



Asignature: Pharmacology of Organs and Systems
Code: 32508
Centre: Medicine School
Title: Master in Pharmacological Research
Level: Master
Type: Compulsory
Number of credits: 4 ECTS
Academic Course: 2017-18

1. COURSE TITLE

Pharmacology of Organs and Systems

1.1. Course number

32508

1.2. Content area

Pharmacology

1.3. Course type

Compulsory

1.4. Course level

Master Degree

1.5. Year

First

1.6. Semester

First semester

1.7. Language

English

1.8. Prerequisites

Degree in Medicine, Pharmacy, Biology, Biochemistry, Veterinary, Psychology, Nursery, or other degree related to Health Sciences. Students must have a suitable level of English to read and understand scientific papers.

1.9. Minimum attendance requirement

Attendance to lectures and seminars is mandatory; the student must attend at least 80% of seminars to be evaluated



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1.10. Faculty data

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1.11. Course objectives

In the theoretical part will provide systematic and updated information on the latest experimental findings in the main pharmacological areas, as well as clinical trials to demonstrate its therapeutic efficacy and possible alerts that may appear in relation to its use. The main drug families grouped by systems will be studied, analyzing in detail their mechanisms of cellular and molecular action, their physiological and pathophysiological repercussions, as well as their therapeutic indications and main adverse effects, so that the student acquires the necessary knowledge for the correct follow-up of teaching in the subsequent specialization module. It also seeks to bring the student closer to biological therapy, which is already providing new drugs to the therapeutic arsenal (monoclonal antibodies, recombinant proteins). We also present the current state of cell therapy and gene therapy, as therapeutic strategies still in experimental phase but with potential clinical applicability in the future. The situation of the so-called "orphan drugs" is also analyzed.

1.12. Course contents

Lectures

Lecture 1: Neurotransmission in the Autonomic Nervous System

The autonomic nervous system: adrenergic and cholinergic transmission. Involved receptors. Ganglionic transmission. Neuromuscular transmission.

Lecture 2: Cholinergic drugs

Muscarinic receptors. Muscarinic effects of acetylcholine. Muscarinic agonists. Muscarinic receptor antagonists. Pharmacological effects. Nicotinic receptors. Acetylcholinesterase inhibitors. Pharmacological properties. Toxicology. Neuromuscular blockers. Pharmacological properties. Stimulants and blockers of ganglionic neurotransmission. Nicotine.

Lecture 3: Adrenergic drugs

Concept. Adrenergic receptors. Catecholamines and non-Catecholamines. Direct-, indirect-, and mixed-acting sympathomimetic amines. Selective alfa agonists. Selective beta-2 receptor agonists. Alpha adrenergic receptor antagonists. Selective alpha-1 antagonists. Non-selective beta adrenergic receptor antagonists. Cardioselective beta antagonists. Beta antagonists with additional cardiovascular actions.



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Seminar

Seminar 1: Pharmacology of autonomic nervous system

An experiment with reserpine. The cocaine paradox. Myocardial infarct at a football match: beta blockade. Cardiac rate and atropine-propranolol interaction. Catecholamines and blood pressure. The experiment of Otto Loewi. Atropine and the placental barrier. Atropine and hexamethonium. A family poisoned with mushrooms. Autonomic control of the eye.

Lecture 4: Neurotransmission in the CNS and its pharmacological interference

Central nervous system. Historic review. Types of neurotransmission: stimulant and inhibitory. Involved receptors. Relevance in health and disease.

Lecture 5: Antipsychotic drugs. Drugs for Parkinson' disease

The nature of schizophrenia: etiology and pathogenesis. Classification of antipsychotic drugs: 1) first-generation or typical antipsychotic drugs, and 2) atypical antipsychotic drugs. Receptor types on which act these drugs to produce their therapeutic and adverse effects. Pharmacological effects, pharmacokinetics properties, interactions, and adverse effects. Features of Parkinson's disease: neurochemical basis and pathogenic mechanisms. Therapeutic targets for Parkinson's disease: 1) counteracting deficiency of dopamine in basal ganglia, 2) blocking the central cholinergic hyperactivity, and 3) prevent neurodegeneration. Drug treatment of Parkinson's disease: levodopa, inhibitors of dopa-decarboxylase (DDC), inhibitors of catechol-O-methyl-transferase (COMT), dopamine agonists and monoamine oxidase-B (MAO-B) inhibitors. Mechanism of action, pharmacological effects, pharmacokinetics properties, interactions, adverse effects, and therapeutic indications

Lecture 6: Antidepressant and antimanic drugs

Nature of depression and classification of depressive syndrome: unipolar and manic-depressive (bipolar) disorders. Pathogenic theories of depression. Classification of antidepressant drugs according with their mechanisms of action: 1) monoamine uptake inhibitors (tricyclic antidepressants, serotonin uptake inhibitors and newer inhibitors of noradrenaline and serotonin uptake), 2) monoamine receptor antagonists, and 3) monoamine oxidase (MAO) inhibitors. Pharmacological effects, pharmacokinetics properties, interactions and unwanted effects. Drugs used to control the mood swings characteristic of bipolar disorder (lithium, several antiepileptic drugs and some atypical antipsychotic drugs).



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Lecture 7: Hypnotic drugs and sedatives

General mechanisms of action and therapeutic targets of benzodiazepines and barbituric. Classification by chemical and pharmacodynamics aspects. The problem of the tolerance. Benzodiazepine drugs: Pharmacokinetics and Pharmacodynamics. Barbituric drugs: Pharmacokinetics and Pharmacodynamics. Examples of patch clamp experiments in single cell and single channel of chloride current upon benzodiazepine treatment.

Lecture 8: Antiepileptic drugs

The nature of epilepsy: the neurobiological mechanisms underlying it and the animal models of disease. Classification of classical and newer antiepileptic drugs according to their mechanism of action: 1) inhibition of sodium channel function, 2) inhibition of calcium channel function, 3) enhancement of GABA action, and 4) other mechanisms. Main difficulties of prescription and treatment with antiepileptic drugs: pharmacokinetic interactions and unwanted effects.

Lecture 9: Opioid drugs

Historical overview. Central and peripheral nociceptive pathways. Opioid receptors. Classification of opioid drugs: pure agonists, partial agonists, mixed agonists-antagonists, pure antagonists. Pharmacological effects. Pharmacokinetics. Tolerance and dependence. Adverse effects.

Lecture 10: Drugs of abuse: tolerance and dependence

Major drugs of abuse, which are consumed with stimulant and/or recreational purposes. These drugs are used: 1) by their marked effects on mental function and behavior, causing excitement and euphoria, reduced feelings of fatigue, and increased motor activity (CNS stimulant drugs, such as amphetamines, cocaine, and crack), or 2) to affect, at low doses, mechanisms normally involved in the thought patterns, perception and cognition (Psychotomimetic drugs, like cannabis and its derivatives, and LSD). Designed drugs (NDMA or ecstasy) share pharmacological effects of the two groups. The study of each drug includes its pharmacological effects, pharmacokinetics properties, unwanted effects, as well as the dependence type and tolerance extent that chronic consumption of the drug could produce.

Lecture 11: Drugs for migraine

Concept of migraine. Theories implicated in the pathophysiology of migraine (Vascular, Neurogenic and Trigeminal-neuroinflammatory). (I) Drugs used for acute migraine: AINEs, ergotics and triptans. (II) Drugs used for migraine prevention: beta-blockers, calcium antagonists, valproic acid, antidepressive drugs, topiramate.



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Lecture 12: General and local anaesthetics

Concept of general anaesthesia. Mechanisms of action of general anaesthetics. Principles of anaesthesiology. Preanaesthetic medication. General anaesthetics: classification, pharmacokinetics, side effects. Analgesics and muscle relaxants used in anaesthesia. Monitoring of anaesthesia. Concept of local anaesthesia. Chemical structure of local anaesthetics. Mechanisms of action. Pharmacokinetic properties. Pharmacological actions and adverse effects.

Seminar

Seminar 2: Neurotransmission in the CNS and its pharmacological interference

Students should obtain information on chemical transmission and drug action in the CNS. On this basis, the student will solve a series of related experiments: 1) historical overview of the main findings regarding the pathogenesis and treatment of Parkinson's disease, 2) experiment that mimics the motor symptoms of Parkinson's disease after administration of MPTP to monkeys, 3) pharmacokinetic problem of general anesthesia, 4) a problem of induction of general anesthesia.

Lecture 13: Anti-anemic and colony stimulant factors

Metabolism of iron, folic acid, and vitamin B12. Characteristics and therapeutic approaches for iron, folic acid, or vitamin B12 deficiencies. Pharmacological applications of erythropoietin and other colony stimulant factors

Lecture 14: Drugs interfering with blood clotting

Anticoagulants: mechanisms of action. New anticoagulants. Antiplatelet drugs: mechanisms of action. Fibrinolytic and antifibrinolytic: mechanisms of action.

Lecture 15: Nonsteroidal anti-inflammatory drugs (NSAIDs)

Classification based on their chemical structure and their selectivity for cyclooxygenase (COX)- 1 and 2. Molecular mechanisms involved in the inhibition of COX-1 and COX-2 by the different drugs. Pharmacological effects: analgesic, anti-inflammatory, antipyretic, uricosuric, antiplatelet, others. Pharmacokinetics. Side effects related with COX-1 or COX-2 inhibition, other side effects.

Lecture 16: Anti-inflammatory steroids

The adrenal cortex. Regulation of the synthesis and release of glucocorticoids. Cortisol and analogues. Synthetic corticosteroids: structural modifications. Mechanism of action. Pharmacological effects. Pharmacokinetics. Adverse effects.



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Lecture 17: Immunoregulatory drugs

Cellular and humoral immunity. Immunosuppressant drugs: immunophilin inhibitors, antimetabolites, monoclonal antibodies, cytokine antagonists, soluble receptors analogues, other immunosuppressant. Immunostimulant drugs: interferons, interleukins, other drugs. Mechanisms of action, pharmacological effects, pharmacokinetics and pegylation, adverse effects.

Seminars

Seminar 3: Pharmacology of pain and inflammation

Historical review of the discovery of aspirin and its mechanism of action. Studies on NSAIDs selectivity for COX isoforms. Clinical trials on the adverse effects produced by coxibs, and the possible involved mechanisms. Cellular mechanisms of cytokine-induced inflammation and its prevention by glucocorticoids. Experimental studies on opioid receptors and their antagonists.

Lecture 18: Pharmacology of the respiratory system

Asthma: early response and late inflammatory response. Drugs used in asthma: (I) Broncodilators: β_2 adrenergic agonists (salbutamol), theophylline. Muscarinic antagonists (Ipratropium bromide). (II) Corticoides. (III) Antileukotienes (zafirlukast..). (IV) Inhibitors of the release of inflammatory mediators: disodium cromoglycate, nedocromil. (V) Omalizumab: humanized monoclonal antibody against IgE. Expectorants and anti-cough drugs.

Lecture 19: Pharmacology of digestive system

Control of gastric acid secretion. Antiulcer drugs, mechanism of action, pharmacokinetics, secondary effects, interactions. Pharmacological groups: (I) Anti histaminic H_2 (ej. ranitidin, famotidin). (II) Inhibitors of the proton pump (ej. omeprazol, lansoprazol). (III) Antiacids (solubles and insolubles). (IV) Others: misoprostol, sucralphate. Drugs that increase intestinal motility-Laxatives: (i) Bulk-forming agents. (ii) Osmotic agents (iii) Irritative o stimulants. Drugs that reduce intestinal motility-Antidiarreic drugs: (i) Drugs that modify hydroelectrolitic transport. (ii) Opioid derivatives. (iii) Adsorbent drugs. Anti-emetics: (i) D_2 dopaminergic antagonists (domperidon, metoclopramide). (ii) $5HT_3$ -antagonists (ondasetron) (iii) NK1 antagonists (aprepitant). Emetic drugs: (i) Dopaminergic drugs (Apomorfin). (ii) Ipecacuana.

Lecture 20: Diuretics and plasma expanders

Diuretics. Concept of diuresis. Classification. Mechanisms of action. Physiopharmacological effects. Pharmacokinetics. Adverse reactions. Interactions. Plasma expanders. Classification. Properties. Pharmacokinetics. Adverse reactions.



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Lecture 21: Pharmacology of the renin angiotensin system

Importance of the renin angiotensin system (RAS) in the cardiovascular pathophysiology. Description of the different components of RAS and its importance as targets in the treatment of cardiovascular diseases. Angiotensin converting enzyme Inhibitors (ACEI). Angiotensin II receptor subtype AT1 antagonists. Direct renin inhibitors. Antagonists of aldosterone. Classification of drugs included in the different groups, mechanisms of action involved in its pharmacological action, pharmacological effects, adverse effects, interactions, pharmacokinetic properties.

Lecture 22: Vasodilators and calcium antagonists

Pathophysiologic basis explaining the therapeutic use of vasodilators in cardiovascular diseases. Nitrite and nitrate: classification, mechanism of vasodilator action related to activation of the pathway, pharmacological effects, adverse effects, pharmacokinetics. Calcium antagonists: classification, mechanism of action based on the blockade of Ca^{2+} channels of subtype L, pharmacological effects at the level of vessels and heart of the different drugs, adverse effects, pharmacokinetic characteristics, interactions and. Other vasodilators.

Lecture 23: Lipid-lowering drugs

Plasma lipoproteins: definition and types. Cholesterol and triglycerides transport. Hyperlipoproteinemia types. Inhibitors of HMG-Co-a-reductase: statins. Ion-exchange resins. Derivatives of fenoxi-ixobutyric acid (fibrates) and probucol. Nicotinic acid. Ezetimibe and new lipid modulating agents. Classification of drugs included in the different groups, mechanisms of action involved in its pharmacological action, pharmacological effects, adverse effects, interactions, pharmacokinetic properties.

Lecture 24: Inotropic and antiarrhythmic drugs

Concept. Hemodynamic changes in congestive heart failure. Cardiac glycosides. Digoxin. Mechanisms involved in the positive inotropic effect. Effects on the autonomic nervous system. Pharmacokinetics and toxicity. Dopamine and dobutamine. Inhibitors of phosphodiesterase III. General concepts of the ionic currents involved in cardiac action potential and of the mechanisms of production of arrhythmias. Classification of antiarrhythmic drugs: Group IA, IB and IC (sodium channel blockers), Group II (β -adrenergic receptor blockers), Group III (drugs that prolong duration of action potential), Group IV (calcium antagonists), others.



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Seminar

Seminar 4: Pharmacology of cardiovascular system

Pharmacology of high blood pressure. Drugs involved (diuretics, beta blockers, calcium antagonists, inhibitors of the renin angiotensin system, others), which can be used in different physiological or pathological situations that may present hypertensive patients. A problem of coronary vasoconstriction and nisoldipine. The experiment of Robert Furchgott on EDRF and nitrovasodilatation. The cascade experiment of Salvador Moncada. Albrecht Fleckenstein's experiment with verapamil. The experiments of D. G. Allen and J. R. Blinks with acetylstrophantidine in the heart of the frog. Probes for measuring calcium signals in the frog heart. An experiment with calcium channel agonists.

Lecture 25: Pharmacology of sexual hormones

Oestrogens and progestogens. Classification, synthesis, and secretion. Mechanism of action. Physiopharmacological actions. Pharmacokinetics. Adverse reactions. Antioestrogens. Mechanism of action. Pharmacokinetics. Therapeutic applications: contraceptive agents Androgens and anabolic steroids. Physiological and pharmacological actions of androgens. Mechanisms of action. Adverse effects of androgenic preparations. Pharmacological effects and mechanisms of action antiandrogens.

Lecture 26: Drugs that control bone metabolism

Bone remodeling. Regulation of bone formation: actions of Vitamin D, calcitonin and parathormone. Pharmacological groups: (I) Anticatabolic or antiresorptive drugs: Biphosphonates, Estrogens, Selective modulators of estrogen receptors (raloxifen). (II) Anabolic or bone formation drugs: Parathormone and analogues. Teriparatide. (III) Drugs with mixed actions: Stontium ranelate.

Lecture 27: Antidiabetic drugs

Regulation of glycaemia. Diabetes Mellitus: types and involved mechanisms. Insulin: history, structure, synthesis and regulation. Insulin receptors and related signalling pathways: physiological and pharmacological effects. Insulin preparations. Insulin analogues. Mechanisms of action, pharmacokinetic aspects, pharmacological actions, adverse effects. Insulin resistance, type 2 diabetes and metabolic syndrome. Sulphonylureas. Metiglinide derivatives. Biguanides. Glitazones. Alpha-glucosidase inhibitors. Incretin analogues. Dipeptidylpeptidase-4 inhibitors. Mechanisms of action; pharmacokinetic aspects; pharmacological effects; adverse effects. Drugs for treating obesity: orlistat. Other drugs.



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Lecture 28: Anticancer drugs I: cytostatic drugs

General concepts of antineoplastic chemotherapy. Resistances. General adverse effects of cytostatic drugs. Cytostatic drugs: antibiotics, antimetabolites, alkylant agents, platinum compounds, antimitotics, topoisomerase inhibitors, hormonal therapy.

Lecture 29: Mechanisms of action for antibacterial drugs

Characteristics and the mechanisms of action of the betalactamic antibiotics. Description of chemical characteristics and mechanisms of action of aminoglycosides, macrolides, tetracyclins, cloramphenicol, and lincosamines. Antimicrobial spectrum. Description of chemical characteristics and mechanisms of action of quinolones and sulphamides. Main characteristics of other antibiotics: vancomicine, phosphomicine, polypeptidic.

Lecture 30: Classification of antibacterial drugs

Classification, types of penicillins, groups and characteristics. Cephalosporins. New betalactamics and betalactames inhibitors. Classification of the diverse types and groups of of aminoglycosides, macrolides, tetracyclins, cloramphenicol, and lincosamines. Classification of quinolones and sulphamides.

Lecture 31: Antifungal and antiparasitic drugs

Brief historical review of the antifungal drugs. Classification of antifungals according to the mechanism of action and resistance acquisition, chemical structure and use. Most relevant groups studied: polyene antifungals (amphotericin B and their different formulations, and nystatin), azoles (imidazoles and triazoles), terbinafine, echinocandins, flucytosine and griseofulvin. Antiparasitic drugs. Amoebic dysentery and malaria are parasitic diseases of increased morbidity and mortality worldwide. Life cycle of the parasite in the aspects related to the mechanism of drug action. Pharmacological approach (quinine, mefloquine, chloroquine, primaquine, metronidazole, iodoquinol ...). The problem of resistance and the development of new drugs.

Lecture 32: Antiviral drugs

Antiviral drugs: general mechanisms of action and therapeutic targets. Classification of antiviral drugs: chemical and pharmacodynamics aspects. The problem of the resistance against antiviral drugs. Anti-DNA virus drugs: Pharmacokinetics and Pharmacodynamics. Anti-RNA virus drugs: Pharmacokinetics and Pharmacodynamics.



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Seminars

Seminar 5: Rational use of antibacterial drugs

Several cases of fungal infections are presented: a pregnant women with a periodontal infection, a woman with an acute cystitis, a child with a meningococcal meningitis, a man with a sepsis secondary to an urinary infection fro E. Coli, a child with meningitis for H. influenza, a man with a hospital infection by a meticilin-resistant staphylococcus, a sepsis produced by gram-negative bacteria, etc. Possible causal agents and treatment options are described, as well as their advantages and disadvantages. The most appropriate drug association are studied, as well as the most important adverse effects and the measures for prevention/control. Some cases of fungal infections are presented: a Tinea pedis, a vaginal candidiasis secondary to antibiotic therapy and a systemic fungal disease in an immunocompromised patient. Possible causal agents and treatment options are described, as well as their advantages and disadvantages. A case of TB prophylaxis in a patient with recent Mantoux conversion and other of a patient with active tuberculosis are presented.

Lecture 33: Biological therapy

Monoclonal antibodies. Tyrosine kinase inhibitors. Pharmacokinetic aspects. Adverse effects. Therapeutic indications.

Lecture 34: Gene therapy

Gene therapy. Transferable nucleic acids and vectors. Gene expression and suppression, enzyme prodrug therapy. Perspectives for genetic therapy. Applications of Herpesviruses in gene therapy. Applications of Lentiviruses in gene therapy.

Lecture 35: Stem cells

Concept. General considerations of cell therapy. Isolation and characterization of stem cells. Cell therapy in cerebral and medular reparation. Cell therapy in scar formation. Crohn disease.

Lecture 36: Orphan drugs

Concept of rare disease and orphan drug. Therapeutic relevance. Clasification. Legal considerations.

Lecture 37: New Pharmacological perspectives

Therapeutic innovation. Future milestones in pharmacological research.



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1.13. Course bibliography

- **Goodman and Gilman´s: The Pharmacological Basis of Therapeutics.** LL Brunton, B Chabner, B Knollman, 12th Edition, McGraw-Hill, 2011
- Edición española: **Las bases farmacológicas de la terapéutica. Goodman Gilman.** LL Brunton, B Chabner, B Knollman, 12ª Edición. McGraw-Hill Interamericana, 2012
- **Farmacología Humana.** J Flórez, JA Armijo y A Mediavilla, 5ª Edición, Elsevier 2008
- **Rang and Dale´s. Pharmacology.** HP Rang, MM Dale, JM Ritter, RJ Flower, G Henderson, 7th Edition, Elsevier, 2012
- Edición española: **Rang y Dale. Farmacología** HP Rang, MM Dale, JM Ritter, RJ Flower, G Henderson, 7ª Edición, Elsevier, 2012
- **Fundamentos de Farmacología Básica y Clínica.** Fernández-Alfonso MS, Gallo M. 2ª Edición, Panamericana, 2013.
- **Velázquez. Farmacología Básica y Clínica.** Lorenzo P, Moreno A, Leza JC, Lizasoain I, Moro MA. 18ª Edición. Panamericana, 2008.
- Edición española: **Principios de Farmacología.** David E. Golan, Armen H. Tahjian, Ehrin J. Armstrong, April W. Armstrong. 5ª Edición, Wolters Kluwer/Lippincott, 2012
- Edición española: **Farmacología.** Michelle A. Clark, Richard Finkel, José A. Rey, Karen Whallen, 5ª Edición, Wolters Kluwer/Lippincott, 2012

2. Teaching methodology

LECTURES

Lectures will provide organized and structured information elaborated by the Lecturer. The lecture content will include the knowledge already established or in very advanced situation, obtained from textbooks, bibliographic reviews, and relevant original papers. Lectures will take 50 minutes, using audiovisual presentations that can be available in the teaching web page.

SEMINARS

Seminars will provide complementary information to Lectures, including practical exercises and problems to stimulate active student participation, under the supervision of a lecturer. During the Seminars, original research papers, describing classical pharmacological experiments or more recent scientific findings, as well as clinical studies, will be discussed in order to stimulate critical and rigorous scientific analysis by the students. Seminars will take 60 minutes. The content of every Seminar will be previously available in the teaching page web, and the students must work previously on them. Therefore, during the Seminar, the students will expose and discuss the



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provided solutions. Moreover, the students will answer and review several multiple choice questions, similar to those of the Objective evaluation test.

3. Student workload

TOTAL HOURS OF PHARMACOLOGY OF ORGANS AND SYSTEMS			
		N° OF HOURS	%
Activities	Lectures	37	37%
	Seminars	10	10%
	Exams	3	3%
Student work	Weekly study and exam preparation	50	50%
Total work load		100	100%

4. Evaluation procedures and weight of components in the final grade

The Pharmacology of Organs and Systems course will be evaluated in the ordinary and extraordinary calls attending the following criteria:

- a) **Objective evaluation test** will include a multiple-choice test based on the contents given in the Lectures and the Seminar's discussion, to determine the knowledge of the subjects acquired by the students. Short written questions may also be included, similar to those explained in the Seminars. To pass the objective evaluation test, the mark should reach at least 50% of the maximal possible mark.
- b) **Continuous evaluation** will be performed during the whole course by the faculty members. This evaluation will have two quantitative components: (1) as the attendance to Seminars is mandatory, the student with less than 80% participation will not be evaluated, with the exception of extraordinary reasons that should be approved by the Department; (2) in every Seminar, the resolution and exposition of the practical exercises will be evaluated. Final marks will be the



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arithmetic mean of the respective evaluation for every Seminar. To pass the continuous evaluation, the mark should reach at least 50% of the maximal possible mark.

- c) For the course of Pharmacology of Organs and Systems, the objective evaluation will be 70% of the final mark and the continuous evaluation will 30 % of the final mark.

5. Course calendar

Timetable will be indicated in the website:

<http://www.uam.es/otros/mfarma/mfarma/Principal.html>