Chapter 6
Application of Nanoparticles as a Drug Delivery System

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ABSTRACT

Small colloidal particles having their diameter in the range of 50 to 500nm are defined as Nanoparticles. These are usually prepared either by using biodegradable or non-biodegradable polymers and are usually classified in two broad categories: (1) Nanocapsules: a type of reservoir system in which an oil or aqueous core is surrounded by a polymeric membrane. (2) Nanospheres: a type of matrix system. Preparation of nanoparticle as a drug delivery system is one of the most widely accepted approach since the prepration of nanoparticle were easy and convenient to scale up. Their high stability and conveniently easy to freeze-dried their preparations provide some additional advantages to choose Nanoparticles as a good drug delivery system. Inspite of them Nanoparticles were were able to achieve with success tissue targeting of many drugs (antibiotics, cytostatics, peptides and proteins, nucleic acids, etc.).

1. INTRODUCTION

In microcapsules drug is encapsulated as small particles or as a drug solution in a polymer fi lm or coat, whereas microspheres are solid polymeric spheres which entrap drug. Equivalent structures with particle diameters ranging from 50 to 500 nm are referred to as nanocapsules and nanoparticles. Nanoparticles (NPs) of different size and physicochemical properties have been introduced to many fields of life and biomedical sciences over the last decade (Oberdörster et al., 2005). It is worth noting that nanoparticles can be made from a fully variety of bulk materials and that they can explicate their actions depending on both the chemical composition and on the size and/or shape of the particles (Brunner et al., 2006). The literature on the ecotoxicity of nanoparticles and nanomaterials as well as the chemistry of both manufactured and natural NSPs is summarized in recent reports (Handy et al. 2008, Yu-Nam & Lead

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2008). Medical therapies have become more tailored to specific diseases and patients in recent years. Most pharmaceutical agents have primary targets within cells and tissues; ideally, these agents may be preferentially delivered to these sites of action within the cell. Selective subcellular delivery is likely to have greater therapeutic benefits. Cytosolic delivery, for instance, is desirable for drugs that undergo extensive exportation from the cell via efflux transporters such as multi-drug resistance proteins and P-glycoproteins (Faraji & Wipf, 2009).

2. PREPARATION OF NANOPARTICLES

Polymer nanoparticles including nanospheres and nanocapsules (Figure 1) can be prepared according to numerous methods that have been developed over the last 30 years. The development of these methods occurred in several steps. Historically, the first nanoparticles proposed as carriers for therapeutic applications were made of gelatin and cross-linked albumin (Scheffel et al., 1972; Marty et al., 1978). Then, to avoid the use of proteins that may stimulate the immune system and to limit the toxicity of the cross-linking agents, nanoparticles made from synthetic polymers were developed. At first, the nanoparticles were made by emulsion polymerization of acrylamide and by dispersion polymerization of methylmethacrylate (Birrenbach, Speiser 1976; Kreuter, 1976). These nanoparticles were proposed as adjuvants for vaccines. However, since they were made of non-biodegradable polymers, these nanoparticles were rapidly substituted by particles made of biodegradable synthetic polymers. Couvreur et al., proposed to make nanoparticles by polymerization of monomers from the family of alkylcyanoacrylates already used in vivo as surgical glue. They succeeded in making nanoparticles by polymerization of the monomers in oil-in-water type emulsions prepared with an acidified aqueous phase (Couvreur et al., 1979).

During the same period of time, Gurny et al., proposed a method based on the use of another biodegradable polymer consisting of poly(lactic acid) used as surgical sutures in humans (Gurny et al., 1981). In this method, nanoparticles were formed directly from the polymer. Based on these initial investigations, several groups improved and modified the original processes mainly by reducing the amount of surfactant and organic solvents. At that time, the methods developed were only able to produce nanospheres (Figure 1) (Legrand et. al. 1999). A breakthrough in the development of nanoparticles occurred in 1986 with the development of methods allowing the preparation of nanocapsules corresponding to particles displaying a core-shell structure with a liquid core surrounded by a polymer shell. From 1986, there was also an acceleration in the development of new methodologies for the preparation of all types of nanoparticles.

The nanoprecipitation technique was proposed (Fessi et al., 1986) as well as the first method of interfacial polymerization in inverse microemulsion (Gasco & Trotta, 1986). In the following years, the methods based on salting-out, (Alle´man, 1992) emulsion–diffusion, (Quintanar & Guerrero, 1998) and double emulsion (Zambaux, 1998) were described. Finally, during the last decade, new approaches were considered to develop nanoparticles made from polysaccharides based on the gelation properties of these natural macromolecules (Vauthier & Couvreur, 2000a). These nanoparticles were developed for peptides and nucleic acid delivery. Another goal was the development of surface modified nanoparticles to produce long circulating particles able to avoid the capture by the macrophages of the mononuclear phagocyte system after intravenous administration (Gref, 1997).

All the methods can be classified into two groups depending on whether the nanoparticles are formed at the same time than the polymer itself requiring a polymerization reaction or are directly obtained