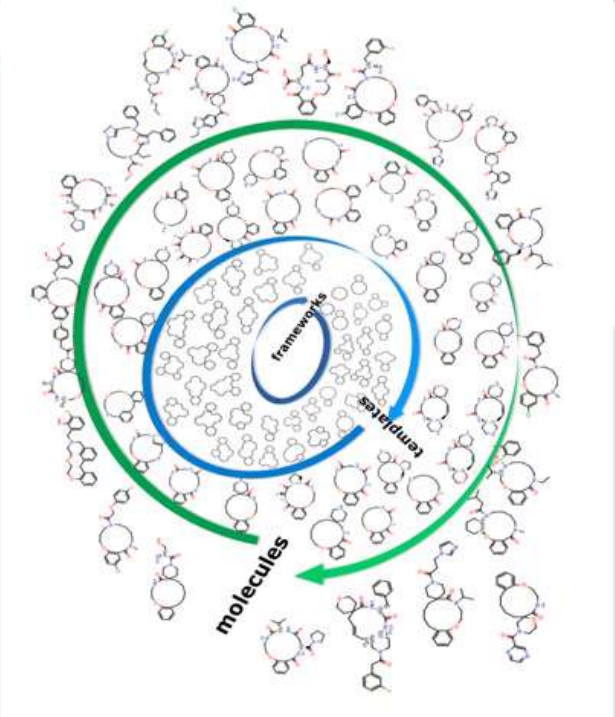
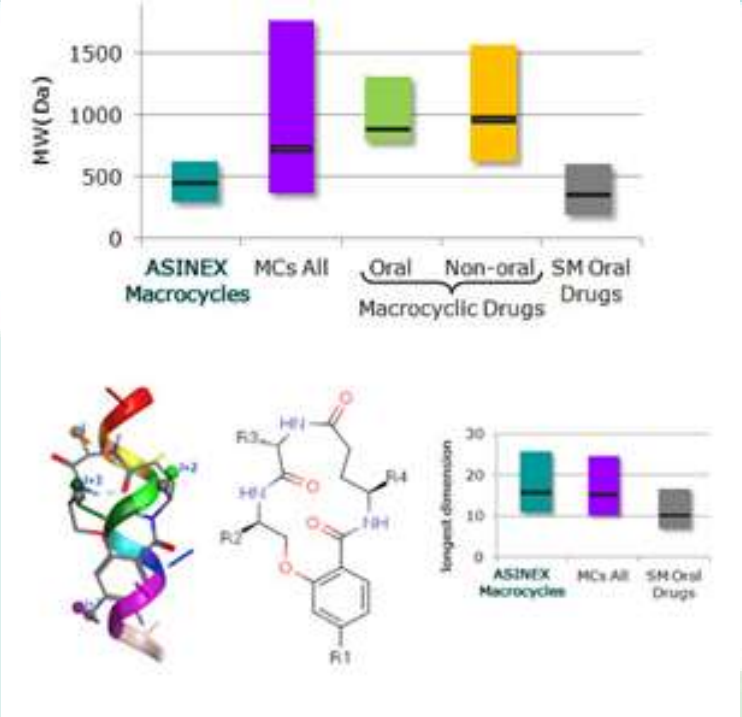
Macrocycles

ASINEX

Medicinal chemists have long considered compounds with medium- and large-sized rings to be a discrete class of molecules, not only due to their interesting physico-chemical and biological properties, but also due to the challenge of their synthesis. To address the issue of synthetic accessibility, ASINEX has elaborated a library of diverse macrocles using an effective tool box of synthetic methods including solid phase-supported synthesis, RCM, click-chemistry, and ring expansion. The resulting scaffolds are novel and have allowed us to generate tremendously diverse, medchem-relevant, macrocyclic frameworks.

Macrocyles tend to be larger than traditional screening molecules which makes them perfect discovery tools for targets with shallow or extended binding sites. At the same time, their unique character based on restricted flexibility and ability to form intra-molecular hydrogen bonds allows for design approaches effectively optimizing properties such as aqueous solubility and membrane permeability. Many of our macrocycles have been tested for aqueous and DMSO solubility with cut-offs applied at 10 mM in DMSO and 50 µM in PBS (pH 7.4) followed by PAMPA permeability assay.





Due to their restricted conformational flexibility accompanied by a favorable orientation of peripheral substituents, many macrocycles effectively mimic the α-helical or β-hairpin topology of biologically relevant proteins. Our Macrocyclic Library provides a very rich source of peptidomimetics and is ideal for probing challenging target classes including: protein-protein interactions, proteases, and antibacterials.

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