Doctorate in Pharmaceutical Sciences
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DEPARTMENT
OF PHARMACEUTICAL SCIENCES

Doctorate in Pharmaceutical Sciences

Course Program (XXXVI cycle)

Ad hoc Teaching Activities

[...ut civitas Perusii sapientia valeat elucere...]

Partner of the European Pharmacoinformatic Initiative europin
Partner of the Paul Ehrlich Euro-PhD Network

AA 2022-2023

January, 13- February 2, 2023
Dr. Remo Simonetti, Janssen
Prof. Emidio Camaioni, University of Perugia

Advanced analytics tools supporting pharmaceutical oral solid dosages manufacturing (2 CFU, 12h)

Over the past few years, the role of advanced analytics tools in the pharmaceutical oral solid dosages manufacturing has become crucial. Starting from the process analytical technology (PAT) applications passing through the process modeling in use for the batch manufacturing this course will also elucidate the control strategy based on a combined use of PAT and Residence Time Distribution into continuous manufacturing. The course will also focus on integrated quality strategies where the combination of multivariate data analysis, spectroscopic analytical techniques and surrogate models are used for the Real Time Release of the product on the market allowing significant timing reductions.

June, 29- 30, 2023
Dr. Franco Lombardo, CmaxDMPK, LLC Consulting

Short Course on ADME and Physicochemical Properties of Drugs (1 CFU, 6h)

This short course will cover all aspects of drugs ADME ranging from in silico, in vitro and in vivo methods to study Absorption, Distribution, Metabolism and Excretion, with reference to the physiological and physicochemical bases underlying the pharmacokinetics of drugs. Each section will be divided in two modules covering different topics. Great emphasis will be placed on physicochemical properties of drugs, with lipophilicity impact at the core, and structure properties relationships (QSPRs). Some pharmacokinetics aspects and calculations, with reference to human PK and dose prediction will be covered in all sections.

July, 10-11 2023
Prof. Paola Signorelli, University of Milan

Lipid metabolism alteration in human proteinopathies (1 CFU, 6h)

To maintain proteome integrity and cellular health, protein synthesis, folding, and degradation must be in proper balance and the abundance of each protein species carefully controlled. Aberrant folding has been linked to a rapidly expanding list of pathologies and protein aggregation has emerged as a process of enormous medical relevance. Two groups of these diseases must be distinguished: loss-of-function and toxic gain-of-function diseases. The first group of diseases is characterized by protein dysfunction resulting from mutations that may render proteins metastable and prone to degradation, as in the case of cystic fibrosis and a wide range of metabolic defects. In the disorders of the second group, metastable proteins undergo aggregation in a process associated with cellular toxicity. These pathologies include the neurodegenerative diseases that cripple our aging societies, most prominently Alzheimer disease (AD) and Parkinson disease (PD), as well as type II diabetes and certain forms of heart disease and cancer. Aggregation may be caused by heritable mutations in disease proteins, as in the case of Huntington disease (HD) and in early onset AD and PD. However, the majority of cases are stochastic and manifest in an age-dependent manner, apparently facilitated through a decline in the capacity of the proteostasis network that occurs during aging, or through the occurrence and/or accumulation of nucleation motifs.
Among most relevant nucleation motifs, lipid molecules arise as key determinant of protein interaction and aggregates formation. Within a cell, lipids are self aggregating molecules, interacting with proteins to give rise to water partitioning structures. In an up-side-down view, lipids may function as "chaperones" for protein folding and aggregation. Thus, protein-lipids interaction occurs in forming intracellular structures and membrane functional domains, as well as in giving rise to abnormal association when including altered proteins and ectopic lipid molecules. Lipidophaty and proteinophaty are therefore connected and altered lipid metabolism derives from and sustains altered protein metabolism and assembly.
Lipids profile is modulated according to signals and stress and specific lipid intermediates can accumulate in temporal/spatial partitions, originating a priming motif for protein-lipids aggregation. Among signalling lipids, sphingolipids moiety has a major role in protein interaction and membrane domains formation.

Disease-modifying therapy is a treatment that at a minimum slows down the progression of the disease and at best cures the disease completely. It can achieve these goals by affecting the cause of the disease, or in some cases, the target of the disease. Literature evidences suggest that modulation of lipid metabolism may be used as a disease-modyfing approach and that sphingolipids and their manipulating enzymes are effective targets.

September, 15 and 18, and October 2, 9 and 23, 2023
Dr. Valerio Mammoli, Aptuit (Verona) Srl, an Evotec Company

Pharmacokinetics: theories and techniques to explore in vivo characterization (2 CFU, 12h)

Pharmacokinetics and pharmacodynamics are the essential components of pharmacology. To obtain in vivo robust data, sample preparation and sample analysis can be a challenge and therefore extraction and analytical method development are vital to allow an adequate bioanalysis. Due to, an increasing use of PK prediction tools, the use of in vivo experiments in animals is slowly decreasing, on the other hand, in vitro ADMET is essential to ensure reliability of in-silico prediction. The high demand of in vitro data has increased the volume of the throughput, the use of automation can definitely play a crucial role in supporting the high demand as well as ensure precision, limiting human errors.

October, 12 and 13, 2023
Prof. Luca Giovanni Regazzoni, University of Milan

Theory and practice of the interpretation of high-resolution mass spectra (1 CFU, 6h)

Nowadays, people working in mass spectrometry (MS) must cope with the overwhelming amount of information produced. First, the number of spectra collected per single experiment is increasing over the years because the scan rate of the new instruments is becoming faster and faster and MS is now applied in fields that require high throughput analyses (e.g., quality control, fragment-based drug discovery, omics). Second, the information included in a single spectrum are becoming higher and higher, especially since the marketing of high-resolution (HR) spectrometers. The logical consequence is that automation is now quite popular, with the associated risk of having unskilled spectrometrists.
In fact, modern spectrometers are becoming more and more user friendly, and unlike for the early instruments it's often not necessary to have skilled operators. Guided or standardized procedures have been included into the software packages first as alternatives, then as a replacement of the manual procedures for data collection, processing, and interpretation. As a result, several spectrometrists are nowadays not fully aware of the potential of the instruments they are working on. This especially affects data interpretation. In fact, the working environment and how it changes over time (i.e., the ecological dynamic framework) has a great impact on MS data. Few examples of framework factors that must be considered during data interpretation are the type of ionization and scan features used to produce the spectrum, the spectrometer conditions (e.g., instrument cleaning and calibration), whether the sample was analyzed also by using different instrument configurations, how the sample have been processed, or which contaminations are expected as carryover from previous analyses.
Without such a knowledge, the information included in a mass spectrum can't be correctly processed. Since it's hard if not impossible to include an ecological dynamic framework into data processing pipelines, having a skilled MS operator is desirable at least to critically review automatically processed data.
This tutorial is intended to give fundamental skills in HR-MS data processing, through theory and practice of the manual interpretation of high-resolution spectra collected in experiments aimed at structural confirmation or de novo identification of small molecules and impurities.

Room and timetable, as well as any change, will be communicated to PhD students by e-mail and published on the website.