Peptides from the Nature to the Laboratory

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Peptides have experienced a remarkable renaissance as therapeutic agents in recent years. They are situated between small molecules (<1000 Da) and proteins, two of the most extensive classes of well-established therapeutic agents.

Peptides provide both the specificity and potency of larger protein biologics but with zero or low immunogenicity. Furthermore, they are smaller, more accessible and cheaper to manufacture using chemical methods, thus presumably combining the advantages of the two therapeutic approaches. While nature has been fine-tuning the bioactive chemical structure of these structures for thousands of years, peptide chemists and protein engineers have the exciting challenge of improving the intrinsically unfavorable pharmacokinetic properties of the majority of native peptides. The drawbacks of peptides as therapeutic agents are associated with their generally high conformational instability.

In this presentation, we will review our current research devoted to the synthesis of natural cyclic peptides (pipecolidepsin, baringolin, teixobactin,….) as well as the design and synthesis of cyclic peptides with improved properties. In this regard, we will discuss the strategies carried out in our laboratory for improving the potency and the stability of peptides. In addition to homodetic cyclizations, we will show as common techniques used in conventional organic chemistry can be applied to peptides for that purposes. Thus, Pd catalyzed coupling reactions allows the efficient preparation of linked, constrained and stapled peptides through C-H Pd activation processes.