MONASH University

CENTRE FOR DRUG CANDIDATE OPTIMISATION

PHYSICOCHEMICAL PROFILING

The physicochemical properties of drug candidates, including solubility, partitioning, ionisation and stability, underpin all aspects of drug formulation, delivery and disposition. Poor physicochemical properties can contribute to low bioavailability and unfavourable distribution properties.

Research platforms include:

- in silico calculations of physiochemical properties (pKa, Log P, Log D, PSA, FRB, H bond donor, H bond acceptor)
- kinetic solubility (nephelometry)
- equilibrium solubility (pH range)
- solubility in simulated biological fluids (FaSSIF, FeSSIF, SGF conditions)
- chromatographic Log D estimate
- Shake-flask LogD
- chromatographic protein binding estimate (HSA, α1-acid glycoprotein)
- pKa determination (potentiometric titration)
- short-term solution stability with degradant identification
- solid-state characterisation
- salt-form screening
- impurity profiling

Physicochemical profiling has become an integral part of drug discovery, leading to property optimisation and rank ordering for ‘drug-like’ characteristics.

The structural and physicochemical characteristics of drug candidates underpin:

- interactions with biological systems, including absorption across biological membranes
- metabolism by the liver and other organs
- distribution throughout the body
- interactions with their intended biological target, as well as 'off-target' interactions, which often lead to unwanted effects or toxicity

Through analysis of structural and molecular properties related to a compound's physicochemical characteristics, it is possible to gain qualitative insight into many of these interactions, and to use this information to design molecules with favourable characteristics for a specific disease area.

Initial physicochemical profiling at the CDCO is conducted using in silico and high throughput in vitro physicochemical screening methods that utilise only small quantities of material to provide rapid and cost-effective data on the “drug-like” properties of a structural series.

The CDCO has adapted experimental methods to handle small-scale quantities of material, assessing their physicochemical, biopharmaceutical, solid-state and stability characteristics.