Introduction

In order to induce structural conformation in peptides many scientists have utilized cyclization due to the versatile methods of peptide synthesis and availability of protecting groups which can be orthogonally removed. Constrained peptides have been shown to have improved the biological properties compared to the linear peptides.

For example, cyclic peptides have shown:
1. Enhanced receptor affinity and efficacy
2. Improved cell permeability and enzyme stability

In addition, these constraints provide a conceptual approach towards designing of peptidomimetics.

<table>
<thead>
<tr>
<th>Peptide</th>
<th>Type of Modification</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>α - Conotoxin</td>
<td>N-to C- terminus cyclization</td>
<td>Increased stability in human plasma¹</td>
</tr>
<tr>
<td>BID BH3</td>
<td>Hydrocarbon stapling using ring closing metathesis</td>
<td>Increased protease resistance and serum stability²</td>
</tr>
<tr>
<td>NOTCH1</td>
<td>Hydrocarbon stapling using ring closing metathesis</td>
<td>Increase binding affinity towards NOTCH transactivation complex³</td>
</tr>
<tr>
<td>DP178 (HIV35)</td>
<td>Side chain to side chain i, i+7 lactam bridge formation</td>
<td>Increase HIV inhibitory activity as a result of stabilized α-helical conformation⁴</td>
</tr>
</tbody>
</table>

Conclusion:

It is scientifically evidenced that constrained peptides in form of stapled or lactam-bridged have attractive biological properties superior to their linear counterparts and introduced a unique technique for studying protein-protein interactions which mediates most of biological actions.

In order to further study peptides with these promising properties, BIOSYNTHESIS, INC. has recently launched a peptide conformation screening tool called positional cyclization scanning.

This technique is aimed at identifying the receptor-bound conformation of various biological peptides by constraining specific segment of the peptide and studying its effect on the biological activity.

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References: