Doctorate in Pharmaceutical Sciences
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DEPARTMENT
OF PHARMACEUTICAL SCIENCES

Doctorate in Pharmaceutical Sciences

Course Program (XXXVIII 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.

AA 2023-2024

January 26 and 13 February, 2024
Prof. Benedetta Pasquini, University of Florence

Pharmaceutical Analysis and Regulatory Affairs of a new medicine: from laboratory to patient (1 CFU, 6h)

The research and development of a new drug represent a very long and complex process. After the initial screening phase of drug discovery, preclinical research in the form of laboratory experiments is carried out. If all preclinical criteria are met and regulatory approval to conduct clinical trials is obtained, the extensive clinical trial process with human volunteers and patients begins. New medicines are typically evaluated in many thousands of patients before receiving regulatory agency approval. Before new medicines are available to patients in Europe, they must undergo regulatory evaluation prior to gaining marketing authorization, and national or regional review and decisions on market access. The course aims to show the contribution of pharmaceutical analysis in preclinical and clinical research in order to guarantee quality, safety and efficacy, the three prerequisites that any medicinal product must possess at every stage. Crucial topics of regulatory sciences will be addressed: from the Quality by Design in the development and validation of analytical methods for the determination of active ingredients and their impurities for the quality control of pharmaceutical specialties up to the evaluation of these analytical methods in the European registration dossier of a new drug.

The Regulation (EU) n. 536/2014 on clinical trials of medicinal products for human use and the innovative platform clinical trial information system (CTIS) will be introduced together with real examples of documentation that Authorities are called to evaluate.

Finally, the skills required for the emerging professional figures in the regulatory field will be presented, with the final scope of supporting the employability of the participants and facilitating their future transitions towards the labour market. Good Clinical Practice (GCP) certificate could be acquired.

February 27 and 28, March 1, 2024
Dr. Silvia Vernotico, Farmaceutica Younger-GUNA S.p.A. Dr. Giovanni Maurizi, Dompè Farmaceutici
Dr. Anna Tolomeo, Itelpharma
Dr. Michele Cianchini, Baxter/Takeda
Prof. Vittorio Maio, Thomas Jefferson University, Philadelphia

Medicines: from the rules of production to therapy (2 CFU, 12h)

This course aims to follow the path of the drug from its production to its use in therapy. The rigid rules of production must guarantee efficacy and safety, while the rules of politics and economics guide medicine use in therapy. The five speakers will discuss the following topics: introduction to GMP, production of proteins in GMP, preparation and quality control of radio pharmaceuticals, health and pharmaceutical outcomes.

13 march, 10 April and 15 May, 2024
Prof. Sabine Groesch, Goethe-Universität Frankfurt, Germany

Sphingolipids in inflammation and cancer (1 CFU, 6h) (on-line)

1. Lesson: Introduction to Sphingolipids-> subgroup of lipids, components of cellular membranes, influence on cellular processes, signaling molecules, formation of membrane domains (lipid rafts, ceramide-enriched microdomains). De novo synthesis and salvage pathway, main enzymes, main products.

2. Lesson: Sphingolipids in inflammation; which cells are important, what do we know about sphingolipids and their influence on inflammatory processes (e.g. sphingolipids in T-cells, macrophages)

3. Lesson: Sphingolipids in inflammation; which cells are important, what do we know about sphingolipids and their influence on inflammatory processes (e.g. sphingolipids in T-cells, macrophages) (Continuation)

4. Lesson: Sphingolipids in cancer development, how they influence apoptosis, proliferation, cancer progression, clinical data, differences between tumors of different tissues

5. Lesson: Sphingolipids in cancer development, how they influence apoptosis, proliferation, cancer progression, clinical data, differences between tumors of different tissues (continuation)

6. Lesson: Influence of sphingolipids on drug resistance

June 3-6, 2024
Prof. Andrea Carotti, University of Perugia

Introduction to open source and free *in silico* tools useful in drug discovery (2 CFU, 12h)

Nowadays the drug discovery process is a complex workflow full of risks that even the majority of the big pharma company cannot deal with. In this view a big opportunity is given by the computational approaches. In the last 25 years the molecular modeling scenario was enriched by the release of open source and free modeling software. The course will provide some theoretical basis to deeper understand the applications to perform molecular visualization, docking and use artificial intelligence (AI) algorithms. Moreover, with hands-on tasks, some practical and standard scenarios in the drug discovery process will be reproduced.

July, 2024
Dr. Vittorio Maglione, IRCCS Neuromed, Pozzilli (IS)

Metabolic alterations in neurodegenerative disorders: new insight into pathogenic mechanisms and potential therapies (1 CFU, 6h)

Homeostasis of neuronal cells is largely dependent on the dynamic compartmentalization of the endomembrane system (ER, GOLGI, endosomal-lysosomes system). Emerging evidence indicates that defects in endomembrane trafficking is impaired in different neurodegenerative disorders, including both Huntington (HD) and Parkinson disease (PD). As matter of fact, proteins like LRKK2, alpha-synuclein and huntingtin are involved in vesicular dynamics, and their mutations may affect the homeostasis of both neuronal and non-neuronal cells at multiple levels. Among the lipids that make up the endomembrane compartments, (glyco)sphingolipids play a critical role. They are both regulators of the endomembrane system and a product of the same. Coherently, abnormal levels of glycosphingolipids, described in both HD and PD, are attributable to a defective homeostasis of membranes and altered lipid recycling.
In this context, over the last fifteen years, our research group has demonstrated that the alterations in (glyco)sphingolipids are shared by different HD settings, including central and peripheral tissues from human patients. Importantly, we have also developed a "lipid-based" therapy in vivo, and provided the evidence that such an approach is effective in HD pre-clinical models. Since the endomembrane compartments are also involved in the regulation of protein post-translational modification, we are currently investigating the metabolism of some glycoproteins essential for brain development and functions. A number of studies supports the concept that the alteration of glycoconjugate pathways may contribute to the pathogenesis of neurodegenerative diseases and may be eventually pharmacologically targeted.
This is supported by the evidence that some drugs, whose molecular targets belong to these pathways, are already in clinical trial for different other diseases and could be eventually repurposed for the treatment of neurodegenerative conditions and/or serve as a tool for the development of new ones.

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

AA 2024-2025

November, 2024
Dr. Anna Donnadio, University of Perugia

Solid state characterization of pharmaceuticals (2 CFU, 12h)

The course will be addressed to introduce some of the solid state characterization techniques (X-ray diffraction, thermogravimetric analysis, differential calorimetry scanning, scanning electron microscopy and hot stage microscopy) routinely utilized in the pharmaceutical field, together with examples of the information provided by each. The aim is to provide the basic principles and typical applications of these commonly employed analytical tools for characterization of pharmaceutical solids for understanding the physical properties and ensure optimal physical form.

May, 2025
Dr Luisa Mattoli, Aboca
Concepts in Metabolomic Analysis. Applications to the analysis of medicinal plants and complex natural products *(2 CFU, 12h)*

Natural substances and plant metabolites. Mass spectrometry in the Metabolomic Analysis. Identification of metabolites. Targeted and untargeted metabolomics. Identification of metabolites and their quantitative determination. Regulatory implications and study of biological activity. Analysis of metabolites by phytochemical class: the case of alkaloids and phenols. Research applications and examples for quality control.

May-June, 2025
Prof. Anna K. H. Hirsch, Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), Germany
Prof. Sabatini Stefano, University of Perugia

Classical and innovative approaches to address Anti-Microbial Resistance (2 CFU, 12 h)
Antimicrobial resistance (AMR) represents a global health issue threatening our social lifestyle and the world economy. The course will show the results of some recent approaches, both classical and innovative, aimed to contrast microbial resistance. Among the innovative approaches, a particular focus will entail Target-guided synthesis (TGS), a powerful approach in which the target selects its own inhibitors, and its two main methods: kinetic target-guided synthesis (KTGS) and dynamic combinatorial chemistry (DCC).

June 23-27, 2025
Prof. Francesca Blasi, University of Perugia
Prof. Aurélie Schoubben, University of Perugia

Bioactives from Agri-Food Waste (2 CFU, 12h)

The course intends to provide information on the valorization of agri-food waste as source of bioactive compounds. Lectures will focus on bioactive compounds and their functional properties, paying particular attention on: eco-friendly methods for their extraction, analytical methods to evaluate their composition, spectrophotometric methods to determine their in vitro bioactivity. The use of bioactives from agri-food waste suffers from several hurdles such as poor stability and solubility. In the second part of the course knowledge on technological strategies proposed to overcome these limitations will be reviewed according to the hydrophilic or lipophilic nature of the bioactives. Advantages of using encapsulation approaches to solve stability problems and at the same time improve bioactive delivery will be illustrated.

July , 2025
Prof. Claudia Zadra, University of Perugia
Prof. Maria Carla Marcotullio, University of Perugia

Plant extracts (2 CFU, 12h)

Plant secondary metabolites are important leads in the drug discovery and the formulation of food supplements, and to use plant metabolites for these purposes is fundamental the correct preparation of plant extracts. Besides the traditional extracting methods, in these last years, new eco-friendly

techniques have been developed with the aim of reducing the use of polluting solvents and energy-consuming strategies. Plant extracts are often used as such for the preparation of plant-based medicines and food supplements, so the occurrence of residues and contaminants in medicinal herbs and their products is of great importance. Different classes of contaminants (natural toxicants, heavy metals, pesticides, mycotoxins..) could have adverse effects on human health and also represent an index of quality for the product.
In this context, information will be provided about the legislation and the requirements for the safety assessment of these materials.

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