Chapter 14
Liposome-Encapsulated Antimicrobial Peptides:
Potential Infectious Diseases Therapy

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ABSTRACT

The purpose of this chapter is to review the potential use of liposomes and peptides to address the ongoing challenges in infectious diseases involving antimicrobial resistance. The First section of this chapter describes and discusses the use of liposomes as model membrane to gain an insight on the membrane binding and disruption behavior of the potent peptides. Under this section, various biophysical techniques used to characterize the interactions are reviewed. In the second section, the use of antimicrobial peptides as an alternative to conventional antimicrobial therapy is presented. The final section of this chapter reviews liposomal encapsulation of antimicrobial peptides as an effective delivery strategy.

INTRODUCTION

Over last few decades, nanotechnology has emerged as a novel method and is gaining importance in many areas of medical field, particularly in infectious disease. Nano-based antimicrobial drug delivery systems to address the issue of antimicrobial resistance have been an extensive area of research. Its application in antimicrobial-resistant biofilms and device-centered infections is also gaining interest lately. Given the vast scope of pharmaceutical nanotechnology and nano-based therapies, this chapter focuses only on potential use and implications of liposomes and antimicrobial peptides as antimicrobial drug delivery systems.

Before the discovery of liposome in early 1960s, researchers struggled to formulate drugs that could be transported effectively to intracellular

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targets. After its discovery, the application potential of liposome was recognized and since then, liposome systems became a popular drug delivery platform. Liposome-based antimicrobial delivery systems are designed to reduce the antimicrobial toxicity and to increase their therapeutic index. Currently, there are few liposome-based antimicrobials that are approved by US Food and Drug Administration (FDA) and available in market for clinical use. Other liposome-based formulations are in various stages of clinical testing or are under development. Liposomes are biodegradable delivery vesicles that can entrap both hydrophobic and hydrophilic antimicrobials agents in their hydrophilic or hydrophobic phases respectively and create a protective environment. This property help to increase their efficacy, improve solubility and stability, enhance bioavailability, lower cytotoxicity thus reducing side-effects of conventional antimicrobials and make them more target specific. Most important of all, Liposome-based antimicrobial delivery would to prolong the useful lifespan of antimicrobials.

Another area of antimicrobial drug research that does show significant promise is in the discovery and development of antimicrobial peptides (AMPs).

The antimicrobial peptide field is growing rapidly in response to the demand for novel antimicrobial agents. To date, thousands of antimicrobial peptides have been discovered both at gene and protein levels and reported in literature. Some of these peptides are potent antimicrobials exhibiting bactericidal activity. At the time of writing this chapter, there were 1931 antibacterial, 147 antiviral, 864 antifungal, 62 antiparasital and 94 anti-HIV1 peptides discovered and reported on the Antimicrobial Peptide Database version 2 (The Antimicrobial Peptide Database, 2014). These peptides, which are about 12-100 amino acid residues in length, are produced by a large number of organisms and serve as a first line of defense. They exhibit bactericidal effect against a wide range of pathogens.

The next few sections of this chapter will review in greater detail the development and application of liposome and antimicrobial peptides as novel antimicrobial agents.

LIPOSOMES: DRUG DELIVERY PLATFORM

The use of liposomes as a drug delivery platform is an area of extensive research and to a certain extent successful too. Some of the most widely used liposome-based antimicrobial agents includes AmBisome® (Gilead Sciences, Inc, San Dimas, CA), Amphotec® (Ben Venue Laboratories, Inc, Bedford, OH) and Abelcet® (Sigma-Tau PharmaSource, Inc, Indianapolis, IN). Liposomal formulations exhibit enhanced activity against pathogens since the incorporated antimicrobial agent becomes less prone to the inactivation by bacterial enzymes. The other theory to support enhanced activity is the reduced electrostatic repulsion of liposomal antibiotics (Nacucchio, 1985). Clinically it has been noted that due to the release of drug upon target attainment, the antimicrobial related toxicity in-vivo is much lower (Uhumwangho et al., 2005).

With the on-going research on liposomes, there are certain challenges that have been identified with the designing of liposomes. One of them is related to the premature drug release from liposome before reaching the target. The other challenge is that higher liposomal volume is needed when the encapsulation efficiency is low to achieve clinical dosages (Mirzaee et al., 2009). Development of resistance like in any other antimicrobial agent is another issue that can reduce the efficacy of liposomal formulations. Resistance can develop due to enzymatic inactivation by bacterial enzymes, alterations on molecular target preventing the drug to enter the cell and rapid extrusion of drug (Nikaido, 1994, Immordino et al., 2006). Various types of liposomes were also found to interact with the blood coagulation system in-vivo. They