Bio-Pharmacology Program
Pharmacology 4A03 – Drug-Receptor Interaction: WINTER TERM 2024

Instructors: Manali Mukherjee (course coordinator) and Mahmood Akhtar

PHARMAC 4A03 C01
Mahmood Akhtar
Bachelor of Health Sciences Program
Email: akhtarm@mcmaster.ca

PHARMAC 4A03 C02
Manali Mukherjee
Assistant Professor
Department of Medicine
E Mail: mukherj@mcmaster.ca
Phone: 905-522-1155 x 35927
Cell: 289-456-8669

Overview:
The overall theme of this course is to provide students in the Bio-Pharmacology program familiarity with the molecular principles of drug receptor interaction and signal transduction. Students will increase their critical thinking skills in the context of basis of receptor classification, receptor theories, signaling mechanisms, gene expression, drug metabolism and drug elimination.

Class will commence on 11 Jan 2024 and be conducted weekly (Thursday 2:30-5:00 pm).

Three separate problems developed for this course offer students the opportunity for self-directed learning in drug-receptor interactions and signal transduction. Students are expected to set and attain objectives to fit their own educational needs, and a component of the work in the course should be directed to these ends. In addition, there are minimal objectives that every student will be expected to attain. Upon completion of this course, students will be able to have comprehensive knowledge of receptors in relation to the action of drugs and signal transduction, and translation to clinical medicine.

1. Serotonin Punch.(Two research scientists start fighting at a cocktail party over **two receptors of serotonin**)**This problem** encompasses receptor classification based upon various criteria, namely IUPHAR classification; operation, structural and transductional classification. G proteins coupling, 2nd messengers, GTPASE cycle pharmacological tools to establish coupling of receptors with specific G proteins, molecular differences between drug receptors and uptake sites. Species homologies of the receptors, concepts of drug affinity, IC50, Ki values, drug efficacy and potency.

15 December 2023

2. Freddie Freeloader. (In the back room of a dingy North Carolina bar two disreputable-looking, long-lost friends are talking about their all-consuming passion) **This problem** encompasses various theories for drug receptor interaction, for example rate theory, occupancy theory, Two state model, Three state model, Ternary complex model, Cubic ternary complex model, Allosteric ternary complex model and Quaternary complex model. Differences between Linear and Collateral efficacy, Constitutive receptor activity, classical versus neutral antagonist, biased agonism, β-arrestin and other signaling pathways.

3. Big Car Blues. (A co-op student studies the wrong topic in preparation for a new work term.) **This problem** deals with the nuclear receptors such as CAR and PXR. Their role in endobiotic and xenobiotic mechanisms. Concepts of drug absorption, distribution, metabolism, elimination and toxicity (ADMEtox). Various domains of nuclear receptors such as DNA binding domain, ligand binding domain and hinge regions. Role of nuclear receptors in gene expression for the enzymes involved in endobiotics and xenobiotics metabolism and elimination.

Course objectives and learning outcomes:

1. To develop skills and critical thinking for the understanding of various concepts of drug receptor interaction by regularly participating in the tutorial groups
2. To develop and enhance skills for communication and dissemination of scientific knowledge
3. To apply molecular pharmacological principles for the targeted drug action
4. To develop skills in scientific writing and presentation
5. To develop skills for problem solving and peer evaluations

Participation in Tutorials

Each student will complete a Tutorial Self-Evaluation Sheet at the end of each tutorial.

The self-evaluation will be discussed with the group, revised if necessary and a record kept by the student and instructor. A mid-course evaluation will be performed on TBA during which, each student and the tutor will assess all other students in the group in the categories: Responsibility, Information, Communication, Critical Analysis and Self- Assessment. The tutor will keep a record of the evaluation, but the purpose of this evaluation is strictly formative. At the final tutorial, evaluation will be performed exactly as described for mid-course evaluation. In this case, evaluation will be summative and grades will be used to compute the overall mark.

Problem Summaries for 1 and 3 (10 marks for each problem summary)

A Problem Summary must be submitted to your tutor for every problem **two weeks** after your group completes that problem. It should be neat, free of spelling and grammatical errors and contain your name, your tutor's name, and the title of the problem discussed.

Part A: TUTORIAL SUMMARY (written format required for problem 1 and 3)

Please provide a brief outline of the class engagement and what issues the class/group could generate about this problem. Briefly provide a succinct summary of which of the course objectives were met during the study of this problem. Please identify if there were additional objectives identified during this study, in particularly, related to currently used drugs or diseases? Provide a

general schematic of the flow of the class in how the different objectives were identified/discussed (maximum 1.5 page)

Part B: DISCUSSION (written format required for problem 1 and 3)
In this section choose three key references (published articles) that you came across during your study group discussion of the problem. One reference should be directly associated with a drug/disease. Briefly summarize each of the articles to indicate which course learning objective it helped you understand/identify (250 words per reference/article). In a final conclusion paragraph write a concise summary of your current knowledge of this issue (500 words maximum) and supplement with a summary figure that helped you understand the learning objectives.

Do not exceed three 1.5-spaced pages (excluding references, figures and tables).

Problem summary for 2: (10 marks)
The assessment for problem summary 2 will be in a Poster/visual presentation format. The instructor will divide the class into 2-3 small groups, and each group will present a visual presentation of the problem 2 summary (5 min + 5 Q&A format). Assessment will be based on clarity of the visual aids used to communicate the problem objectives, and explanation of questions posed by fellow students. There will also be peer-marking.

Provide thorough references and use figures and tables. Internet references are NOT acceptable.

Midterm Exam I (FEBRUARY 15th, 2024
On February 15th students will perform a problem-based evaluation exercise (Mid –Term Test). In essence this is just like a regular problem, except that you will work individually, and write your thoughts down. You will be expected to identify one important learning objective, which you will work on during the following week, and you will return a written summary to the next tutorial. After completion of in class test on February 15th we will also do mid-term evaluations.

Novel Problem
You will be expected to write a novel problem for use in Pharmacology 4A03. Your problem must be an appropriate vehicle for students to learn the principles of receptor classification and will be based upon a particular receptor system. It should also raise other issues pertinent to pharmacology that you think students ought to learn. Each student will be given a separate receptor system that will be assigned randomly from a list similar to the following (SUBJECT TO CHANGE):

α-adrenoceptors
β-adrenoceptors
bradykinin receptors
dopamine receptors
leukotriene receptors
melatonin receptors
nicotinic acetylcholine receptors
opiod receptors
tachykinin receptors

15 December 2023

You must list the learning issues you would expect a good tutorial group to identify **directly** from the problem on first reading.

Novel Problems will be marked by all students in the course, except the authors, according to the following scheme.

Does the problem raise issues that are pertinent to the appropriate receptor system?	15%
Does the problem raise issues that are pertinent to receptor classification?	20%
Does the problem raise a sufficient breadth of other issues?	20%
Is the problem original and well-presented?	15%
Is the list of learning issues given by the author consistent with the problem?	15%
Is it realistic to expect a good tutorial group to identify the listed learning issues directly from the problem on first reading?	15%

Final Exam

A problem-solving exercise based on objectives A or B or C will be completed at the end of the course. ***The date will be arranged by the Registrar's Office.***

Evaluation (Grades):

Final marks for this course will be awarded according to the following scheme (subject to change after the class discussion):

Participation in Tutorial	20%
Problem Summaries (10% for each problem)	30%
Midterm Exam	15%
Novel Problem Write-up	15%
Final Exam	20%
Total	**100%**

Academic Dishonesty

Academic dishonesty consists of misrepresentation by deception or by other fraudulent means and can result in serious consequences, e.g. the grade of zero on an assignment, loss of credit with a notation on the transcript (notation reads: "Grade of F assigned for academic dishonesty"), and/or suspension or expulsion from the university.

It is your responsibility to understand what constitutes academic dishonesty. For information on the various kinds of academic dishonesty please refer to the Academic Integrity Policy, specifically Appendix 3, located at:

http://www.mcmaster.ca/policy/Students-AcademicStudies/AcademicIntegrity.pdf

The following illustrates only three forms of academic dishonesty:

1. Plagiarism, e.g. the submission of work that is not one's own or for which other credit has been obtained.
2. Improper collaboration in group work.
3. Copying or using unauthorized aids in tests and examinations.

Students will be required to submit some of their work electronically and in hard copy so that it can be checked for academic dishonesty.

<u>Note</u>

"The instructor and university reserve the right to modify elements of the course during the term. The university may change the dates and deadlines for any or all courses in extreme circumstances. If either type of modification becomes necessary, reasonable notice and communication with the students will be given with explanation and the opportunity to comment on changes. It is the responsibility of the student to check their McMaster email and course websites weekly during the term and to note any changes."