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# A Review on Synthesis and Preparation of Nanoparticles

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## ABSTRACT

Nanotechnology defined as a tiny science. Now a day, there has been an exponential interest in the development of novel drug delivery systems using nanoparticles. Several techniques are used for preparation of nanoparticles like Solvent evaporation, Double emulsification method, Emulsions - diffusion method, Nano precipitation, Coacervation method, Salting out method, Dialysis and supercritical fluid technology. This review focuses on various synthesis and preparation methods of nanoparticles.

**Keywords:** Nanotechnology, Nanoparticles, Synthesis of nanoparticles, Preparation techniques

## INTRODUCTION

Nanoparticles can be defined as objects ranging in size from 1-100 nm that due to their size may differ from the bulk material [1]. Nanoparticles are defined as particulate dispersions or solid particles drug carrier that may or may not be biodegradable [2]. Nanoparticles are having application in various fields of life sciences such as separation technologies, histological studies, clinical diagnostic assays and drug delivery systems [3]. The major goals in designing nanoparticles as a delivery system are to control particle size, surface properties and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen. Though liposomes have been used as potential carriers with unique advantages including protecting drugs from degradation, targeting to site of action and reduction toxicity or side effects, their applications are limited due to inherent problems such as low encapsulation efficiency, rapid leakage of water-soluble drug in the presence of blood components and poor storage stability [4].

## SYNTHESIS OF NANOPARTICLES

Nanoparticles can be synthesized chemically or biologically. Many adverse effects have been associated with chemical synthesis methods due to the presence of some toxic chemical absorbed on the surface. Eco-friendly alternatives to chemical and physical methods are biological ways of nanoparticles synthesis using microorganisms, enzymes, fungus and plants or plant extracts [5-8].

### Biosynthesis of nanoparticles

Biosynthesis of nanoparticles by microorganisms is a green and eco-friendly technology. Diverse microorganisms, both prokaryotes and eukaryotes are used for synthesis of metallic nanoparticles [9]. The synthesis of nanoparticles may be intracellular or extracellular according to the location of nanoparticles [10].

### Intracellular synthesis of nanoparticles by microbes

This method involves transport of ions into microbial cells to form nanoparticles in the presence of enzymes. As compared to the size of extracellularly reduced nanoparticles, the nanoparticles formed inside the organism are smaller. The size limit is probably related to the particles nucleating inside the organisms [11].

### Extracellular synthesis of nanoparticles by microbes

Extracellular synthesis of nanoparticles has more applications as compared to intracellular synthesis since it is void of unnecessary adjoining cellular components from the cell. Mostly, fungi are known to produce nanoparticles extracellularly because of their enormous secretory

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components, which are involved in the reduction and capping of nanoparticles [11].

## PREPARATION TECHNIQUES

### Solvent evaporation

Solvent evaporation method first developed for preparation of nanoparticles [12]. Polymer dissolved in organic solvent. Drug is dispersed in this solution. Then this mixture emulsified in an aqueous phase containing surfactant make an ion in water emulsion by using mechanical stirring, sonication or micro fluidization. After formation of emulsion the organic solvent evaporates by increased the temperature and reduced pressure with continuous stirring [13].

### Double emulsification method

Double emulsification technique is prepared by addition of aqueous drug solution to organic polymer solution with continuous stirring. This prepared emulsion another aqueous phase with vigorous stirring, results emulsion prepared, then organic solvent removed by high centrifugation [14].

### Emulsions - Diffusion method

In this method polymer dissolved in water-miscible solvent and saturated with water. Polymer-water saturated solvent phase is emulsified in an aqueous solution containing stabilizer. Then solvent removed by evaporation or filtration [15].

### Nano precipitation method

In this method precipitation of polymer and drug obtained from organic solvent and the organic solvent diffused in to the aqueous medium with or without presence of surfactant. Firstly drug was dissolved in water and then solvent was added into this solution. Then another solution of polymer and propylene glycol with chloroform prepared and this solution was dispersed to the drug solution. This dispersion was slowly added to 10 ml of 70% aqueous ethanol solution. After 5 min of mixing, the organic solvents were removed by evaporation at 35° under normal pressure, nanoparticles were separated by using cooling centrifuge, supernatant were removed and nanoparticles washed with water and dried at room temperature in a desiccator [16].

### Coacervation method

By using biodegradable hydrophilic polymers nanoparticle prepared by Coacervation method. This nanoparticle was prepared by ionic gelation method which involves two aqueous phases. First phase contain polymer like chitosan, a di-block co-polymer like ethylene oxide or propylene oxide. Second phase contain polyanion sodium tripolyphosphate. Between these two phases electrostatic interaction occurs which forms coacervates [17]. Drug and protein solution (2% w/v) incubated for one hour at room temperature and pH adjusted to 5.5 by using 1 M HCl. In this solution ethanol was added in 2:1 ratio (v/v) in a control rate 1 ml/min. Resultant coacervate hardened with 25% glutaraldehyde (1.56 µg/mg of protein) for 2 h which allow cross-linking of protein. Rotary vacuum evaporation at reduced pressure organic solvents were removed then nanoparticle were collected and purified by centrifugation at 4°C. Pellets of nanoparticles were then suspended in phosphate buffer (pH 7.4; 0.1 M) and lyophilized with mannitol (2% w/v) at –48°C and $28 \times 10^{-3}$ M Bar pressure for 24 h [18].

### Salting out method

This technique based on the separation of water-miscible solvent from aqueous solution by salting out effect. In this method toxic solvents are not used. Polymer and drug dissolved in a solvent which emulsified into a aqueous solution containing salting out agent but salting out can also be produced by saturation of the aqueous phase using colloidal stabilizer/emulsion stabilizer/viscosity increasing agent such as polyvinyl pyrrolidone or hydroxyethylcellulose, PVA, PLGA and poly(trimethylene carbonate). After preparation of o/w emulsion diluted with addition of sufficient water to allow the complete diffusion of acetone into the aqueous phase, thus inducing the formation of nanospheres. This technique does not require an increase in temperature and stirring energy required for lower particle size. Disadvantage of this technique is exclusive application to lipophilic drug and the extensive nanoparticles washing steps [15].

### Dialysis

Dialysis is an effective method for preparation of nanoparticles. In this method firstly polymer and drug dissolved in an organic solvent. This solution added to a dialysis tube and dialysis performed against a non-solvent miscible with the former miscible. The displacement of the solvent inside the membrane is followed by the progressive aggregation of polymer due to a loss of solubility and the formation of homogeneous suspensions of nanoparticles. Dialysis mechanism for formation of nanoparticle is not fully understood at present. It may be based on a mechanism similar to that of nanoprecipitation [16].

### Supercritical fluid technology

Supercritical fluid technology method is alternative method because in this method organic solvents are not used which are hazardous to the environment as well as to physiological systems. Supercritical fluids define as a solvent at a temperature above its critical temperature at which the fluid remains a single phase regardless of pressure.

Mainly supercritical fluid used in two main techniques:

1) Supercritical anti-solvent (SAS)

2) Rapid expansion of critical solution (RESS)

**Super critical anti-solvent**

In SAS process liquid solvents are used, which should completely miscible with the supercritical fluid. The process of SAS employs a liquid solvent, e.g. methanol, which is completely miscible with the supercritical fluid, the extract of the liquid solvent by supercritical fluid leads to the instantaneous precipitation of the solute, it results the formation of nanoparticles [18].

**Rapid expansion of critical solution**

In RESS high degree of super saturation occur by dissolving solute in a supercritical fluid to form a solution, followed by the rapid expansion of the solution across an orifice or a capillary nozzle into ambient air by the rapid pressure reduction in the expansion which results in homogenous nucleation and thereby, the formation of well-dispersed particles [15].

## CONCLUSION

Nanoparticle technologies have great potentials, being able to convert poorly soluble, poorly absorbed and labile biologically active substance into promising deliverable substances. Nanoparticle is novel approach for drug delivery which we can achieve better therapeutic action, better bioavailability, reduce toxicity. Today nanoparticles are successfully used in brain targeting, in cancer therapy, etc.

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