Chapter 1

# Introductory Chapter: Application of Peptides in Biomedical Sciences

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Additional information is available at the end of the chapter

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## 1. Introduction

The application of peptides in the pharmaceuticals and medicinal field is thrivingly emerging nowadays. Over the past few years, the development of peptides such as the major compounds in medicines and biotechnology research has been widely utilized due to its high selectivity, good efficiency, predictable metabolism, and affordable prices, compared to other classes of drugs such as small compounds or natural products [1]. Nevertheless, the extensive bioactivities that peptide class possessed are promising and interestingly worthy to be investigated and developed further in the future.

Peptides are biopolymers which composed of amino acids as the monomers that connected through peptide bonds. The length of amino acids is varying from 2 (commonly known as dipeptide) to 50 amino acids (known as a polypeptide). The composition and order of amino acid sequences determine their properties, both physical and chemical, and also their pharmacological activities [2]. Regarding the structure, peptides can be classified into two categories: linear peptide and cyclic peptide. The linear peptide is prone to be hydrolyzed by exopeptidases and endopeptidases. Thus, lowering its effective half-life in the human body. The peptide cyclization is a familiar technique to increase the peptide stability and effective half-life. However, this treatment is also modifying the peptide bioactivity, either by lowering or raising its activity due to fixed flexibility and conformation, which have to be measured later on by *in vivo* experiments [3].

## 2. Peptide as therapeutics agents

The development of peptides as the therapeutic agents had arisen since the early 1980s when natural peptides such as insulin and adrenocorticotrophic hormone (ACTH) were isolated widely and became the popular therapeutics approaches at that time. Since then, several synthetic peptides (i.e., vasopressin and oxytocin) and natural peptides (i.e., snake venom) have been introduced and identified for their use in pharmaceuticals and biotechnology fields [4]. As for today, more than 60 peptides have been approved for their use as drugs from Food and Drug Admission (FDA) and widely marketed, with other 140, and 500 peptides are still in clinical trials and preclinical development [1]. Therapeutic peptides have various known pharmacological and biological activities, including an antioxidant, antimicrobial, anti-inflammatory, and antihypertension [5]. Currently, the antiviral activity of peptides is also investigated as well, such as an anti-HIV agent [6].

One of the most significant challenges on the development of peptides as the therapeutic agents is to increase their oral bioavailability. Due to their enormous molecular weight, high polarity, low intestinal permeability, and hydrolysis susceptibility (especially for linear peptide), almost all therapeutic peptides are administrated through injection. Although considerable efforts have been made in the advancement of peptides research, so far there are only eight peptide drugs that have currently sold in the market which orally administrated. The well-known examples of this kind of peptide are linaclotide, an oligopeptide which used to treat irritable bowel syndrome with constipation, and cyclosporine, which widely utilized as an immunosuppressant (**Figure 1**) [7]. To date, two approaches have been established to improve the oral bioavailability of the respective peptides: the first strategy would be the optimization of peptide structure, followed by the lead peptide alteration into its derivate that possessed high oral bioavailability. The second strategy, which involves the development of the orally available peptide backbones, has not obtained the same success as the previous strategy, although the potency of this strategy cannot be underestimated yet [3].

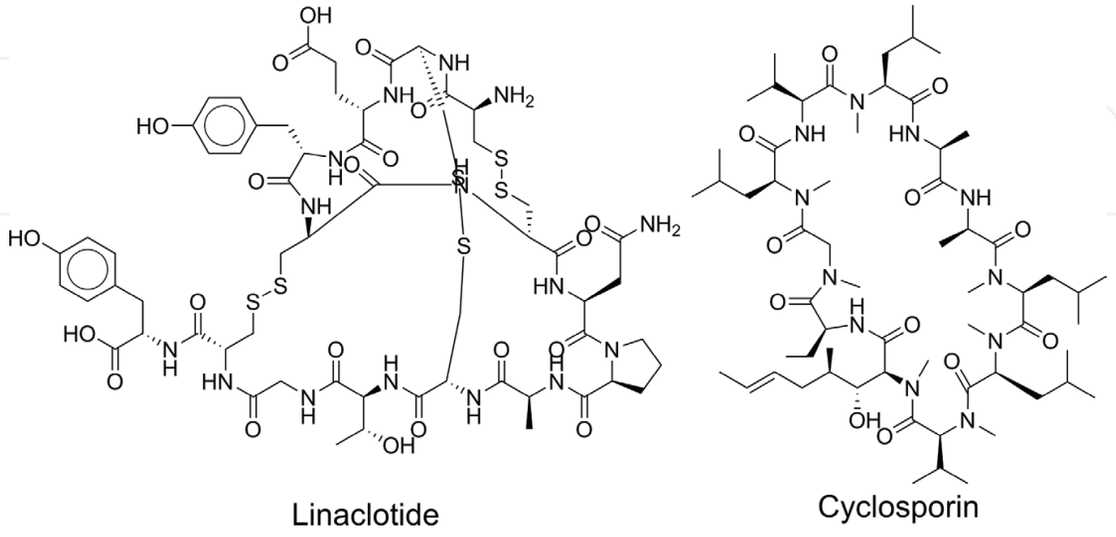


**Figure 1.** The molecular structure of linaclotide (left) and cyclosporine (right), one of the examples of orally administrated peptide drugs.

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