Review

Production of protein nanoparticles for food and drug delivery system

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Proteins nanoparticles are one of the new methods for food delivery systems. The protein nanoparticles which represent promising carriers for delivery are fabricated based on different methods. Synthetic protein nanostructure acts as surrogate mimics such as viruses and plasmid for food and drug delivery system. The benefits of protein nanoparticles include non-toxicity, stability for long duration, nonantigenicity and biodegradability. The purpose of this paper was to explain different ways of fabrication of nanoparticles in the unique range which is suitable for the food and drug delivery system

Key words: Biological nanoparticles, food and drug delivery, coacervation method, drug loading.

INTRODUCTION

Nanobiotechnology have wide range of application, one of them is application of nanoparticles for delivery system (Rieux et al., 2006). Nanoparticles were first developed around 1970. They were initially devised as carrier for vaccines and anticancer (Mageti and Ravikumar, 2000). Over the past few decades, there has been considerable interest in developing biodegradable nanoparticles (liposome, virus like particle (VLP), protein, etc.) as effective food and drug delivery device (Barat et al., 2008; Jung et al., 2008; Kumaresh et al., 2001; Jahanshahi et al., 2004). Nanoparticles have become an important area of research in the field of food and drug delivery vehicles (Hans and Lowman, 2002). The major advantage of colloidal food or drug carrier systems is the possibility of food (drug) targeting by a modified body distribution as well as the enhancement of the cellular uptake of a number of substances and their ability to deliver a wide range of drugs to varying areas of the body for sustained periods of time (Hans and Lowman, 2002; Weber et al., 2000). Nanoparticles generally vary in size from 10 to 1000 nm (Kumaresh et al., 2001; Couvreur et al., 2006). Recently protein nanoparticles have been shown efficacy as biodegradable carrier (Rahimnejad, 2006a; Jahanshahi et al., 2008), which can incorporate variety of

drugs in relatively non-specific fashion. The food or drug is dissolved, entrapped, encapsulated or attached to a nanoparticles matrix and depending upon the method of preparation, nanoparticles, nanospheres or nanocapsules can be obtained. Nanocapsules are vesicular systems in which the drug is confined to a cavity surrounded by a unique polymermembrane, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed (Kumaresh et al., 2001; Hans and Lowman, 2002). Figure 1 shows the schematic diagram of nano-capsulated and nanosphere particles loaded with food or drug.

Among these colloidal system those based on protein may be vary promising since they are biodegradable and non-antigenic relatively easy to prepared and their size-distribution can be monitored easily (weber et al., 2000). A wide variety of drugs can be delivered using nano-particulate carriers via a number of routes. Nanoparticles can be used to deliver hydrophilic drugs, hydrophobic drugs, proteins, vaccines, biological macromolecules, etc (Hans and Lowman, 2002). Advantages of nanoparticle for drug and food delivery systems:

1. Biodegradability
2. Lack of toxic
3. Non-antigenic
4. Stable and have long shelf life
5. Higher loading capacity for hydrophilic molecules compared other colliodal systems

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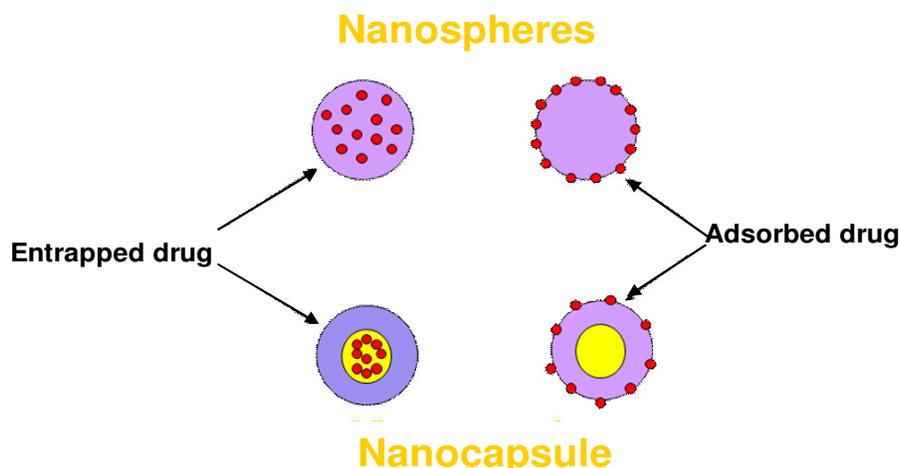
Nanospheres

Figure 1. Schematic diagram of encapsulated and coated nanoparticle in drug delivery system (Rahimnejad, 2006a).

6. Control Release of drugs
7. Ability to deliver proteins, peptides and gene
8. Carrier of DNA in gene therapy.

Another promising class of nano-sized vehicles that have been considered in food and drug delivery application is liposomes (Kumaresh et al., 2001; Hans and Lowman, 2002; weber et al., 2000). These vesicles prepared from lipids have been used as potential drugs carrier because of the protection they can offer drugs contained in their core. However liposomes have shown a low encapsulation efficiency, poor storage stability and rapid leakage of water-soluble drugs in the blood (Kumaresh et al., 2001; Hans and Lowman, 2002)

The bio distribution of intravenously injected carriers is mainly influenced by their physicochemical properties, e.g. particle size and surface characteristics (Langer et al., 2003). Larger particles are more rapidly removed by the liver and spleen than smaller particles. Reducing the particle size of colloidal carriers below a threshold of 100 to 200 nm introduces the possibility of escaping the vascular system via fenestrations or cavities in the lining of blood vessels (Muller et al., 1996).

And also polymeric materials used for the formulation of nanoparticles include synthetic (poly(lactic acids) (PLA), poly(lactic-coglycolic acids) (PLGA), poly(ε-caprolactone) (PCL), poly(methyl methacrylates) and poly(alkyl cyanoacrylates)) or natural polymers (albumin, gelatin, alginate, collagen or chitosan). Polyesters, alone and in combination with other polymers, are the most commonly used for the formulation of nanoparticles (Rieux et al., 2006; Walter, 2001).

FABRICATION METHODS

Protein nanoparticels can be obtained by different

methods (Aghajani et al., 2004; Rahimnejad, 2006b). Protein noparticles have been extensively studied as suitable for drug delivery since they are biodegradable, non-toxic and non antigenic, because of their defined primary structure and high content of charged amino acids (that is, lysine). The protein-based nanoparticles could allow the electrostatic adsorption of positively or negatively charged molecules without the requirements of other compounds. In addition, protein nanoparticles can be easily prepared under soft condition, by coacervation or controlled desolvation processes (Arnedo et al., 2002; Aghajani et al., 2004)

Among the available potential colloidal drug carrier systems covering the size range described, protein-based nanoparticles play an important role (Rahimnejad et al., 2006c; Langer et al., 2003). Biopolymers, such as proteins, are commonly used to encapsulate oil-in-water emulsions (Mageti and Ravikumar, 2000). Simple and complex coacervation, spray drying and heat denaturation represent three major microencapsulation techniques based on proteins. Their principles are quite similar: emulsification of the core material (oil) is followed by microcapsules wall formation induced by environmental conditions changing. Concerning simple coacervation method, the protein precipitation around oil droplets is obtained by changing pH and temperature or by the "salting-out" technique. Widespread presence of microcapsules based on animal proteins such as gelatin, casein or albumin contrasts with a very limited use of plant proteins. Wheat gliadin was one of the rare plant storage proteins used for encapsulation of dispersed oil phase by simple coacervation method (Lazko et al., 2004). Figures 1 to 7 shows the schematic diagram of different methods for fabrication of particles.

The disadvantage of the emulsion method for particle preparation is the need for applying organic solvent, for the removal both of the oily residues of the preparation
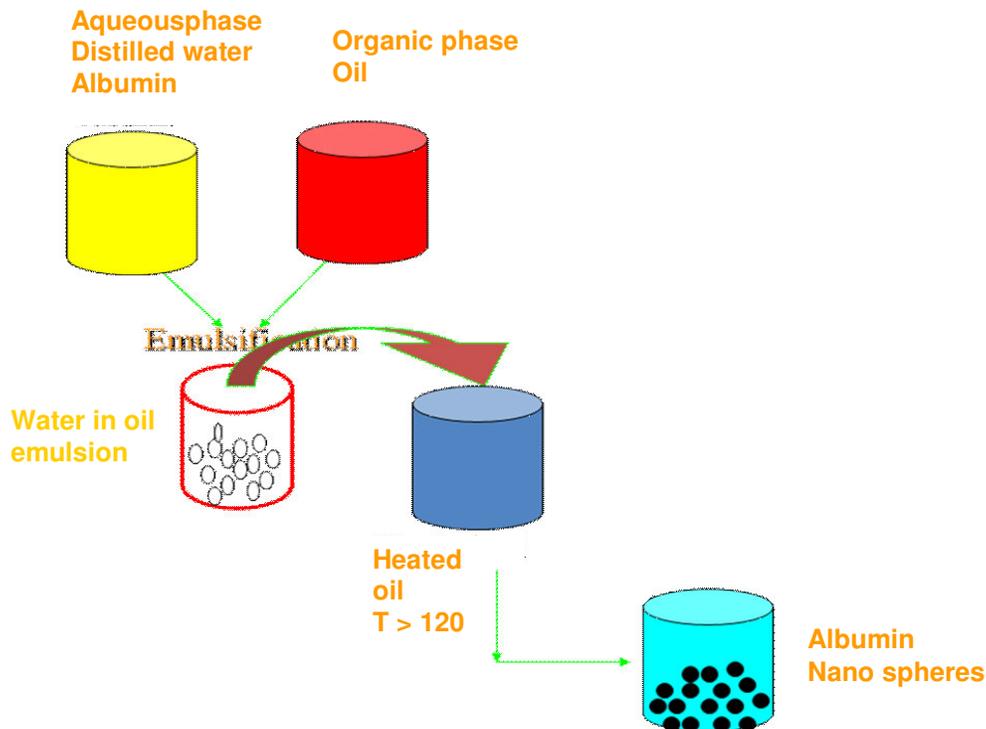
Figure 2. Production of nanoparticle by thermal denaturation. Drawbacks: Particles must be submitted to several washings using large amounts of organic solvent for complete removal of the oil and also some drugs are heat-sensitive (Rahimnejad, 2006b).
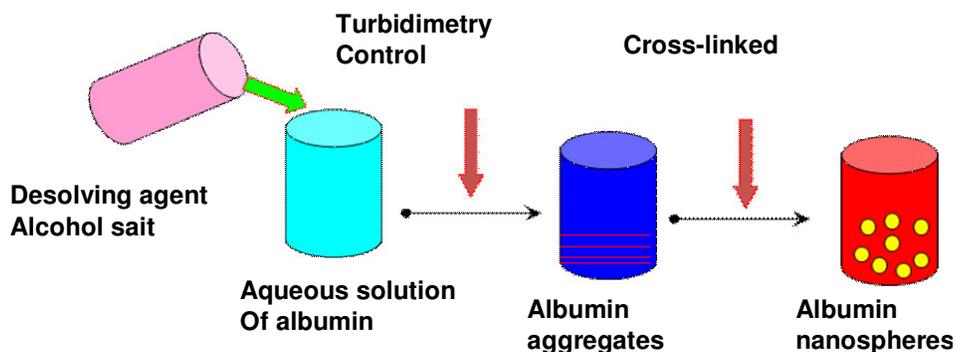

Figure 3. Preparation of nanospheres by desolvation (simple coacervation) method (Rahimnejad, 2006b).

process and surfactants required for emulsion stabilization (Langer et al., 2003) and it is difficult to obtain protein nanoparticle less than 500 nm by emulsification cross linking method (Kumaresh et al., 2001). The size and surface charge of the nanoparticles are crucial for their uptake (Hans and Lowman, 2002)

Coacervation is the separation into two liquid phases in colloidal systems (Kruif et al., 2004). The phase more concentrated in colloidal component is the coacervate and the other phase is the equilibrium solution. Associative phase separation of two polymers in water occurs if there is an electrostatic attraction (Kruif et al 2004,

Mohanty and Bohidar 2003). Complex coacervation is a process of spontaneous phase separation that occurs when two oppositely charged polyelectrolytes are mixed in an aqueous solution. The electrostatic interaction between the two species of macromolecules results in the separation of a coacervate (polymer-rich phase) from the supernatant (polymer-poor phase). This phenomenon can be used to form microspheres and encapsulate a variety of compounds. The encapsulation process can be performed entirely in aqueous solution and at low temperatures, and has a good chance, therefore, of preserving the bioactivity of the encapsulant.
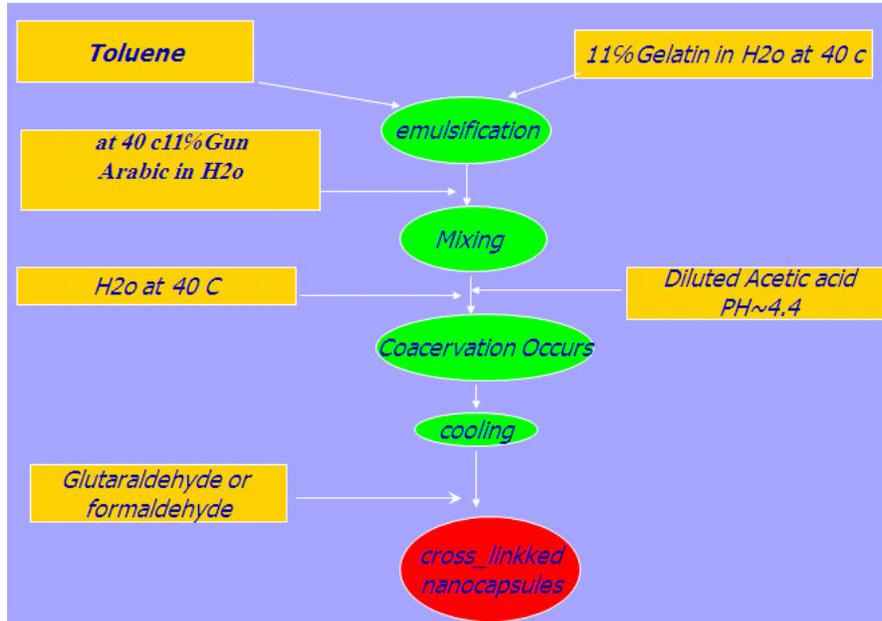
Figure 4. Preparation of nanospheres by Complex Coacervation. The electrostatic interaction between the two species of macromolecules results in the separation of a coacervate (polymer-rich phase) from the supernatant (polymer-poor phase).
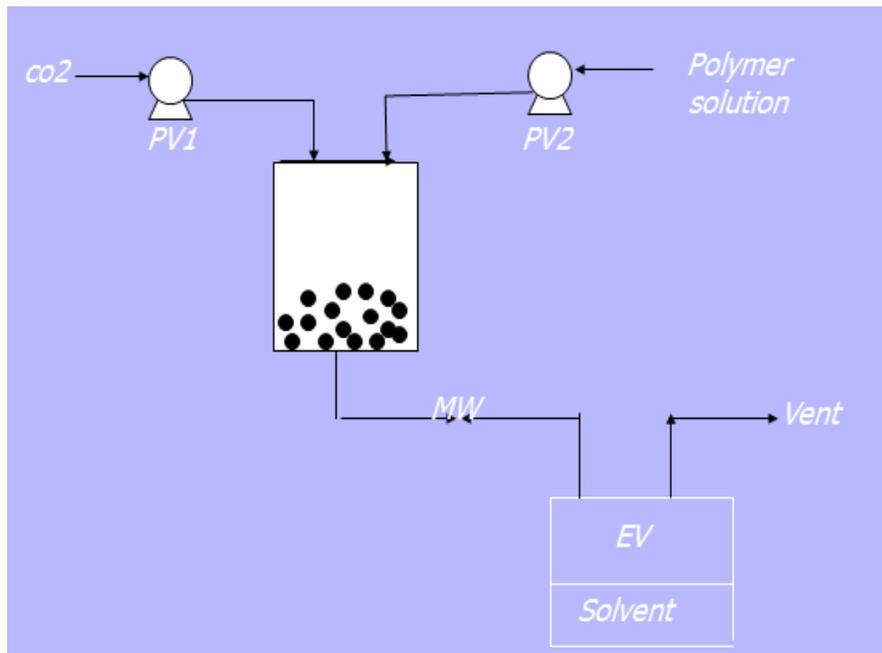

Figure 5. Preparation of nanoparticles by Supercritical fluid technology. The substances solved in supercritical fluid, then pass through the nozzle and expand.

Concerning simple coacervation method, the protein precipitation around oil droplets is obtained by changing pH and temperature or by the "salting-out" technique (Lazko et al., 2004) .

As consequence, a major aspect in preparing a colloid-dal carrier system has to be establishing preparation conditions which control the resulting particle size and which lead to particles of a narrow size distribution, with special emphasis on size of 100 - 200 nm (Langer et al., 2003; Zhang et al., 2000).
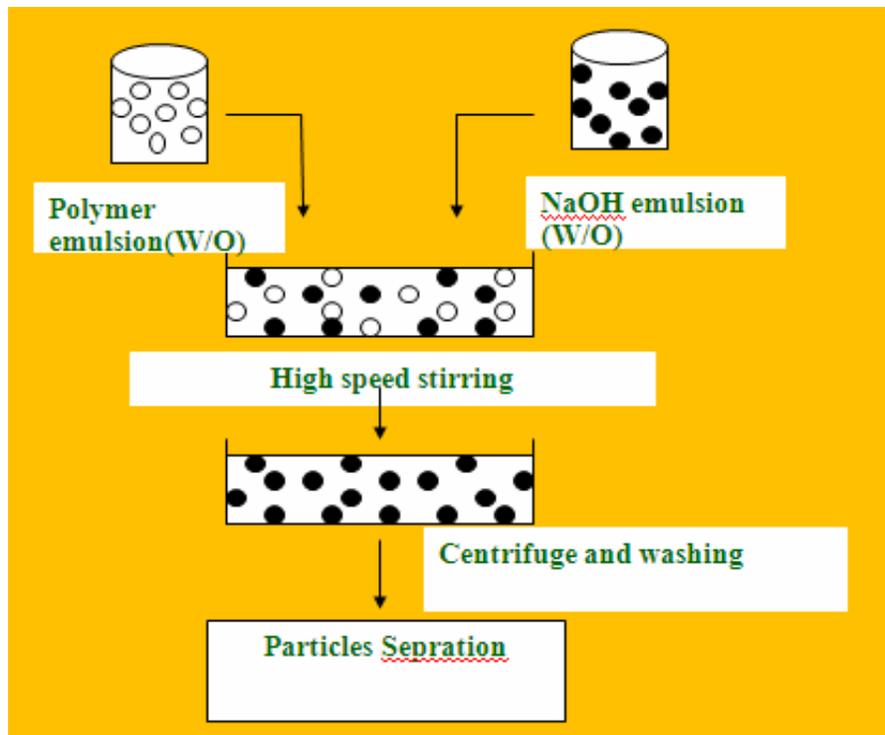
Figure 6. Fabrication of nanoparticles by emulsion- droplet Coalescence method.
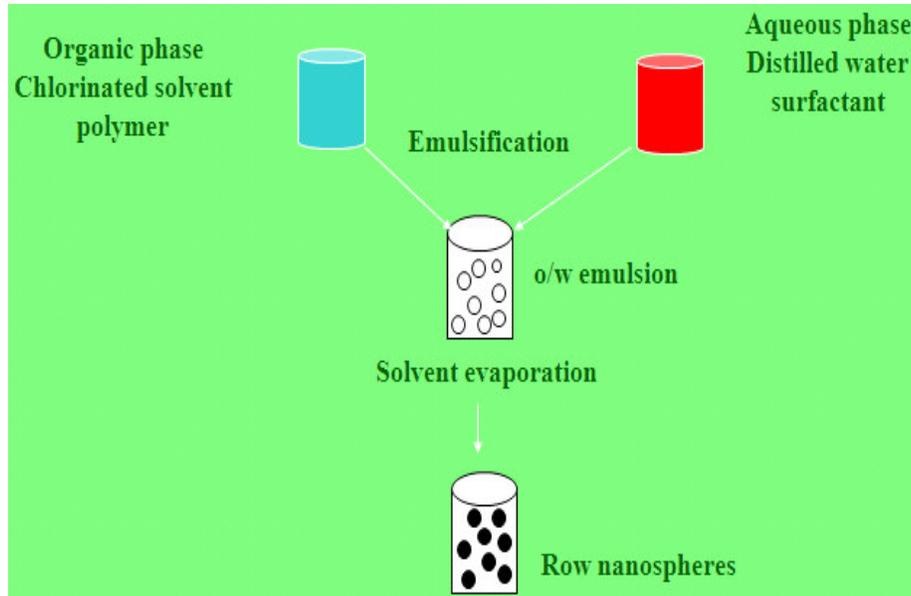

Figure 7. Solvent evaporation emulsification technique. Polymer is dissolved in organic solvent, then emulsified in aqueous solution. The emulsion is dried under pressure or continues stirring or increasing temperature (Rahimnejad, 2006b).

Conclusion

Control of the nanoparticle size and the size distribution has several important implications for controlled-release in food and drug delivery systems. For example, there is typically an ideal sphere size that provides the optimal release rate and route of administration. Several metho-dologies for microcapsule preparation have been

described, such as precipitation, spraying, phase separation and emulsion techniques. The emulsion approach is commonly using on both bench and industrial scales.

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