Chapter

Introductory Chapter: Peptide Synthesis

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1. Introduction

Peptide science is presently witnessing an enormous growth in its synthetic developments. Many synthetic peptides have commercial and pharmaceutical applications. But the synthesis of these peptides is a difficult task. The advent of solid-phase peptide synthesis has changed the face of peptide synthesis by opening the way to the extensive use of synthetic peptides in chemical and biomedical applications. Along with this landmark discovery, many other developments such as improved synthetic strategies, selection of protecting groups, automated synthetic methods, and advanced purification and analytical techniques were also evolved [1]. This book is intended essentially for those investigators who wish to make use of synthetic and antimicrobial peptides in their research and also provide practical information regarding the synthesis of difficult sequence-containing peptides. At the same time, it is addressing the common problems relating the synthesis and applications of synthetic peptides.

2. Methods of peptide synthesis

Methods for the chemical synthesis of peptides are divided into two groups: classical solution phase and solid-phase peptide synthesis (SPPS). Solution phase is the traditional way for large-scale synthesis of peptides. But these methods are labor-intensive and time-consuming because of its intermediate purification procedures and unforeseeable solubility issues. Hence many researchers who need to synthesize peptides choose the more convenient solid-phase approach. One of the main difficulties in solid-phase assembly of peptides is that of obtaining reasonable quantities of pure peptides. Investigations dealing with the quantitative aspects of polymer-supported reactions have shown that the insoluble support does have a significant dynamic influence on the bound substrates. An efficient polymeric support for peptide synthesis should have optimum hydrophobic-hydrophilic balance compatible with the peptide being synthesized. Systematic studies on the polymer-supported reactions show that the use of a flexible polymer support enhances the reactivity [2]. But the design and development of polymer supports having appropriate hydrophobic-hydrophilic balance is a difficult task.

3. *O*-isoacylpeptide method

Various methods are reported for the efficient synthesis of long-chain and difficult peptide sequences. These peptides have a tendency of aggregation and low solubility, making its synthesis and purification laborious. Native chemical

ligation (NCL) renders a highly effective and powerful method for the preparation of long-chain peptides [3]. This book introduces a novel "*O*-isoacylpeptide" method for the effective synthesis of long and difficult peptide sequences as in [4]. *O*-isoacylpeptides having ester bonds can be converted into the parent peptides under physiological condition *via* the *O* to *N* intramolecular migration. In addition a new approach called segment condensation with no racemization using the *O*-isoacylpeptide method is also introduced excellently [5]. This segment condensation can be treated as a substitute for NCL method.

4. Synthetic peptides

This book gives a detailed review on synthesis and applications of synthetic peptides. Various aspects of solid-phase peptide synthesis including different resins, linkers, and synthesis techniques are discussed in detail. Applications of synthetic peptides as peptide vaccines, radio-theranostic agents, radio-labeled peptide analogues, and radio peptides for imaging therapy are featured as part of the synthetic peptide chapter. This chapter also presents an excellent discussion on cell-penetrating peptides (CPP) [6] as molecular carriers. It not only illustrates the use and applications of cell-penetrating peptides but also provides different aspects of various cell-penetrating techniques. A more in-depth description of factors affecting the mechanism of cellular uptake and various molecular detections of CPPs are also included in this chapter.

5. Antimicrobial peptides

Antimicrobial peptides are a growing group of natural and synthetic peptides with a broad spectrum of targets including viruses, bacteria, fungi, and parasites [7]. Another interesting feature of this book is a comprehensive discussion on antimicrobial activity of defensin-like peptides [8]. These antimicrobial peptides act mainly by damaging the bacterial cell membranes and are found in many parts of the body. The chapter on defensins presents a discussion on mammalian defensins, their antimicrobial mechanisms, and its various evaluation techniques. This section also compares the antimicrobial activity of defensins in free form and immobilized on material surfaces along with pictorial representation of various immobilization methods. Furthermore, several of the concepts discussed can be easily adopted for the next-generation antimicrobial surfaces as coatings for medical devices and implants.

Peptide synthesis has come a long way from the invention of solid-phase synthesis to the present day. Each chapter in this book portrays one major aspect of peptides including its synthesis and applications. This book is intended to provide the researchers with various new methods for the synthesis of long and difficult sequence peptides.

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