

ADME and hERG in Medicinal Chemistry

"Succeeding Through the Literature"

Outline

Day 1: Introduction to ADME

ADME Made Simple

A colourful voyage through the digestive system outlining the elements of ADMET, absorption, permeability, pgp, CYP's, phase 1&2, enteropathic cycling, toxicity, renal excretion, glomerular filtration, oral absorption, first pass.

Round Table Discussion

Route of administration. Detection of pharmacologically active metabolites in drug discovery. Ames test.

Pharmacokinetics - Definitions and Assays

A useful, easy to follow yet comprehensive guide to elimination (half-life, extraction ratio, clearance, AUC) Distribution (volume of distribution, half-life) absorption (bioavailability, iv, po), and overview of corresponding assays methodologies.

Making the correct Diagnosis - ADME and the Medicinal Chemist

A step by step guide to correctly diagnosing the perennial issues in lead optimization for drug design.

Workshop: ADMET Issues - Solutions that Work

Making the diagnosis and abstracting working solutions to recurrent ADME issues from a range of key medicinal chemistry papers. This team exercise provides a range of quality ideas that have been successfully applied in topical research projects taken from a broad spectrum of pharmaceutical companies.

Roundup Session and Outstanding Questions.

Day 2: hERG – La Bête Noire

hERG – An Introduction

hERG and IKr, ECG, TDP, QTC. The hERG channel structure, in silico models, site directed mutagenicity studies. Assay methodologies. Regulatory issues, current issues.

The hERG 4 Commandments – Designing out hERG Activity

An up to date overview of the literature and summary of key approaches employed by the major players in the field. Lecture illustrated with numerous worked examples on designing out hERG activity.

Round up Session

WORKSHOP - Strategies for Diluting out hERG

A productive group session aimed at working through real life projects designing out hERG activity. The 'hERG 4 Commandments' will be evaluated in parallel and discussed.

Round up Session: Conclusions and Recommendations

In addition to maintaining their sound synthetic organic chemistry knowledge, Medicinal Chemists have to address complex **ADME** (**A**bsorption, **D**istribution, **M**etabolism and **E**limination) and pharmacology issues on a day to day basis. Although relevant principles of pharmacology can be picked up from traditional medicinal chemistry books, much of the wisdom required to progress projects takes years to acquire and many 'tricks of the trade.' These are often concealed within a profusion of medicinal chemistry papers. Distilling practical help from the literature itself requires experience as well as time.

'ADME - hERG – Succeeding through the Literature' is a new, interactive approach to learning medicinal chemistry.

The course is divided into self-contained blocks that require no prior knowledge of the topic. It spans the foundations of ADME as well as all relevant terms in pharmacokinetics. The hERG topic is treated in two parts: a comprehensive introduction to the topic and a comprehensive up to date review of the literature. Each block first gives sound background to the topic and then focuses on distilling 'solutions' from past and current literature, enabling participants to become effective and productive readers of the literature, thus promoting innovation. New concepts are applied in realistic group sessions which are designed to mimic real life situations.

The uncluttered and highly practical teaching style has been tried and tested in a number of pharmaceutical companies as well as in academia and has received much positive feedback.

Tutor



Corinne Kay read Organic Chemistry at Lyon University, France (1984). She then joined Roche (1984-1990) as a medicinal chemist where she was involved in the Trocade and Saquinavir projects. In addition, she had a key role in establishing a Solid Phase Peptide and Oligonucleotide synthesis facility in house. She joined Glaxo in 1990, where she worked on a number of Protease and GPCR drug Discovery projects at various stages of lead discovery and lead optimisation. Corinne then obtained a GlaxoSmithKline sponsored PhD at the University of Cambridge (2000) having worked with Prof S V Ley, FRS on the discovery of novel solid phase amine linkers. She moved to Organon in 2001 where she became responsible for Medicinal Chemistry training of staff and more recently founded Med-Simple, a company specialising in applied Medicinal Chemistry training. She is the author of over 35 publications, book chapters and reviews in these areas. Her research interests include the design of chemical libraries, peptide synthesis, solid phase synthesis and cancer chemotherapy.

Course Aims and Objectives

- An applied knowledge of **ADME** (**A**bsorption, **D**istribution, **M**etabolism and **E**limination) and an understanding to its relevance to drug design
- An overview of pharmacokinetics, biological assays and a grasp of biological results interpretation
- An understanding of major issues associated with hERG and QT prolongation
- A good working knowledge of tackling hERG related issues in a lead compound
- A method for productive reading of the literature

Topics Covered in the Course

- Overview of the human digestive system and its relevance to ADME issues
- Diagnosing ADME issues in a medicinal chemistry programme
- Working solutions to ADME issues taken from the literature
- Introduction to all key pharmacokinetics terms and their associated assay methodologies
- Overview of hERG and its impact on the drug discovery process
- Up to date hERG 'wisdom' on diluting out IKr activity from lead compounds

Who Should Attend?

This course will be valuable to both industrial and academic researchers currently involved with, or intending to become active in the area.

Fees

Fee includes lunch & refreshments, course dinner and course manual.

Accommodation

Scientific Update use high quality venues around the world. Preferential room rates including bed & breakfast are usually available.

Please check the Course Schedule on our website for venues, dates and availability.