Chapter 7
Pharmacokinetics of Polymeric Nanoparticles at Whole Body, Organ, Cell, and Molecule Levels

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ABSTRACT
Polymeric nanoparticles have been increasingly studied and applied in a variety of areas, most commonly in biomedicine. The efficiency and toxicity are two aspects that need to be considered for nanoparticles, and both are closely related to the pharmacokinetics of nanoparticles. In this chapter, the pharmacokinetics of polymeric nanoparticles were introduced at the whole body level (including absorption, distribution, metabolism, and excretion), organism level (transportation within organs and pass through physiological barriers), cell levels (binding to cell surface, endocytosis, intracellular transition, and exocytosis), and molecule level (protein binding and ligand-receptor binding). Examples were also given to illustrate the modeling of the pharmacokinetics of polymeric nanoparticles at different levels. A comprehensive understanding of the pharmacokinetics of polymeric nanoparticles will facilitate the applications in various areas such as drug delivery and disease diagnosis.

1. INTRODUCTION
Nanoparticles, according to their chemical compositions, could be classified into three categories: polymeric, non-polymeric, and hybrid particles. Non-polymeric nanoparticles are commonly used for imaging and diagnosis in medicine, but they are very limited to modifications. Polymeric nanoparticles are very flexible, and could be prepared using numerous polymers to achieve very complicated properties and functions, which make them very advantageous for drug delivery. Hybrid nanoparticles contain both polymeric and non-polymeric materials with the purpose to retain the advantages and functions of both.

It is difficult to distinguish polymeric nanoparticles from non-polymeric and hybrid nanoparticles in terms of pharmacokinetics, although there

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are certainly some differences such as degradation. However, it is not in the scope of this chapter to compare the pharmacokinetics of nanoparticles with different chemical composition. This chapter will focus on the pharmacokinetics of polymeric nanoparticles, while research about non-polymeric and hybrid nanoparticles will be mentioned only when they are helpful in understanding the pharmacokinetics of polymeric nanoparticles. On the other side, most general statements in this chapter also apply to non-polymeric and hybrid nanoparticles, unless indicated specifically.

Polymeric nanoparticles are increasingly used in diverse areas, such as cosmetics, foods, and especially medicine (Nitta & Numata, 2013). There are two aspects of nanoparticles that need to be understood thoroughly before they can be used on human body: how efficient they are for the purposes and what is the toxicity. Both aspects are closely related to the fate of nanoparticles in the human body, which could be generally described as ADME (absorption, distribution, metabolism, and excretion). ADME of polymeric nanoparticles, similar as those of small molecules, are dynamic processes, involving numerous interactions between the nanoparticles and the human body. Mathematical description of the kinetics of these processes enhances our understanding of the interactions between polymeric nanoparticles and the human body, and further promotes the designation and optimization of nanoparticles with higher efficiency and low toxicity (M. Li, Al-Jamal, Kostarelos, & Reineke, 2010).

The pharmacokinetics of polymeric nanoparticles depends on their properties including size, surface charge and modifications, chemical composition, and shape. There are a few comprehensive reviews have discussed this in full detail (Duan & Li, 2012; Owens & Peppas, 2006). Many studies have been done to show the relationships between nanoparticle properties and their ADME within animal bodies and interaction with cells (Duan & Li, 2012; Moghimi, Hunter, & Andresen, 2012; Yue et al., 2011). These studies significantly advanced the understanding of nanoparticle pharmacokinetics within the human body. Based on these studies, mathematical models were established or improved to describe and illustrate the kinetic processes of these particles inside the living systems.

2. PHARMACOKINETICS OF POLYMERIC NANOPARTICLES

2.1 The Pharmacokinetics at Whole Body Level

Nanoparticles entering the human body can be classified by two ways of exposure: unintentional and intentional. The former includes airborne pollutants and nanomaterials in working environments, or in food and cosmetic products. Intentional exposure is mostly for medical applications, especially drug delivery and imaging. In most cases, polymeric nanoparticles were engineered and intentionally given to human for designed applications such as drug delivery and diagnosis. Nanoparticles may be given through various routes, such as through the respiratory tract, gastrointestinal tract, and skin. Nanoparticles can also be injected into the body, mostly for medical purposes. Numerous studies have shown that the properties of nanoparticles have complicated influences on the pharmacokinetics (Figure 1).

2.1.1 ADME of Polymeric Nanoparticles

The most common route is through the respiratory tract, especially for pollutants (Yue et al., 2011). Due to the physiological structures of the lungs, pharmacokinetics of inhaled nanoparticles is very complicated and under numerous studies, as discussed later in this chapter. According to the physiological structures, the lungs could be divided into the airways (trachea, bronchi, and bronchioles) and the alveoli. Particles could deposit in the airway surface, and then be cleared...
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