CHAPTER 16

Nanoparticle Formulations and Delivery Strategies for Sustained Drug Release in the Lungs

MARÍA L. CUESTAS[a] • TOMÁS BRITO DEVOTO[a] • MARÍA A. TOSCANINI[b] • MARÍA J. LIMERES[a] • GERMÁN A. ISLÁN[c] • GUILLERMO R. CASTRO[c,d]
[a]University of Buenos Aires, CONICET, Institute for Research in Microbiology and Medical Parasitology (IMPaM), Buenos Aires, Argentina, [b]University Buenos Aires, Faculty of Pharmacy and Biochemistry, Institute of Nanobiotechnology (NANOBIOTEC), Buenos Aires, Argentina, [c]Laboratory of Nanobiomaterials, CINDEFI, Department of Chemistry, Faculty of Exact Sciences, National University of La Plata-CONICET (CCT La Plata), La Plata, Argentina, [d]Max Planck Laboratory for Structural Biology, Chemistry and Molecular Biophysics of Rosario (MPLbioR, UNR-MPIbpC), Partner Laboratory of the Max Planck Institute for Biophysical Chemistry (MPIbpC, MPG), Center for Interdisciplinary Studies (CEI), National University of Rosario, Rosario, Santa Fe, Argentina

1. INTRODUCTION

Inhalation therapy is one of the ancient medical approaches to treat pulmonary diseases. The inhalation of therapeutic vapors and aerosols and the smoking of herbal preparations for medicinal purposes have been used for thousands of years. It is estimated that the origins of inhalation therapy for asthma and other lung diseases dated back more than 2000 years to Ayurvedic medicine in India, although the introduction of the first pressurized metered-dose inhaler (pMDI) in 1956 opened the era of the modern pharmaceutical aerosol industry [1]. One of the first and most notable drug delivered by the respiratory tract was opium that was used for therapeutic and recreational purposes [2]. Remarkable advances in the technology of devices, aerosol formulations, and nanotechnology for pulmonary drug delivery (PDD) have occurred since then (Fig. 1).

The unique anatomical and physiological features of the lungs (i.e., large surface area of the pulmonary epithelium of 100–140 m^2, an extremely thin absorptive mucosal membrane of <1 μm in the alveoli, and high vascularization) and the minimal interactions between the targeted sites and other organs make lungs an appropriate site for drug absorption and an attractive target for both local and systemic drug delivery (DD).

At present, the three main uses of the inhalation therapy are (1) local therapy of asthma and chronic obstructive pulmonary disease (COPD) with bronchodilators and glucocorticoids, (2) local therapy of lung disorders associated with orphan diseases such as cystic fibrosis (CF), and (3) systemic applications such as in diabetes, neurological diseases, blood disorders, and analgesia [3]. Unfortunately, no inhaled therapy for lung cancer has been approved by the US Food and Drug Administration (FDA) so far. Available inhalation DD devices include pMDI, dry powder inhalers (DPIs), nebulizers, and soft mist inhalers (SMIs); each of them with their own advantages and disadvantages, as it will be addressed in Section 5.

PDD formulations based on nanotechnology, such as nanoparticles (NPs, i.e., particles in the size range of 10–1000 nm), constitute a promising approach to circumvent many barriers related to the complexity of the respiratory tract and with the patient's compliance (Fig. 2) [4–6]. Using this approach, the sustained lung release of drugs, peptides, proteins, genes, siRNA, and vaccines might fulfill unmet clinical needs.

This chapter highlights the recent advances in the development of devices and nanotechnologies for PDD, with special focus on the nanoformulations and biomaterials used for the therapy of asthma, COPD, lung cancer, and pulmonary infectious diseases.

This chapter is organized into eight sections. Section 1 is an introductory section. Section 2 presents the benefits and drawbacks of the pulmonary route over other administration routes. Section 3 is about the marketed inhalable products and the patient's compliance. Section 4 highlights the role of formulation in controlled PDD. Section 5 presents the role of inhaler devices in controlled PDD [(1) pMDIs, (2) accessories

Modeling and Control of Drug Delivery Systems. https://doi.org/10.1016/B978-0-12-821185-4.00002-6