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Review

Discovery, structure, and chemical synthesis of disulfide-rich peptide toxins and their analogs

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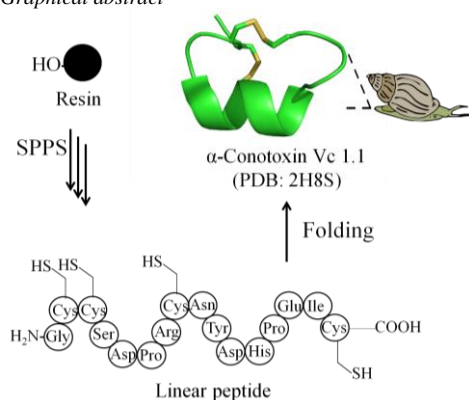
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Graphical abstract



Disulfide bond-rich peptide toxins are promising scaffolds for the development of medicinal peptides because they possess a rigid 3D structure formed by multiple disulfide bonds. In this review, we discuss recent advances in the discovery, structural elucidation and chemical synthesis of disulfide-rich peptide toxins and their analogs.

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ABSTRACT

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Recently, medicinal peptide molecules are of great interest to many international pharmaceutical companies, mainly because of their relatively lower research costs, shorter research cycles, and the greater likelihood of being drugs, when compared with traditional small molecules. Due to the great variety in molecule structures and the diverse biological functions, disulfide-rich peptide toxins have become a shining molecular library for the development of polypeptide drugs. In view of the increasing amount of related publications, here we summarize the discovery, structural elucidation and chemical synthesis of disulfide-rich peptide toxins and their analogs.

1. Introduction

Conventional peptide therapeutic agents have poor stability in serum and are difficult to be administered orally [1]. Disulfide-rich peptide toxins and their analogs exhibit relatively high stability *in vivo* and therefore are becoming promising

scaffolds for the development of peptide-based drugs in many groups. For example, Craik *et al.* found a class of disulfide-rich peptides called cyclotides from plants and used them as platforms for the designing peptide drugs for cancer, pain and various other diseases [2]. By screening and engineering conotoxins, Alewood *et al.* concentrated on screening bioactive

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