

MEDTEC SHOOL

Course: Pharmacology Year: 4th Period: annual Credits: 8

Objectives

Pharmacology is the scientific study of drugs and their action on biological systems, ranging from genes and cells up to tissues and human populations. The Pharmacology course aims to provide the medical student with a core of fundamental information underlying the use of pharmacological agents in the practice of medicine. In the first part, the course will describe the principles related to pharmacokinetic and pharmacodynamic processes. In the second part, the course will be focused on the rational and evidence-based use of drugs in treating various diseases. This includes learning about the main classes of pharmacological tools available for different conditions, their mechanisms of action, and main features. Principles to use drugs in the clinic in a rational fashion will be detailed during the following courses of the MEDTEC school committed to specific diseases.

At the end of the Pharmacology course, the student will be able to:

Knowledge and insight

• describe the basic scientific concepts and principles underpinning the pharmacological sciences including pharmacokinetics, pharmacodynamics, and main individual factors affecting drug response.

• explain how these fundamental pharmacological properties can influence route of administration, drug levels over time in the body, drug action, drug efficacy, drug toxicity, potential for drug interactions, and the appropriate choice of drugs for pharmacotherapy in a given patient.

• elucidate how the determination of the pharmacological parameters can be used to design, monitor, and modify appropriate dosing regimens in specific patient populations.

• list the major drugs and drug classes currently used in medical practice for infectious diseases, cardiovascular diseases, endocrine and metabolic diseases, pulmonary diseases, gastrointestinal diseases, diseases affecting the autonomic nervous system and the central nervous system, and cancers.

• give a general overview about the main classes of anti-inflammatory agents.

• describe the main pharmacological features of the described drugs, with a specific focus on their mechanism(s) of action.

• describe how targeting the pathophysiological mechanisms with the appropriate drug(s) can act to effectively treat, cure, or mitigate the underlying disease causes and/or symptoms.



• demonstrate the ability to link the acquired knowledge on pharmacokinetics and pharmacodynamics with the therapeutic and toxic effects of the various described drugs.

• describe the process by which new drugs are discovered, developed, tested, and finally approved by the regulatory agencies for use in the clinic; understand the scientific rigor, methodological approaches and ethical considerations underlying the development of new drugs.

Applying knowledge and insight

- demonstrate the ability to address problems of pharmacological significance.
- predict pharmacological effects in relation to drug-specific and patient-specific features.

• keep up to date by critically reading and understanding scientific articles, selecting the most reliable sources and performing on-line search queries on reference web sites.

Communication

• articulate ideas and questions and respond to the ideas and questions from the teacher, and/or from other learners.

- interact with medical and research professionals presenting their real-world life experiences.
- use the correct terminology relative to the field of Pharmacology.

Learning skills

• demonstrate the learning capacity required to continue training in MEDTEC school, particularly concerning organ/system diseases.

Prerequisites

To attend the Pharmacology course, the student should be familiar with the molecular, cellular and physiological mechanisms underlying normal cell/organ functions and the pathophysiological changes that occur in the most common disease states, as well as the clinical presentations associated with these diseases. Namely, a deep understanding of the main concepts of anatomy, physiology, biochemistry, cell biology, genetics, microbiology, immunology, physiology and pathophysiology is required.

As a general prerequisite, the student must have passed all the exams of the academic years 1^{st} and 2^{nd} of the MEDTEC school.



Contents

1st SEMESTER

PRINCIPLE OF PHARMACOKINETICS

Faculty member: prof. Maurizio D'Incalci *Number of lessons:* 4 (8 hours) *Programme:*

• Topics covered by clinical pharmacology.

• General aspects of pharmacokinetics. Description of the main pharmacokinetic parameters. Mathematical representation of drug absorption, distribution and elimination. Clinical application of pharmacokinetics.

• ADME processes: Absorption - routes of drug administration and main physical/chemical factors regulating absorption; Distribution - main physical/chemical factors regulating distribution; Metabolism - phase I and phase II reactions of drug metabolism; Elimination - different ways of drug elimination.

- Patient-specific factors affecting pharmacokinetics. Drug-drug interactions. Pharmacogenetics.
- Pharmacokinetics of biologicals.

PRINCIPLES OF PHARMACODYNAMICS

Faculty member: prof. Davide Pozzi *Number of lessons:* 3 (6 hours) *Programme:*

• General concepts of pharmacodynamics: brief history of pharmacology, main principles in pharmacodynamics, the concept of receptor.

• Class of receptors fundamental in pharmacology: nuclear receptors, G-coupled receptors, ion channels (including ligand- voltage-gated channels), membrane transporters and enzymes.

• Dose-response relationship: occupancy theory, the concept of agonist (including full and partial agonist) and antagonist (including competitive, non-competitive antagonist and inverse agonist) drugs. Concepts of tolerance, dependence, sensitization, hormesis and synergism. Kinetics properties of drug-receptor relationship and interactions with agonist and antagonist drugs (examples of dose-response relationships).

DRUG DEVELOPMENT

Faculty member: prof. Maurizio D'Incalci

Number of lessons: 2 (4 hours)

Programme:

• Processes of drug development: target discovery and validation, hit discovery, lead identification and optimization, preclinical studies, clinical studies.



• Adverse effects of drugs: classification, balancing drug benefits and adverse effects, management of adverse effects.

DRUGS ACTING ON THE AUTONOMIC NERVOUS SYSTEM

Faculty member: prof. Michela Matteoli *Number of lessons:* 2 (4 hours) *Programme:*

- Structure and function of central and peripheral synapses.
- The sympathetic and parasympathetic systems: a general overview.
- The cholinergic synapse and the drugs affecting cholinergic neurotransmission.
- The catecholaminergic synapses and the drugs affecting adrenergic neurotransmission.

DRUGS TO TREAT CARDIOVASCULAR DISEASES

Faculty member: prof. Gianluigi Condorelli, prof. Giulio Stefanini, dr. Giuseppe Ferrante, dr. Cristina Panico, dr. Davide Cao, dr. Mauro Chiarito

Number of lessons: 6 (12 hours)

Programme:

- Anticoagulant, fibrinolytic, and antiplatelet drugs.
- Drug therapy for dyslipidemias.
- Treatment of hypertension.
- Antiarrhythmic drugs.
- Therapeutic targets in pulmonary hypertension.
- Pharmacotherapy of chronic heart failure and ischemic heart disease.

DRUGS AGAINST INFECTIOUS DISEASES

Faculty member: prof. Maurizio D'Incalci Number of lessons: 4 (8 hours)

Programme:

• Introduction to antibacterial agents: classification and mechanisms of action of antibacterials. Therapeutic choice. Pharmacokinetic aspects. Antibiotic toxicity, antibiotic resistance.

- Classes of antibacterial agents: drugs targeting folic acid metabolism, inhibitors of cell wall synthesis, inhibitors of nucleic acid synthesis, inhibitors of protein synthesis.
- Antibiotics against tuberculosis.
- Antiprotozoal agents, with a focus on antimalarial agents.
- Introduction to antifungal agents and antihelmintic agents.
- Antiviral agents: drugs against Herpes viruses, Influenza viruses, HIV, Hepatitis viruses, SARS-CoV-2.



MECHANISMS OF ANTI-INFLAMMATORY DRUGS

Faculty member: prof. Maurizio D'Incalci Number of lessons: 1 (1 hour) Programme:

• Introduction to some classes of anti-inflammatory agents: nonsteroidal anti-inflammatory drugs (NSAIDs) and cytokine inhibitors.

MECHANISMS OF PULMONARY PHARMACOLOGY

Faculty member: prof. Maurizio D'Incalci *Number of lessons:* 1 (1 hour)

Programme:

• Introduction to the main classes of drugs used to treat asthma, chronic obstructive pulmonary disease, and cystic fibrosis.

2nd SEMESTER

NEUROPHARMACOLOGY

Faculty member: prof. Michela Matteoli, prof. Davide Pozzi, dr. Erica Tagliatti, dr. Fabia Filipello *Number of lessons:* 12 (24 hours)

Programme:

- General principles of neuropharmacology: synapse as a drug target.
- Pharmacology of neurodegenerative disorders, with a focus on Parkinson's disease.
- Antidepressant drugs and pharmacotherapy of depressive disorders.
- Antipsychotic drugs
- Anxiolytics and hypnotic drugs.
- Mechanisms of action of antiseizure medications.
- Addiction and drugs of abuse.
- Analgesic drugs and pain therapy.
- Pharmacology of the blood-brain-barrier and multiple sclerosis.
- General anesthetic drugs.
- New frontiers in neuropharmacology.

GASTROINTESTINAL PHARMACOLOGY

Faculty member: prof. Maurizio D'Incalci, prof. Alessandro Armuzzi *Number of lessons:* 2 (4 hours) *Programme:*

- Pharmacotherapy for gastric acidity, peptic ulcers, and gastroesophageal reflux disease.
- Pharmacotherapy for motility and functional gastrointestinal disorders.



- Antiemetics.
- Pharmacotherapy for inflammatory bowel disease.

DRUGS AGAINST ENDOCRINE DISEASES

Faculty member: prof. Davide Pozzi, dr. Maria Luisa Malosio *Number of lessons:* 2 (4 hours) *Programme:*

- Introduction to pharmacology of the hypothalamic-pituitary axis.
- Pharmacology of the reproductive tract: estrogens, progestins, and androgens.
- Adrenocorticotropic hormone: adrenal cortex and steroids.
- Pharmacology of prolactin- and GH- secreting adenomas.
- Pharmacology of diabetes (type I and type II diabetes).

ANTICANCER DRUGS

Faculty member: prof. Maurizio D'Incalci, dr. Sergio Marchini,

Number of lessons: 6 (12 hours)

Programme:

- General aspects of antitumor therapy and its limits.
- General principles of personalized therapy.
- Main classes of chemotherapeutic drugs: alkylating agents, platinum coordination complexes, antimetabolites, natural products, miscellaneous.
- Targets and mechanisms of action of conventional chemotherapy.
- Hormones and their antagonists as antitumor agents.
- Conventional chemotherapy and targeted therapy.
- Main classes of small molecules inhibitors, their targets and mechanisms of action.
- General principles of cell therapy against cancers.
- Combinations of drugs and their association with other therapeutic modalities (immunotherapy, surgery, radiotherapy).

IMMUNOSUPPRESSIVE THERAPIES IN NEPHROLOGY

Faculty member: prof. Maurizio D'Incalci *Number of lessons:* 1 (2 hours) *Programme:*

• Immunosuppressive drugs used to treat kidney diseases.

CRITICAL ANALYSIS OF CURRENT USE AND DEVELOPMENT OF DRUGS

Faculty member: prof. Maurizio D'Incalci Number of lessons: 3 (6 hour)



Teaching Methods

The synchronous sessions are organized mainly as lectures (on campus and TEAMS). Students are encouraged to actively participate to the lectures with questions and comments. Guest lecturers provide the insight and perspective of specific fields of pharmacology.

The asynchronous sessions (off campus) are characterized by in-depth articles and investigations related to specific topics.

Assessment

The final test consists of multiple choice questions. Questions will include the whole program of the course (Full exam). Each question will score 0.5 point; no penalties will be applied for wrong answers.

There will be also an intermediate test at the end of the first semester (IT 1^{st} semester exam), that it is not mandatory. Students who will not take or will not pass the 1^{st} semester exam will have to take the Full exam. Students who passed the IT 1^{st} semester exam will be able to take a second test at the end of the second semester (IT 2^{nd} semester exam), to complete the exam. This option can be seized only till the September session, after that students will have to pass the Full exam.

<u>IT 1st semester exam</u>

31 questions (each question 0.5 points) about the contents addressed in the 1st semester lessons. To pass the exam, the student will have to answer to at least 18 questions correctly. Time allotted: 45 minutes.

IT 2nd semester exam

31 questions (each question 0.5 points) about the contents addressed in the 2nd semester lessons. To pass the exam, the student will have to answer to at least 18 questions correctly. Time allotted: 45 minutes.

Full exam

62 questions (each question 0.5 points) about the whole program of the course. To pass the exam, the student will have to answer to at least 36 questions correctly. Time allotted: 90 minutes.

Scores of the Full exam or IT exams (1st semester + 2nd semester) will be based on the number of questions answered correctly as indicated in the table below:

correct answers	points	mark
61-62	30.5-31	30 cum laude
36-60	18-30	18-30
	(numbers with decimal	
	places are rounded up to the	
	nearest integer)	
<36	<18	Not passed



Texts

Title: "Basic & Clinical Pharmacology" *Author:* Bertram G. Katzung, Todd W. Vanderah

Title: "Goodman and Gilman's The Pharmacological Basis of Therapeutics" *Author:* Laurence Brunton, Bjorn Knollmann

Title: "Rang & Dale's Pharmacology" *Author:* James Ritter, Rod Flower, Graeme Henderson, Yoon Kong Loke, David MacEwan, Humphrey Rang

Title: "General and Molecular Pharmacology: Principles of Drug Action" *Author:* Francesco Clementi, Guido Fumagalli