of those interesting events, it is important to examine the events that have led to the development of this field, with their significance. Richard Zsigmondy, Nobel Prize Laureate in Chemistry in 1925, first suggested the idea of a "nanometer". He invented the term nanometer specifically to describe particle size and was the first to use a microscope to quantify particle size like gold colloids.

Current nanotechnology was first historically speaking idea was introduced in 1959 by the well-known educator Nobel Prize Laureate in material science Dr. Richard P.Feynman in his talk "There is a lot of room at the base" at the American Physical Society meeting of the California Institute of Technology on December 29, 1959. In which he introduced the possibility of the nuclear control of the issue. This inventive idea uncovered better approaches for thought and from that point forward, Feynman's thoughts have been demonstrated right. Consequently, he is known as the author of present-day nanotechnology.

The main logical paper on sub-atomic nanotechnology, composed by K. Eric Drexler, an alumni understudy at Massachusetts Institute of Technology (MIT), is distributed in the September 1981 issue of the Proceedings of the National Academy of Sciences (PNAS). In India, conventional restorative frameworks, for example, Ayurveda and Siddha as bhasmas (100 BC-AD 100), the

most old-fashioned use of nanomedicine is recorded. Gold, silver, copper, and different metals were refined into fine powders in these Ayurvedic arrangements, prompting bhasmas that showed various hues and utilized to fix infirmities.

About 15 years after Feynman's talk, In 1974, Norio Taniguchi, a Japanese researcher, was the first to utilize "nanotechnology" to portray semiconductor forms that happened on the request for a nanometer. He pushed that nanotechnology comprised of one iota or one atom preparing, isolating, combining, and disfiguring the materials. The brilliant time of nanotechnology started during the 1980s. Creation of 1981 examining burrowing magnifying lens and the 1985 disclosure of fullerene (C60) prompted nanotechnology development.

In 1990, the world's first-historically speaking companion assessed diary in nanoscale science and building, called Nanotechnology, which is propelled by the Institute of Physics in the United Kingdom.

The mid 21st century saw an expanding enthusiasm for the new fields of nanoscience and nanotechnology. Feynman's height in the U.s and his idea of nuclear level control of issue assumed a noteworthy job in molding national science needs. During a discourse at Caltech on 21 Jan 2000, President Bill Clinton supported subsidizing for investigation into this developing innovation. Start of the 21st century 3 years after the fact George W. Shrub marked into law the Nanotechnology Research and Development Act.

In 1994, Burst and colleagues at the University of Liverpool, UK, lead the amalgamation of thiol-based gold nanoparticles. The enthusiasm for a combination of the gold nanoparticles restores, discovering its utilization in different areas. From that point forward, writing has quickly expanded in the field of gold nanoparticles. To offer an outline of the turn of events, just 11 articles identified with gold nanoparticles were distributed in 1995. Yet, in 2000 the number expanded to 178 distributions, while a lot more were distributed in 2005 (1430 papers), 2010 (3912 papers), and 2014 (5590 papers). Only 11 articles identified with gold nanoparticles were distributed in 1995 to offer a diagram of the turn of events, however, in 2000 the number expanded to 178 distributions, while a lot more were distributed in 2005 (1430 papers), 2010 (3912 papers), and 2014 (5590 papers).

In 1995, Stephen U.S. Choi and Jeffrey A. Eastman, from the Argonne National Laboratory, USA, propose that nanoparticles that help warm liquid conductivity. Which prompts another exploration zone, "nanofluids" Robert F. Twist Jr., Sir Harold W. Kroto, and Richard E smalley are together granted the Nobel Prize in Chemistry "for their disclosure of fullerenes" (Nobel Prize, 1996). In 2000, The National Nanotechnology Initiative (NNI), a US government innovative work activity, is shaped. In 2002, The National Institute for Nanotechnology (NINT), Alberta, Canada, is developed. In 2003, The 12 Principles of Green Engineering were proposing. Ideas of green nanoscience begin building up The Road to Green Nanotechnology" by Barbara Karn of the US Environmental Protection Agency (EPA) is distributed. In 2009, Green Center Canada, subsidized by the administrations of Ontario and Canada, is formed.

Today, nanotechnology impacts human life consistently. In pharmaceutics, ≈ 90% everything being equal, the dynamic fixing is as strong particles. With the headway of nanotechnology, sedate nanoparticles would now be able to be created, which can be utilized in various innovative manners. New medication conveyance courses would now be able to be used to improve sedate viability and diminish symptoms. For example, the U.S. in 2005 Food and Drug Administration affirmed 130-nm intravenously stacked paclitaxel (AbraxaneTM) albumin nanoparticles for malignant growth treatment.

## Nanomaterials -definition and classification

A nanoparticle (or nanopowder, or nanocluster, or nanocrystal) is a microscopic particle with less than 100 nm in at least one dimension. Research into nanoparticles is currently an powerful scientific research area due to a broad range of possible applications in the biomedical, optical and electronic fields. Nanoparticles have been used in a variety of industries, including the electrical, biological, chemical and textile industries. In the electronic system, nanoparticles play an important role, the expression of antimicrobial genes, and the catalytic and electromagnetic properties depending on their size. According to the former definition, there are three fundamental aspects to describe the existence of a nanomaterial, which are size, particle size distribution (PSD) and surface area.

Nanotechnology has been referred to as nanomedicine for medical purposes and is defined as the use of nanomaterials for diagnosis, monitoring, control; disease prevention and treatment. Nanoparticles are particles between 1 and 100 nanometers in size.

**In nanotechnology**, particle is defined as a small object which acts as an entire unit in relation to its transport and properties. Particulate matter is further classified by diameter.

**Nanometer** is about one billionth of a meter, about three or four atoms in width. The human hair is around 25,000 nanometers wide on average

**Nanoscale** materials can be characterized as particles whose characteristic length scale is within the nanometric range, i.e., among one and several hundred nanometers (preferably between 1-100 nm).

Nanostructured materials are classified as zero-dimensional, one-dimensional (graphene, thin film), two-dimensional (carbon nanotubes), and three-dimensional (quantum dots or nanoparticles) nanostructures (fullerene), according to Siegel (1994). Polymeric nanoparticles' structure may be divided into nanocapsules and nanospheres.

Nanoparticles are classified according to their composition as:

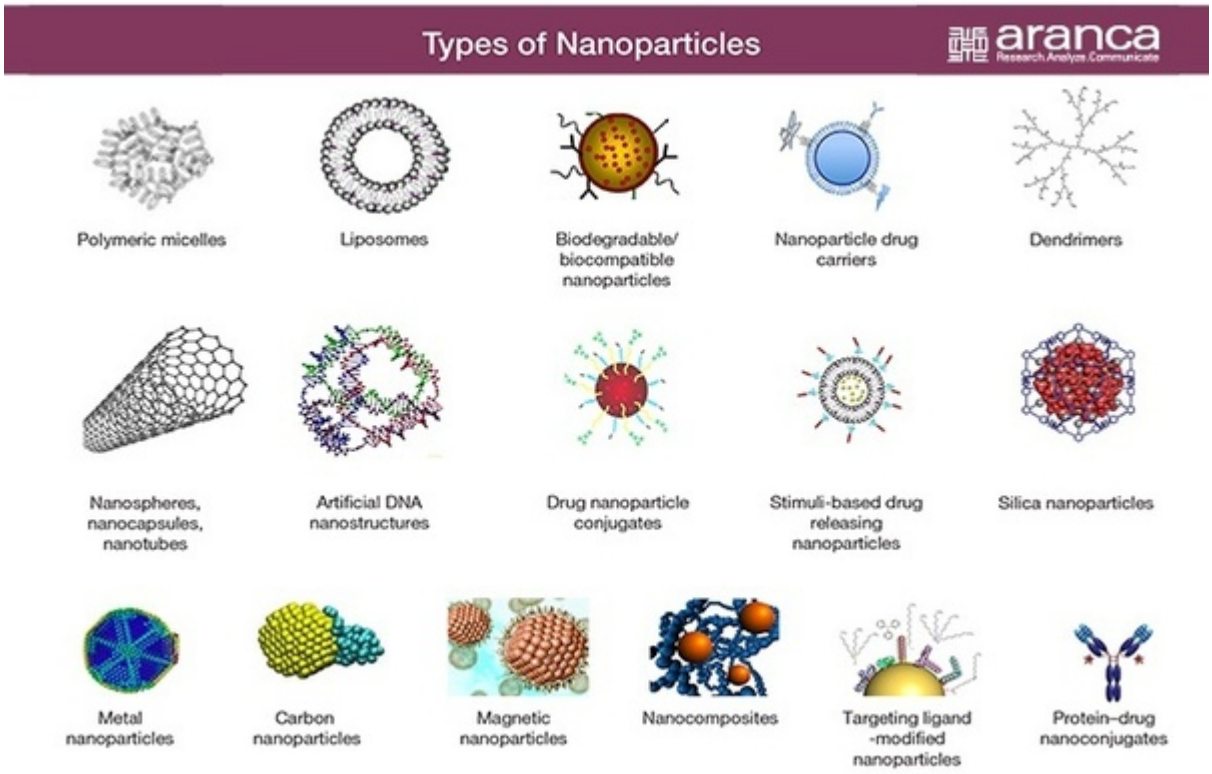
- Organic nanoparticles
- Inorganic nanoparticles
- Organic –inorganic hybrids
- Carbonaceous nanostructure
- Liposome, that can filled with specific materials
- Biological nanoparticles such as proteins and viruses.

There are 1266 commercialized nano product with 714 products in health and fitness, 104 in food and beverages and 28 products for in children, according to the Consumer product inventory as of April 2013. The analysis revealed silver nanoparticles to be the most marketable materials in the world.

The National Science Foundation estimates that the global marketplace of nanotechnology products and services will expand to $1 trillion by 2015. The U.S. invests about $3 billion annually in nanotechnology research and development, which accounts for roughly one-third of the total investment in the public and private sector worldwide.

### Types of nanoparticles

Types of Nanoparticles Developed Since the Late 1960s



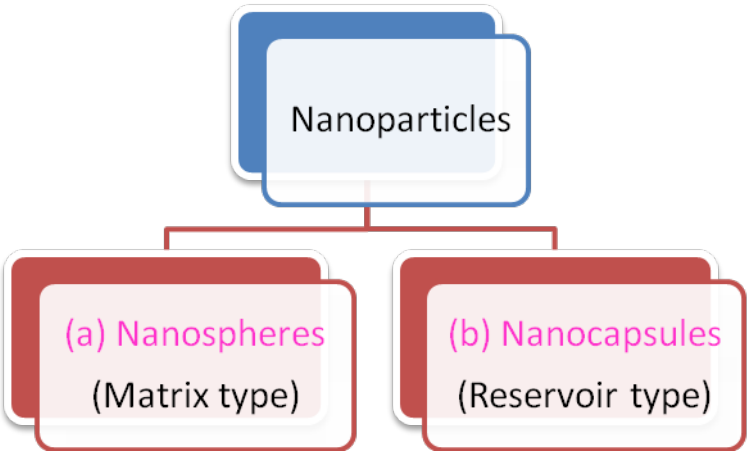

**Advantages and disadvantage**

| S.NO | Advantages | Disadvantages |
|---|---|---|
| **1** | Improve blood circulation, bioavailability, therapeutic effectiveness and decrease side effects. | Polymeric nanoparticles posses limited drug-loading capacity |
| **2** | Nanoparticles can be administered via different routes including oral, nasal, parenteral, intraocular, etc. | Toxic metabolites may be formed during the biotransformation of polymer carriers upon repeated administration. |
| **3** | Nanoparticles conquer resistance across physiological barriers in the body due to small particle size and quickly penetrate cell walls, blood vessels, stomach epithelium and blood-brain barrier. | The polymeric nanoparticles are biodegradable fairly slowly which may lead to systemic toxicity. |
| **4** | Nanoparticles enhance the aqueous solubility of poorly soluble drugs, thus improving drug bioavailability | Disturbance of Autonomic imbalance |
| **5** | Nanoparticles as a targeted drug carrier minimize drug toxicity and increase effective drug delivery | Discontinuation of therapy is not possible |
| **6** | Useful to diagnose various diseases and Enhanced stability of ingredients | Alveolar inflammation |

| | | |
|---|---|---|
| **7** | Change the method of drug delivery to improve customer acceptance or reduce manufacturing costs | Disruption of autonomic imbalance by nanoparticles that have a direct effect on cardiac and vascular function |
| **8** | Prolonged shelf life | Limited targeting abilities |
| **9** | Nanoparticles are regulated and stored at the location site for release, altering the organ distribution of drug compounds. | |

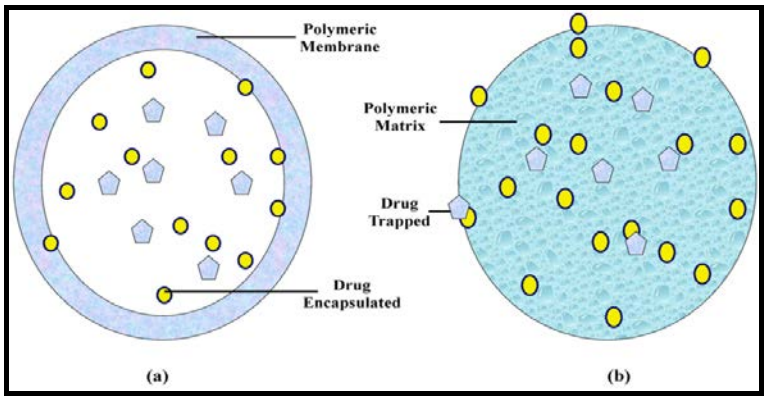
## Based on structure and morphology

Physical chemistry is same as that of colloidal dispersions. Surface charge, dispersibility, density, hydrophobicity and hydrophilicity determine the *in vivo* stability and disposition of nanoparticles.




**(a) Nanosphere:** Nanospheres are solid core spherical particulates containing drugs that are trapped in the matrix or adsorbed to the surface. (Matrix type)

(b) **Nanocapsules:** Nanocapsules are a vesicular device in which the drug is basically located in the central core enclosed by a polymeric sheath. (Reservoir type)

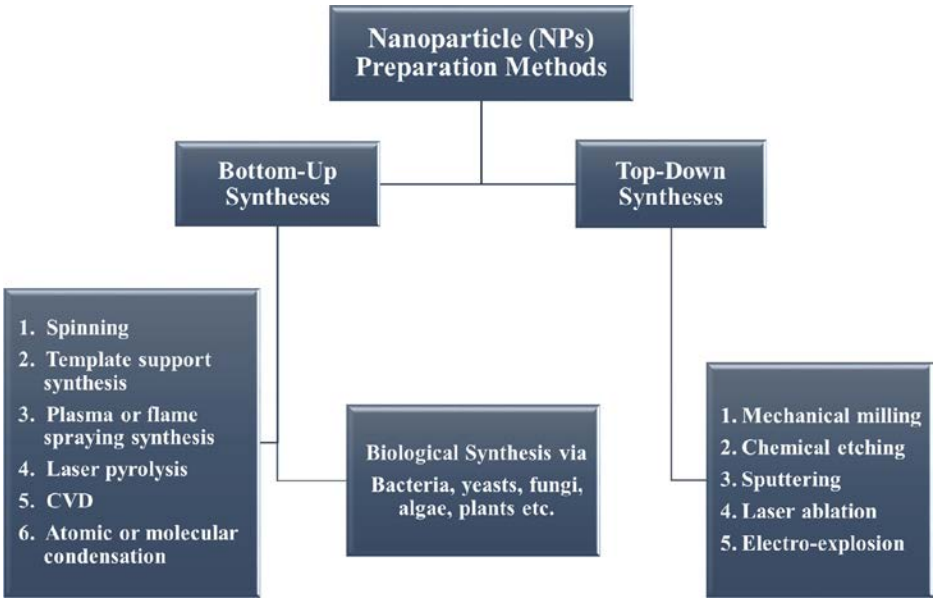


## Strategies used to synthesize Nanoparticles

Different methods can be used for Nanoparticle synthesis, but these methods are commonly divided into two key classes i.e., (1) Bottom-up approach and (2) Top-down approach. These approaches further divide into separate subclasses, based on process, reaction state and protocols adopted.

(1) **Bottom-up syntheses**: Nanosized materials are synthesized in the bottom-up methods by mixing materials on an atom scale.

(2) **Top-down syntheses:** The bulk materials are broken down into nanosize by milling or etching in the top-down method.




## Polymers used for nanoparticles preparation

### (1) Natural polymers

| PROTINES | POLYSACCHARIDES |
|---|---|
| Gelatin | Alginate |
| Albumin | Dextran |
| Lectins | Chitosan |
| Legumin | Agarose |
| Vicilin | Pullulan |

**(2) Synthetic polymers**

| Pre-polymerized | In phase, polymerised |
|---|---|
| Poly (e-caprolactone) | Poly (n-butyl cyanoacrylate) |
| Poly(lactide-co-glycolide) | Poly (isobutyl cyanoacrylate) |
| Poly (lactic acid) | Poly (hexyl cyanoacrylate) |
| Polystyrene | Poly (methyl methacrylate) |

**Polymers used for drug candidates when preparing nanoparticles and their techniques**

| Polymer use | Technique | Candidate drug |
|---|---|---|
| **Hydrophilic**<br>Albumin,<br>gelatin | Heat denaturation & cross linking in w/o emulsion<br>Desolvation &cross linking in aqueous medium | Hydrophilic<br>Hydrophilic & protein affinity |
| Alginate, chitosan | Cross linking in aq. medium | Hydrophilic & protein affinity |
| Dextran | Polymer precipitation in an organic solvent | Hydrophilic |
| **Hydrophobic**<br>Poly(alkylcyanoacrylates) | Emulsion polymerization<br>Interfacial/polymerization | Hydrophilic<br>Hydrophobic |
| **Polyesters**<br>Poly (lactic acid,<br>poly (lactide-co glycolide)<br>poly(e-caprolactone) | (a) Solvent extraction-evaporation<br>(b) Solvent displacement<br>(c) Salting out | Hydrophilic, Hydrophobic<br>Soluble in polar solvent<br>Soluble in polar solvent |

**Preparation of Nanoparticles**

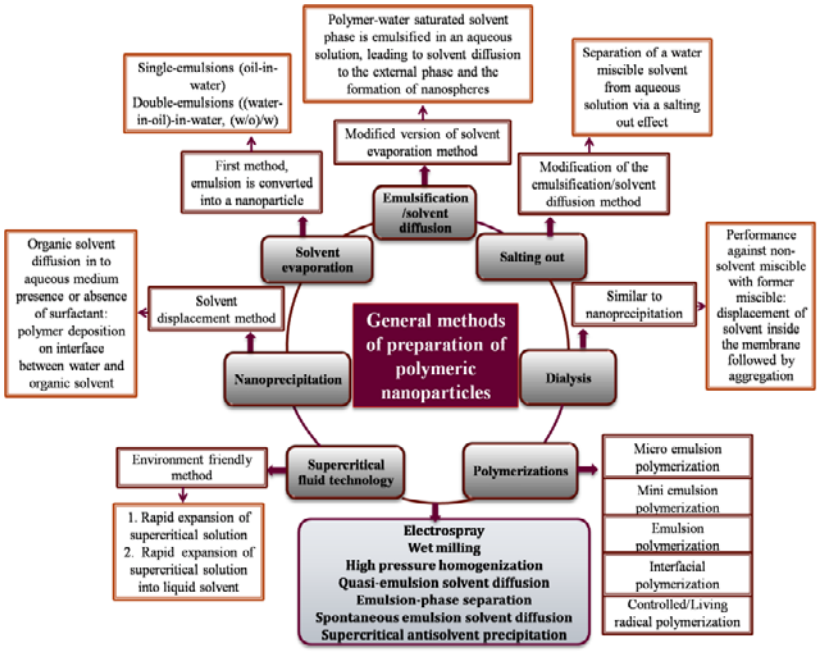
Nanoparticles may be made from a number of materials, including proteins , polysaccharides, and synthetic polymers. The choice of matrix materials depends on a number of factors including

- Size of nanoparticles required;
- Degree of biodegradability, biocompatibility and toxicity;
- Drug release profile desired; and
- Surface features like charging and permeability
- Final product anti-Genicity.
- Inherent properties, e.g. aqueous solubility and stability of the drug;

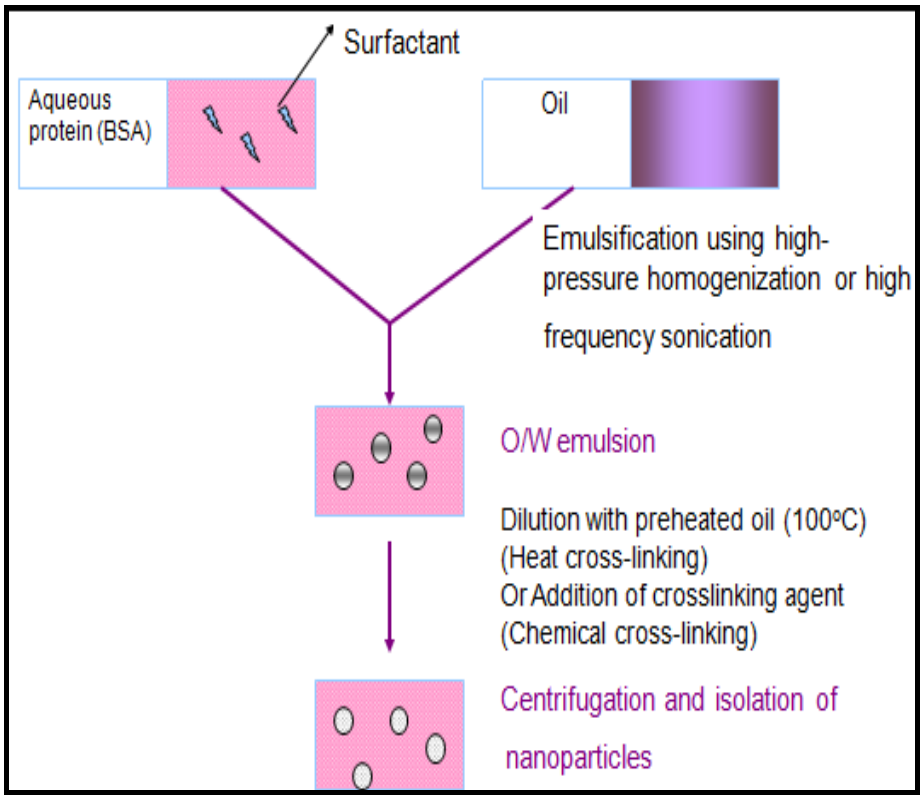
**Methods for preparations of nanoparticles**

1) **Amphiphilic macromolecule cross-linking**
   - Heat cross-linking
   - Chemical cross-linking
2) **Polymerization based methods**
   - Emulsion (micellar) polymerization
   - Polymerization of monomers in situ
   - Dispersion polymerization
   - Interfacial condensation polymerization
3) **Polymer precipitation methods**
   - Solvent extraction/evaporation

- Solvent displacement (nanoprecipitation)
- Salting out




**Amphiphilic macromolecule cross-linking**



**Polymerization based methods**

a) Emulsion (micellar) polymerization

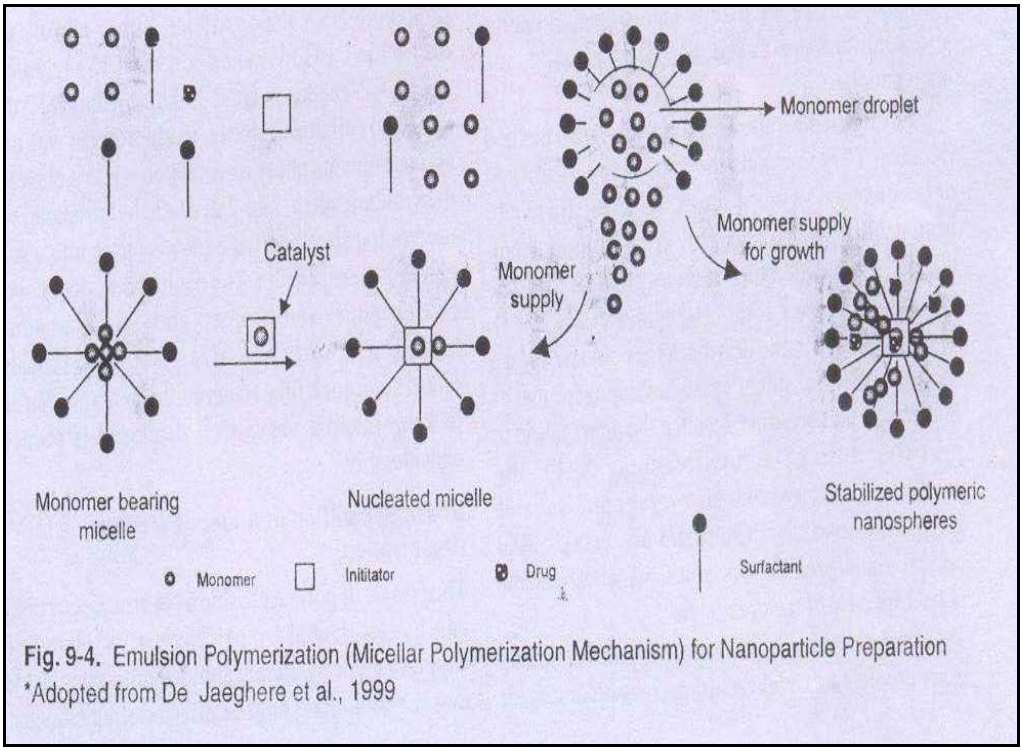



Fig. 9-4. Emulsion Polymerization (Micellar Polymerization Mechanism) for Nanoparticle Preparation
*Adopted from De Jaeghere et al., 1999

**b) Polymerization of monomers in situ**

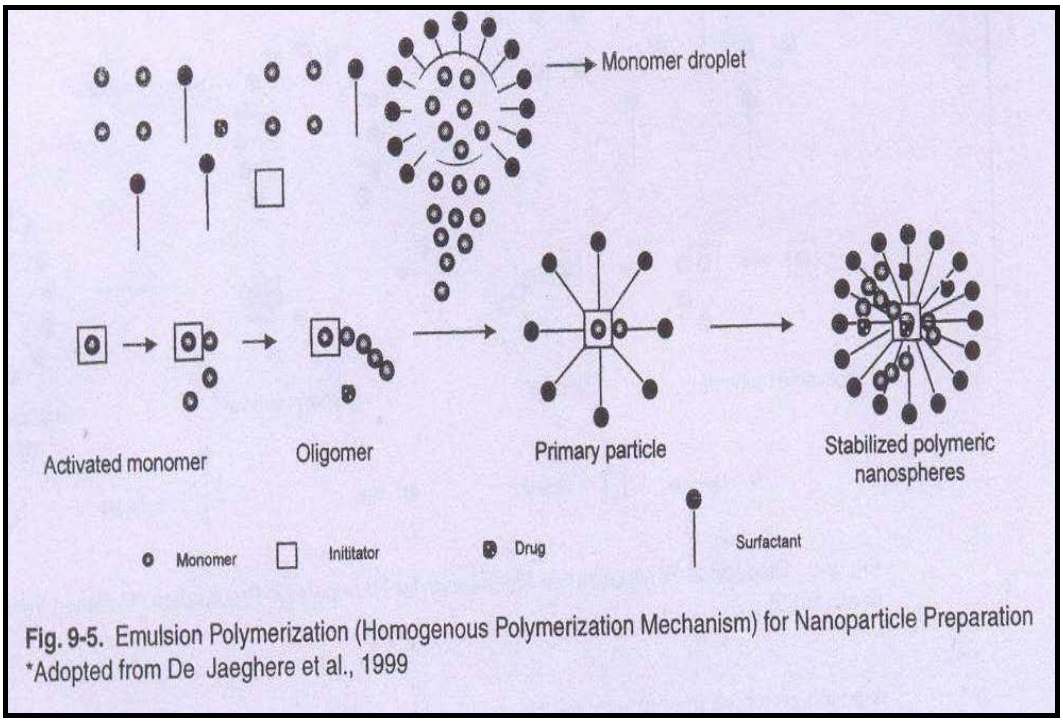
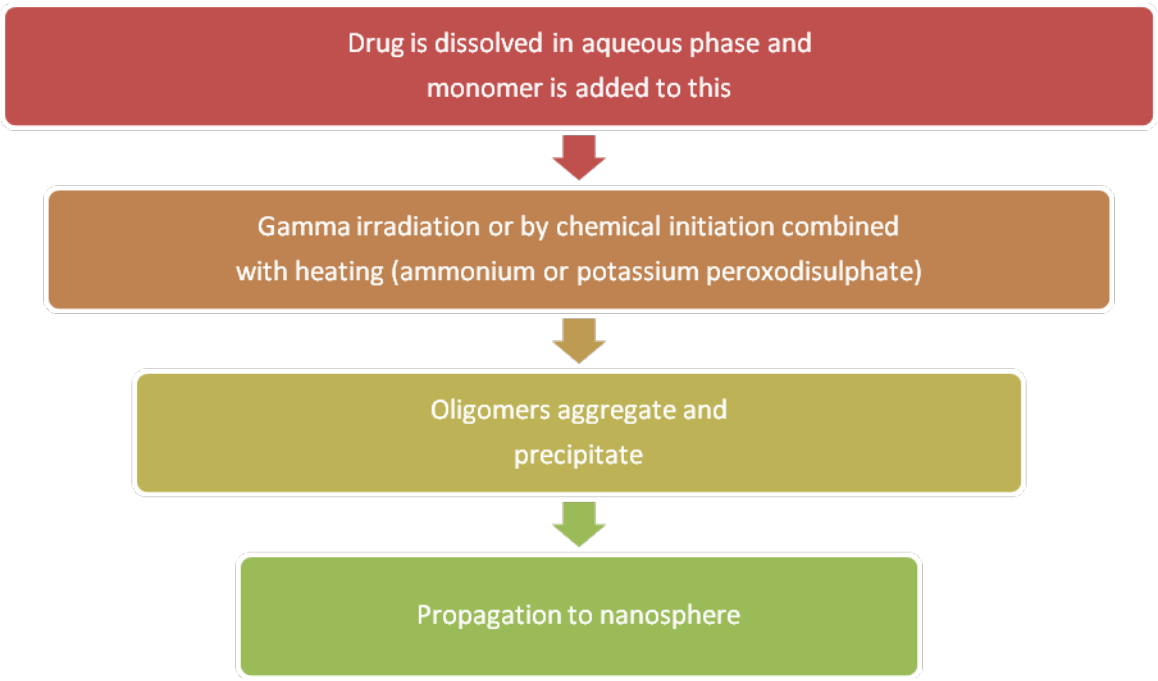



Fig. 9-5. Emulsion Polymerization (Homogenous Polymerization Mechanism) for Nanoparticle Preparation
*Adopted from De Jaeghere et al., 1999

c) Dispersion polymerization




**d) Interfacial condensation polymerization**

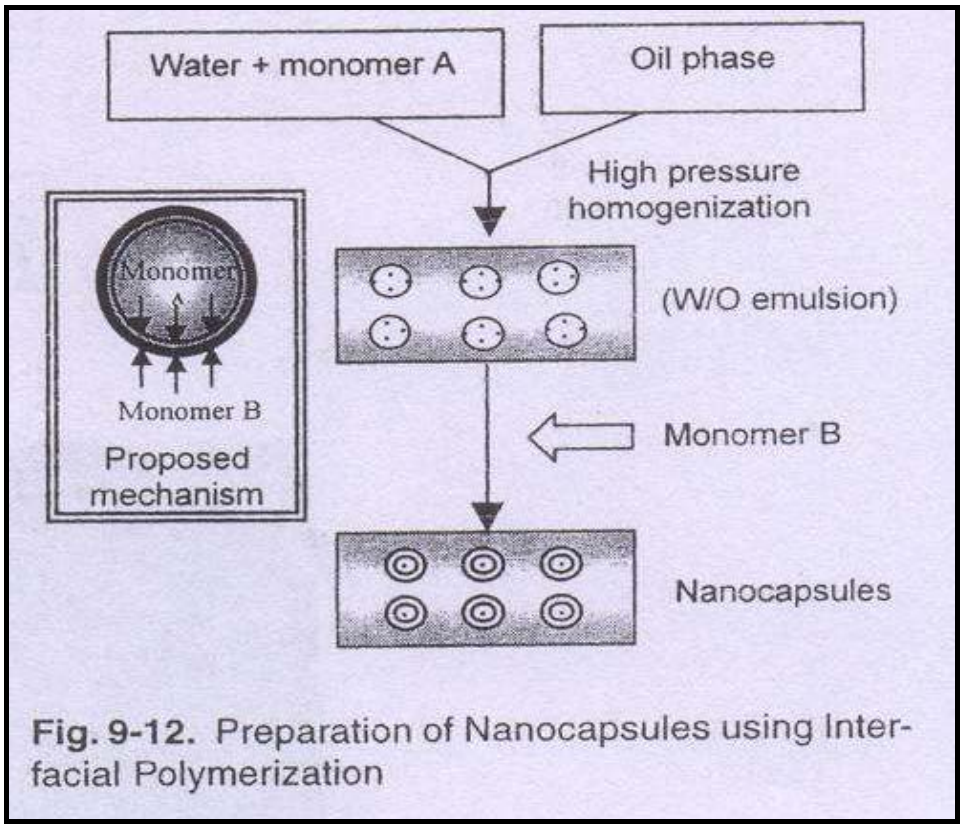



Fig. 9-12. Preparation of Nanocapsules using Inter-facial Polymerization

e) Interfacial complexation

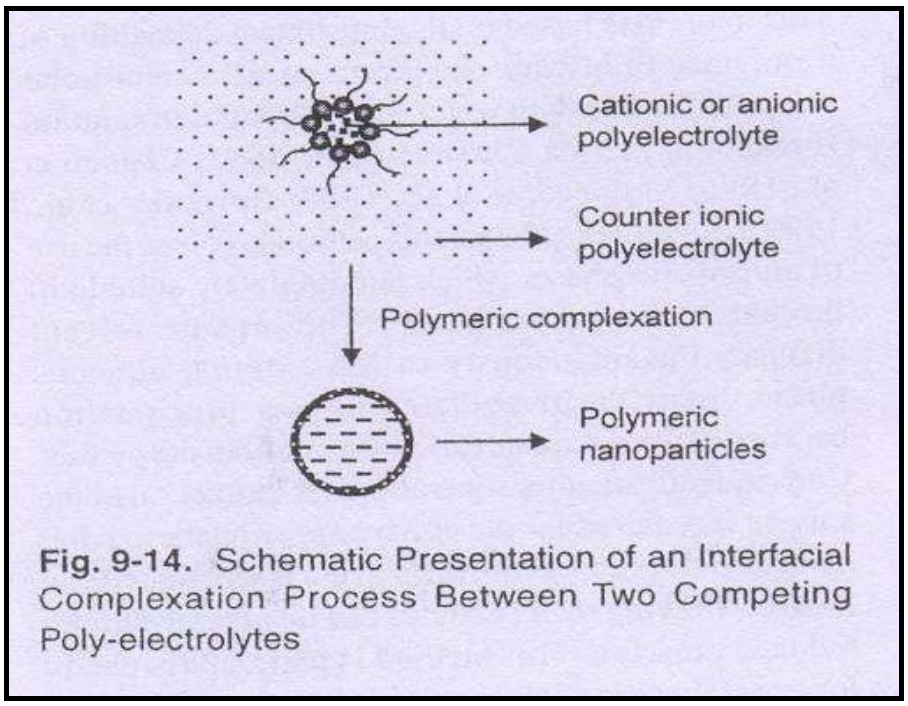



**Fig. 9-14.** Schematic Presentation of an Interfacial Complexation Process Between Two Competing Poly-electrolytes

**1) Polymer precipitation methods**

**a)** Solvent extraction/evaporation

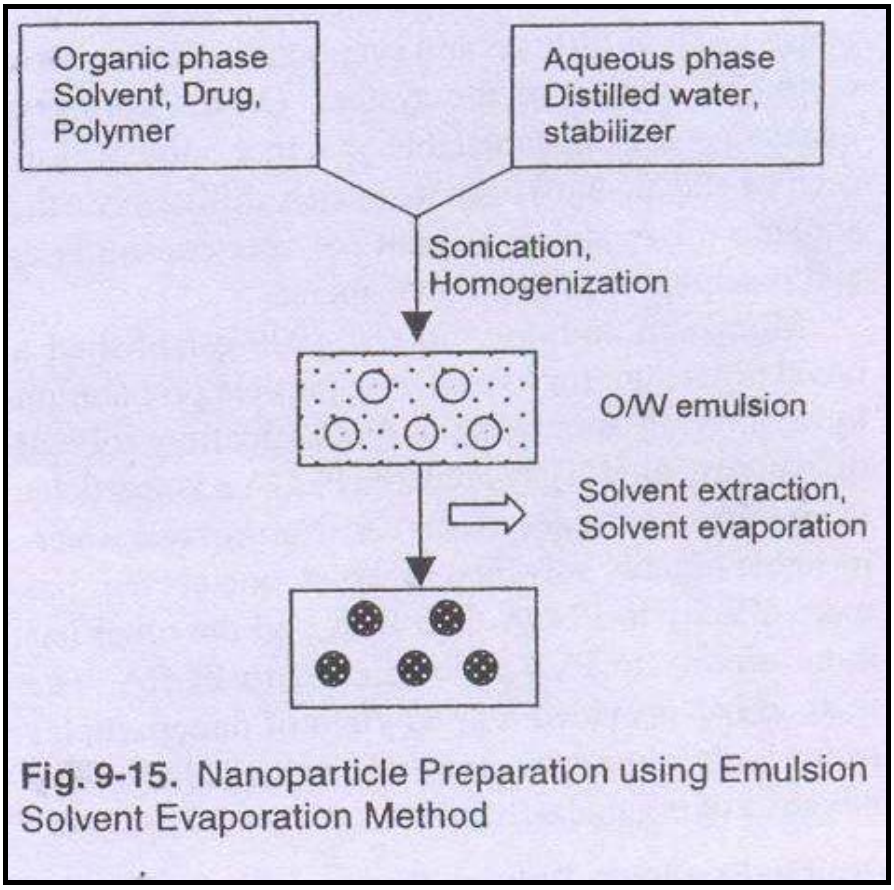



**Fig. 9-15.** Nanoparticle Preparation using Emulsion Solvent Evaporation Method

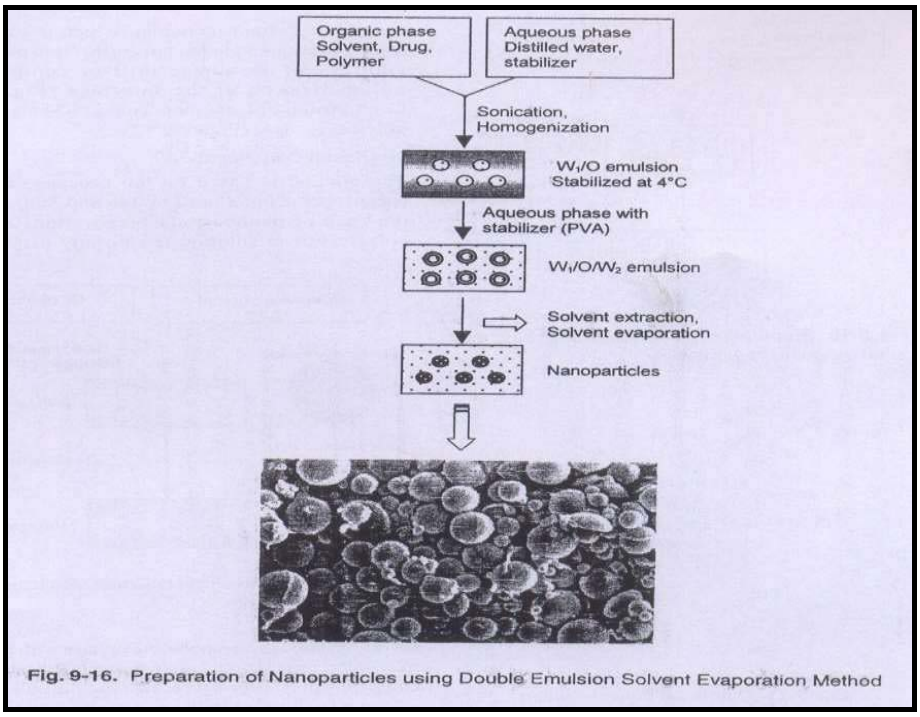



Fig. 9-16. Preparation of Nanoparticles using Double Emulsion Solvent Evaporation Method

b) Solvent displacement (nanoprecipitation)

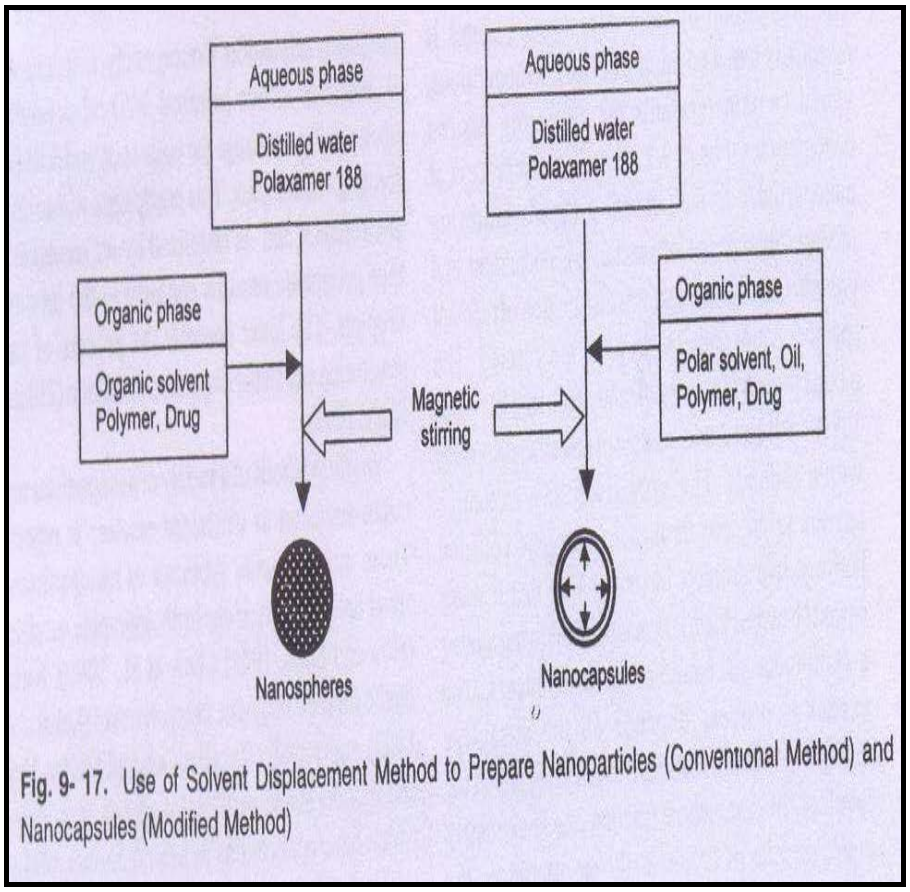



Fig. 9- 17. Use of Solvent Displacement Method to Prepare Nanoparticles (Conventional Method) and Nanocapsules (Modified Method)

c) Salting out

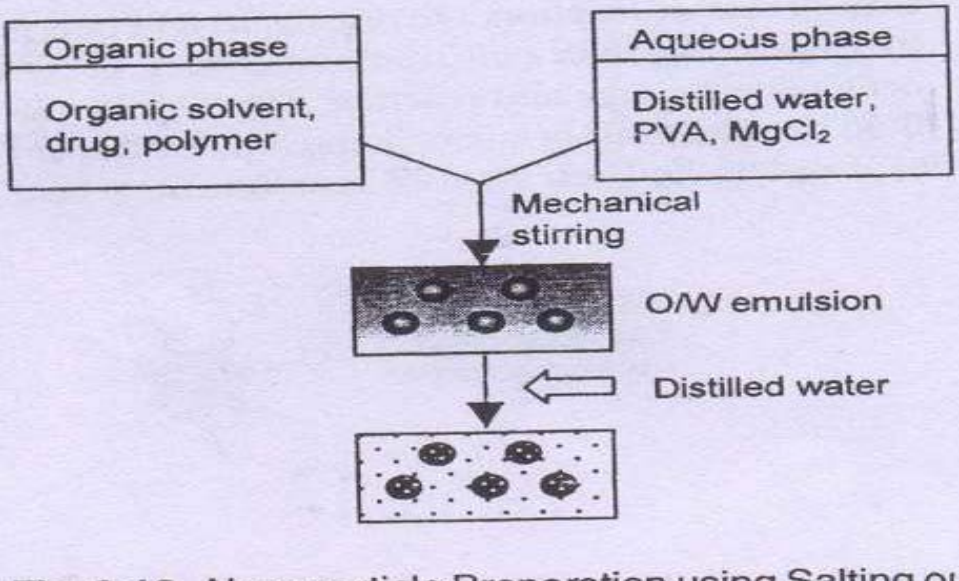



Fig. 9-18. Nanoparticle Preparation using Salting out of Polymer

**Characterization of nanoparticles**

| S.no | Parameters | Technique |
|---|---|---|
| **1** | Particle size | 1. Photon correlation spectroscopy<br>2. Transmission electron microscopy<br>3. Scanning electron microscopy |
| **2** | Specific surface area | Sorptometer |
| **3** | Charge determination | Laser Doppler Anemometry<br>Zetasizer |
| **4** | Surface hydrophobicity | 1. Hydrophobic interaction chromatography<br>2. Water contact angle measurement<br>3. X-ray photoelectron spectroscopy |
| **5** | Density | Helium pycnometer |
| **6** | Molecular weight | Gel permeation chromatography |
| **7** | Nanoparticle dispersion stability | Critical flocculation temperature(CFT) |
| **8** | *In vitro* release | 1. Dialysis bag method<br>2. Diffusion cell<br>a) Frnaz cell<br>b) Side by side diffusion cells<br>3. Ultrafiltration<br>4. Ultracentrifugation |
| **9** | Drug stability | Drug-chemical analysis<br>Bioassay of drug extacted from Nanoparticles |

## Applications of nanoparticles

A list of some of the biological or medicinal applications of nanoparticles is given below

- Fluorescent biological labels
- 2. Delivery of drug and gene
- Pathogens can be detected
- Proteins can be detected

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