

Medicinal chemistry

Mercachem has an experienced group of medicinal chemists headed by Dr. Geert Jan Sterk (Byk Gulden, Altana, Nycomed) offering the following services:

- Design and synthesis of druglike compounds
- Hit optimization, Hit-to-Lead and Lead optimization
- Experimental measurement of physical and chemical properties
- Cheminformatics and computational chemistry
- Structure-guided lead discovery (in collaboration with Proteros)

Mercachem successfully combines in projects its unprecedented knowledge of synthetic and medicinal chemistry as well as clear understanding of the physico-chemical properties of compounds. This strong set of skills enables the synthesis of novel druglike scaffolds, the design and synthesis of small focused libraries for SAR studies and synthetic evolution of fragments.

Experience

The medicinal chemistry team has worked on a large variety of targets and indication areas:

- POP, PARP
- Histamine-H₁, -H₂, -H₃ and -H₄
- PDE₂, PDE₃, PDE₄, PDE₅, PDE₇, PDE₈, PDE₁₁
- Androgenic β 2
- NO donor
- Endocannabinoids
- Opioids
- Anti-infectives (viruses, gram-positive and gram-negative bacteria and parasites)
- Oncology
- CNS diseases
- Inflammation
- GI-diseases
- Pain

Design

For the design of small focused libraries for hit expansion, hit to lead projects and lead optimization several cheminformatics and computational chemistry tools are used to facilitate this process.

The following important properties are calculated or approaches applied when required:

- Lipophilicity (clogD/P)
- Polarity (topological polar surface area)
- Pharmacophore docking
- Diversity analysis

Routinely the following important physico-chemical properties of compounds or small focused libraries are determined experimentally by the analytical department:

- Aqueous solubility
- Lipophilicity eLogD/P
- Acid dissociation constant pK_a
- Permeability (PAMPA)
- Chemical stability

Screening

For biological screening (*in vitro* assays (biochemical and cellular) and *in vivo* pharmacology) and determination of ADME parameters (early ADME assays, pharmacodynamics and pharmacokinetics) Mercachem uses a number of preferred partners that are selected for each project based on the specific needs. Mercachem always remains responsible for project management so that seamless communication about the progress of a project is guaranteed.

SAR analysis

The interpretation of the experimental data, the SAR analysis and prioritization of active compounds is often done in collaboration with the customer on the basis of:

- Biological activity
- Ligand efficiency
- Physicochemical property profile
- Chemical feasibility for parallelization
- Novelty (IP)
- Chemical stability

Working with Mercachem ensures efficient execution of your medicinal chemistry projects.