Imperial College London

BSc in Medical Sciences with PHARMACOLOGY

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Structure for the BSc in Pharmacology

Introduction	
Module 1	**Principles of Pharmacodynamics and Pharmacokinetics**
Module 2	**Cardio-respiratory Pharmacology**
Module 3	**Central Nervous System Pharmacology**

Introduction
This two week course will provide students with an understanding of the scientific foundations of the study of pharmacology.to the basic principles of drug action, including receptor theory, agonism and antagonism, the principal classes of drug targets and signal transduction mechanisms. Concurrently, the course will provide an introduction to pharmacokinetics and drug metabolism.

Lectures covering:
1.   Receptors as drug targets
2.   Hormones as drug targets
3.   Enzymes and ion channels as drug targets
4.   Data handling and statistics
5.   Critical appraisal of scientific writing
6.   Scientific writing

Learning outcomes: At the end of the course the students will be able to:
- understand the nature and purpose of the scientific method and its relation to the practice of medicine
- understand the importance of receptors, enzymes and ion channels as drug targets

Module 1: Principles of Pharmacodynamics & Pharmacokinetics

This course will build upon the information presented in the second year pharmacology course, but will provide more information and will encourage a deeper understanding of the molecular mechanisms involved and insight to the complexities of translating data from animal models to man. The course will provide a more mathematical approach to pharmacokinetic and pharmacodynamic problems, including the use of rate equations and basic calculus. Students will also be introduced to the importance of structural biology in

understanding drug-drug target interactions and the concepts of molecular modelling. Teaching will focus where possible on the use of examples that are pertinent to current scientific and medical issues and will draw upon teaching from several difference disciplines.

Course structure & teaching methods:

Lectures covering:
1. Diffusion and active transport
2. Transport of drugs across biological membranes
3. P-glycoprotein and the removal of drugs from cells
4. The blood brain barrier
5. The placenta, teratogenicity and the fetal origin of disease
6. Drug administration, bioavailability and targeted drug delivery
7. Pharmacokinetics – multi-compartment models
8. Pharmacokinetics – modelling different drug administration routes
9. Drug metabolism and excretion, including, hepatic clearance and first-pass metabolism
10 Molecular basis of receptor agonism, antagonism, inverse agonism, allosteric modulation.
11. Receptor dynamics
12. Enzymes as drug targets
13. Nuclear receptors, including pre-receptor metabolism and steroid response modulators
14. Quantitative analysis of drug action – measurement of efficacy and potency and influence of the physico-chemical environment
15. Mechanisms of tolerance and dependence
16. Principles of drug interactions
17. Biological substances as drugs, including principles of gene therapy.
18. Structural analysis of drugs and their targets and the application of molecular modelling to drug development.
19. Translating pharmacokinetic and pharmacodynamic data from animals models to man.
20. Factors affecting drug actions in man, including the disease state and age.
21. Pharmacogenetics and Pharmacogenomics

PBL sessions
1. Analysis of drug transport across cell membranes (3 sessions)
2. Problems of drug administration during pregnancy, consideration of maternal and fetal metabolism, and the placental barrier (3 sessions)
3. Schild plots and calculation of EC_{50} values from raw data (3 sessions)

Tutorials
1. Structured sessions to reinforce the lectures (4 sessions).

Research Workshop (3 sessions)
Learning objectives: At the end of the course the students will:
1. understand the relative roles of passive diffusion, facilitated diffusion and active transport in, and how physicochemical properties affect, the movement of drugs in the body
2. be able to describe the principal mechanisms of intestinal drug absorption
3. understand the importance of efflux proteins in the removal of drugs from their site of action
4. be able to describe the main features of the blood-brain barrier and the implications this has for the development of drugs targeting the central nervous system

5. be able to describe the main features of the placental barrier and the implications of drug administration during pregnancy
6. understand the use of multi-compartment models to describe drug distribution in the body, and the relative roles of fat storage, protein binding and pH
7. be able to use rate equations to calculate average steady state plasma concentrations following repeated dosing schedules
8. ` understand the processes responsible for drug clearance and the consequences of renal or hepatic failure
9. be able to discuss the pharmacokinetic differences between the different drug administration routes
10. be able to relate the concepts of agonism, antagonism, inverse agonism and allosteric modulation to the effects drugs have on second messenger signalling systems
11. understand the special problems posed by 'biological drugs'
12. understand the value of structural biology in advancing pharmacological science
13. be able to discuss the problems of translating data from animal models to man and how drug action is influenced by the disease state and other medications.

Module 2: Cardio-respiratory Pharmacology

Cardiovascular and respiratory diseases are major causes of global morbidity and mortality. This course will provide students with an understanding of the basic pharmacology of the cardiovascular and respiratory systems and the therapeutic applications of drugs acting on the cardiovascular and respiratory systems. Students will engage in current research issues, including the application of interdisciplinary science to the field, and the processes of translating basic science to the clinic.

Course structure & teaching methods:
Lectures covering:

1. Pharmacology of cardiac electromechanical coupling
2. Vascular physiology and pharmacology, neural and local regulation of blood vessels
   a) Neural control
   b) Nitric oxide and other endothelial mediators
   c) Myogenic tone and local mediators (e.g. adenosine, pH, eicosanoids)
3. Pharmacology of thrombosis and haemostasis
   a) Pharmacology of platelet function
   b) Pharmacology of coagulation and fibrinolysis
4. Renin-angiotensin-aldosterone system (RAAS) and natriuretic peptides
   a) Pharmacology of the RAAS
   b) Natriuretic peptides
5 Lipid lowering agents
6. Anti-obesity agents
7. Treatment of cardiovascular disease
   a) Hypertension
   b) Angina/Ishaemic Heart Disease
   c) Heart Failure
8. Pharmacogenetics & cardiovascular disease
9. Nervous system of the airways
10. Pathophysiology of asthma and COPD
11. Cellular & Molecular mechanisms of glucocorticoids in asthma and COPD
12. Pharmacotherapy for asthma
13. Pharmacotherapy for COPD
14. Hormones to treat lung disease
15. Pharmacology of stem cell research

   a) Introduction to stem cells and regenerative pharmacology
   b) Drugs used for stem cell mobilisation
16. Nanopharmacology

- Self-directed computer based courses (1 session) utilising Pharma-CAL-ogy
- programmes
- CV-respiratory practicals
- Journal Clubs
- Tutorials (4 sessions) structured sessions to reinforce the lectures

Learning outcomes: on successful completion of this module students will have knowledge and understanding of:
1. the scientific principles, techniques and approaches used to study the pharmacology of the cardiovascular and respiratory systems at the molecular, cellular, tissue/organ and whole organism levels, including what constitutes good experimental design and how data are translated to man;
2. how to develop a research plan, including the principles of analysis and presentation of scientific data;
3. how to critically evaluate scientific papers;
4. the current therapeutic approaches used to treat cardiovascular and respiratory disease and their advantages and disadvantages;
5. possible future developments in the pharmacological management of cardiovascular and respiratory disease.

Module 3: CNS Pharmacology

Brain function is the single most important aspect of physiology that defines the differences between humans and other species. Disorders of brain function, whether primary or secondary to malfunction of other systems, are a major concern to human society, and a field in which pharmacological intervention plays a key role. This module aims to give the student a comprehensive knowledge of chemical transmission in the CNS, functions of the major neuronal pathways, how they are affected in neurological disorders and how pharmacological therapies can be used to treat such disorders in the clinic. Considerable attention will focus on the development of novel pharmacological treatments and their translation to man and, ultimately, the clinic.

Course structure & teaching methods:
Lectures covering:
1. Introduction to Chemical transmission and drug action in the CNS
2. Amino Acid Transmitters and drugs which affect their actions
   a) Excitatory amino acids
   b) Glutamate
   c) GABA
3. Epilepsy and its treatment with drugs
4. 5-Hydroxytryptamine pathways in the CNS and their modulation by drugs
5. Anxiety, anxiolytics and hypnotics
6. Depression and therapeutic approaches
   a) Anti-depressant drugs
   b) Is the use of anti-depressants justified?
7) Alzheimer's disease and its treatment
   a) Acetylcholine esterase inhibitors
   b) Targeting the amyloid pathway
   c) Targeting tau
8. Parkinson's disease and its treatment

a) Dopaminergic drugs
            b) Anti-muscarinic drugs
9. Schizophrenia
        a) Historical perspective and introduction to clinical features
        b) The pharmacological treatment of schizophrenia
10. Drugs and alcohol: how they act in the brain
11. Pharmacotherapy for drug and alcohol misuse
12. Addiction:
        a) Systems level approaches, networks and models
        b) Medical aspects
13. Psychosocial interventions in substance misuse disorders
14. Cocaine and other stimulants
15. Contingency management

- CNS practical
- 4Tutorials (4 sessions) structured sessions to reinforce the lectures and other teaching
- Journal clubs at which the students will be required present research papers

Learning outcomes: on successful completion of this module students will be able to:
1. demonstrate in-depth understanding of chemical transmission within the central nervous system
2. demonstrate an understanding of how these neurotransmitter systems are implicated in numerous CNS disorders
3. describe how drugs are utilised to treat these disorders and compare available treatments for specified disorders e.g. efficacy, side effect profile
4. understand the cellular mechanisms of the acute effects of drugs of abuse
5. understand the cellular modifications that occur following chronic administration of certain drugs of abuse
6. understand the mechanisms which underlie drug taking behaviour
7. understand the principles of brain imaging and its role in diagnosis and treatment of brain disorders
8. critically evaluate new neuropharmacological data and the processes of translating novel findings to man
9. appreciate the special difficulties of targeting drugs to the brain.

Past BSc Project Titles in Pharmacology
- Does social isolation induce a dysfunctional neuroendocrine response to subsequent stress
- Do engineered nanoparticles induce a fibrotic response in the human peripheral lung?
- Bitter Taste Receptors and their role in functional responses in the lung.
- Pharmacology of pathogen pathways in human disease; Profiling signalling inhibitors of NOD1 and NOD2 in human tissue
- Metabonomic analysis of methotrexate-induced toxicity in a rodent model of nonalcoholic steatohepatitis
- The role of FUS in chemotherapy response
- Neuroprotective Effects of Histone Deacetylase Inhibitor valproate in the Lactacystin Rat Model of Parkinson's Disease: A Preclinical Magnetic Resonance Imaging Study
- The influence of P2X receptor antagonists on anterior pituitary function