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DIFFERENT TECHNIQUES EMPLOYED FOR THE PREPARATION OF NANOPARTICLES: AN OVERVIEW

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ABSTRACT

Polymeric nanoparticles (PNPs) are defined as particulate dispersion or solid particles with the size in the range of 10-1000nm.In present time nanoparticles are widely used in many dosage forms due to their good solubility, less size and better penetrability. Nanoparticles can be prepared by using various methods such as Solvent evaporation, salting out, dialysis, and supercritical fluid technology. The choice of method depends on particle size, particle size distribution etc. Polymeric nanoparticles have been extensively studied as particulate carriers in the pharmaceutical and medical fields because they have controlled and sustained release properties. In this review the different techniques for preparation of polymeric nanoparticles are described.

Keywords: Polymeric nanoparticles, particulate carriers.

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]

DEFINITION AND CLASSIFICATION OF POLYMERS:

Nanoparticles are frequently defined as solid, colloidal particles in the range 10–1000nm.[5,6] The term PNP is a collective term given for any type of polymer nanoparticle, but specifically for nanospheres and nanocapsules. Nanospheres are matrix particles, i.e., particles whose entire mass is solid, and molecules may be adsorbed at the sphere surface or encapsulated within the particle. In general, they are spherical, but “nanospheres” with a non spherical shape are also described in the literature [7]. Nanocapsules are vesicular systems, acting as a kind of reservoir, in which the entrapped substances are confined to a cavity consisting of a liquid core (either oil or water) surrounded by a solid material shell [8].

Advantages of polymeric nanoparticles [9,10]

- Increase the stability of any volatile pharmaceutical agents, easily and cheaply fabricated in large quantities by multiple methods.
- They offer a significant improvement over traditional oral and intravenous method of administration.
- The choice of polymer and the ability to modify drug release from polymeric nanoparticles have made them ideal candidates for cancer therapy.

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PREPARATION OF NANOPARTICLES:

The selection of appropriate method for the preparation of nanoparticles depends on the physiochemical characters of the polymer and drug to be loaded.

The primary method for the nanoparticles includes:

(A) Solvent evaporation [11, 12]:

Solvent evaporation method first developed for preparation of nanoparticles. 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.

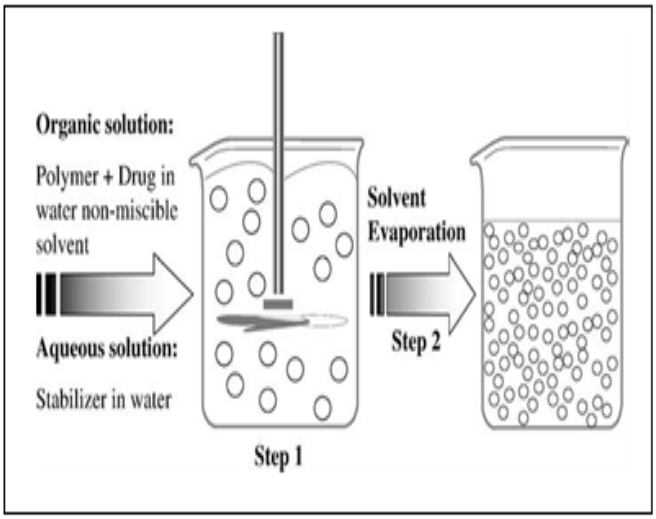

Fig. 1: Schematic representation of solvent evaporation technique [13].

(B)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].

(C) Nanoprecipitation:

Nanoprecipitation is called solvent displacement method. It involves the precipitation of the performed polymer from an organic solution and the diffusion of organic solvent in the aqueous medium in the presence or absence of surfactant [15-18].

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 desiccators [19].

(D) SALTING OUT METHOD:

By using salting-out from aqueous solution the water miscible solvent is separated using this method. Initially in a solvent, polymer and drug are dissolved which is consequently containing the salting out agents (electrolytes such as calcium chloride, magnesium chloride or sucrose as nonelectrolytes) and polyvinylpyrrolidone (PVP) or hydroxyethyl cellulose as a colloidal stabilizer into an aqueous gel. This oil in water emulsion is diluted with water or with aqueous phase to increase the diffusion of solvent which indicates the formation of nanospheres, several parameters such as electrolyte concentration, concentration of polymers in the organic phase. Salting out may be useful for heat sensitive substance because an increase of temperature does not require in this technique. Lipophillic drug and the extensive nanoparticles washing steps are drawbacks of this method (20).

(E)COACERVATION OR IONIC GELATION 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 [21]. 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 × 10^{-3} M Bar pressure for 24 h [22].

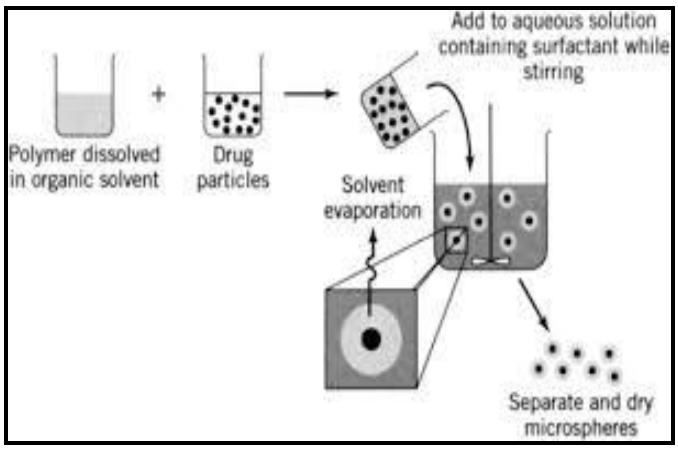

Fig. 2: Schematic representation of coacervation method. [23]

(F) POLYMERIZATION METHOD:

In this method, polymerization of monomer is done in an aqueous solution and after polymerization is completed, drug is incorporated either by adsorption onto the nanoparticles or by being dissolved in the polymerization medium. To remove various stabilizers and surfactants employed for polymerization by ultracentrifugation the nanoparticle suspension is then purified and in an isotonic

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surfactant free medium re suspending the particles. For the preparation of poly (alkyl cyanoacrylate) nanoparticles, this technique is reported. Formation of nano capsule and their particle size affected by the surfactants and stabilizers concentration used [24].

(G) SOLVENT DISPLACEMENT/PRECIPITATION METHOD:

Solvent displacement includes from an organic solution, the precipitation of preformed polymer and in the aqueous medium the diffusion of the organic solvent in the presence or absence of surfactant. In a semi polar water miscible solvent such as acetone or ethanol, polymers, drugs and lipophilic surfactants are dissolved. Then the solution is poured using a magnetic stirrer into a stabilizer containing aqueous solution. Then, by the rapid solvent diffusion nanoparticles are formed. By using reduced pressure solvent is removed from the suspension [25]. Mostly for the poorly soluble drugs nano precipitation is well suited. By adjusting preparation parameters, nanosphere size, and drug release can be controlled effectively. While adjusting concentration of polymer results in good production of smaller sized nanospheres [26].

(H) DIALYSIS:

Dialysis offers a simple and effective method for the preparation of small, narrow-distributed polymeric nanoparticles [27, 28]. Polymer is dissolved in an organic solvent and placed inside a dialysis tube with proper cut off the molecular weight. Dialysis is 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 the polymer due to the loss of solubility and formation of homogeneous suspension of nanoparticles. Though, this mechanism is not fully understood at present.

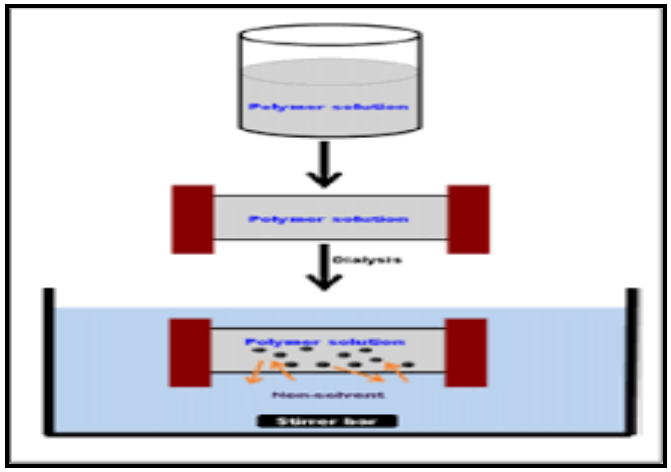

Fig. 3: Schematic representation of osmosis-based method for preparation of polymeric nanoparticles [27].

(I)SUPERCRITICAL FLUID TECHNOLOGY:

This method is an alternative method because in this method organic solvents are not used as they are hazardous to the environment as well as to the biological system. Super critical fluids are defined as a solvent at a temperature above its critical temperature at which the fluid remains at a single phase regardless of pressure.

Mainly super critical fluid used in two main techniques:

- Super critical anti- solvent (SAS)
- Rapid expansion of critical solution (RESS)

Super critical anti- solvent:

In SAS process liquid solvents are used eg: methanol which is completely miscible with the super critical fluid, the extract of the liquid solvent by super critical fluid leads to the instantaneous precipitation of the solute, it results in the formation of the nanoparticles.

Rapid expansion of critical solution:

In RESS high degree of super saturation occur by dissolving solute in super critical fluid to form a solution, which is followed by the rapid expansion of the solution across the orifice or the capillary nozzle, which results in the homogeneous nucleation and thus production of well-deserved polymeric nano-particles.

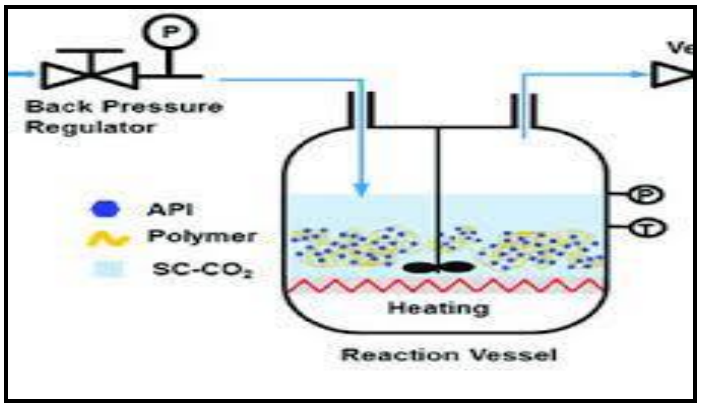

Fig. 4: Schematic representation of super critical fluid technology [28].

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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