# CBMS842

## Medicinal Chemistry

S1 Day 2014

*Chemistry and Biomolecular Sciences*

## Contents

# General Information

Unit convenor and teaching staff
Unit Convenor
Peter Karuso
peter.karuso@mq.edu.au
Contact via peter.karuso@mq.edu.au
F7B232
any time ... for you guys

Credit points
4

Prerequisites
(Admission to MBiotech or MLabQAMgt or PGDipLabQAMgt or PGCertLabQAMgt or MRadiopharmSc or MSc) and permission of Executive Dean of Faculty

Corequisites

Co-badged status
This unit is co-badged with CBMS306 Medicinal Chemistry

Unit description
This unit starts with an overview of the structure and function of important biomolecules that are drug targets and then focuses on how drugs interact with these molecules to bring about their pharmacological activity. The aim of the unit is to integrate chemical biology and organic chemistry to reveal how these are used in medicinal chemistry to design and synthesise new drugs and to understand their mode of action. Case studies are also provided, including antibacterial, psychoactive and anticancer agents. The theory is complemented by a discovery-based laboratory project incorporating synthetic chemistry, spectroscopic and bioassay methods. The unique aspect of this unit is the focus on computational chemistry in drug design and development. This includes aspects of molecular modelling, molecular dynamics, docking, pharmacophore modelling and QSAR as they relate to the understanding of drug action and design of new drugs.

## Important Academic Dates

Information about important academic dates including deadlines for withdrawing from units are available at https://www.mq.edu.au/study/calendar-of-dates

# Learning Outcomes

On successful completion of this unit, you will be able to:

Define medicinal chemistry and what medicinal chemists know
Define the major biological targets for drugs and how these drugs achieve their pharmacological effect
Define where new drugs come from
Describe qualitatively and quantitatively the relationship between structure and biological activity of drugs
Describe qualitatively and quantitatively the factors affecting drug absorption, distribution and metabolism
Be able to design experiments to determine the structure-activity relationship within a class of drugs
Use the chemical literature to find suitable methods to make new compounds
Use analytical techniques to determine the molecular composition of reaction products
Analyse experimental results to solve related problems
Accurately record your laboratory observations in an appropriate scientific manner
Work with colleagues to undertake experiments in a safe and harmonious way
Explain medicinal chemistry concepts clearly in the classes and in written format in exams, tests and laboratory reports
be able to build, edit, manipulate and visualise small molecules and proteins using the MOE suite of programs. • understand the concepts of structure based design, pharmacophore modelling, molecular modelling and simulations, and medicinal chemistry applications as implemented in MOE
be able to develop a Quantitative Structure Activity Relationship using experimental data

# Assessment Tasks

| Name | Weighting | Due |
|---|---|---|
| Practical | 20% | April 11, June 16 |
| Mid Semester Test | 8% | May 16 |
| Assignment | 5% | April 28 |
| Spot Test | 2% | Undated |
| Workshop | 15% | Week 12 |
| Final Examination | 50% | TBA |

# Practical

Due: **April 11, June 16**
Weighting: **20%**

The practical work (synthesis and antibacterial structure activity relationship of sulfonamides) will be conducted in groups, with ~4-6 people per group. For each group a report in the style of a journal article will be produced at the end of the semester. Following your week 1 laboratory preparation session (March 7), in week 2 in the Friday March 14 lecture/tutorial class, each group will be asked to present a short oral presentation on the justification of your group's choice of final target compounds and possible synthetic procedures. In week 6 on Friday April 11 each of you will submit your laboratory notebook and each group will present a formal write up of the experimental procedure for the synthesis of one of your sulfonyl chloride-amine condensation products, including spectral data by the end of the laboratory session. Feedback will be provided on general safety and preparation in the laboratory as well as on the laboratory write up, including proper recording of experimental procedures and spectral data. The feedback will be aimed to help you improve your scientific writing skills and laboratory practices and general understanding of the practical work.

The combined week 2 and week 7 assessment tasks will be worth 5% (3% individual mark, 2% group mark). At the end of the semester (by week 14, Monday June 16, 5pm to Prof Karuso, F7B232), each group will hand in the final report written in journal format and each student will hand in their laboratory notebook. The whole group will get the same mark for the report (7.5%), but each student will be given an individual mark for their laboratory notebook, general safety and participation in the laboratory (7.5%). Proper recording of experimental procedures and spectral data, analysis of results and discussion and conclusion of these will all be taken into account in the marking. Full details on what is expected for assessment of the practical component is provided in the laboratory manual and on the web site (see under "Laboratory Notes").

On successful completion you will be able to:

- Describe qualitatively and quantitatively the relationship between structure and biological activity of drugs
- Describe qualitatively and quantitatively the factors affecting drug absorption, distribution and metabolism
- Be able to design experiments to determine the structure-activity relationship within a class of drugs
- Use the chemical literature to find suitable methods to make new compounds
- Use analytical techniques to determine the molecular composition of reaction products
- Analyse experimental results to solve related problems
- Accurately record your laboratory observations in an appropriate scientific manner
- Work with colleagues to undertake experiments in a safe and harmonious way

- Explain medicinal chemistry concepts clearly in the classes and in written format in exams, tests and laboratory reports

## Mid Semester Test

Due: **May 16**
Weighting: **8%**

There will be a 50 minute test in Week 9, Friday May 16, 1 pm sharp. This will cover up to the end of prodrugs. This is designed to give you specific feedback on your understanding of the topics up to this stage to assist you in your further study of the unit.

On successful completion you will be able to:

- Define medicinal chemistry and what medicinal chemists know
- Define the major biological targets for drugs and how these drugs achieve their pharmacological effect
- Define where new drugs come from
- Describe qualitatively and quantitatively the relationship between structure and biological activity of drugs
- Explain medicinal chemistry concepts clearly in the classes and in written format in exams, tests and laboratory reports

## Assignment

Due: **April 28**
Weighting: **5%**

The assignment consists of a report that summarises the chemical and biological properties of a pharmaceutical agent in current use and how these relate to its function and properties in the body, along with general historical importance of the drug plus an interview/oral defence (~15 minutes) with the unit coordinator.  This assignment is designed to provide skills in searching the literature and understanding the properties of the pharmaceutical agent from a molecular point of view and written and oral communication skills. The written assignment is due Week 7, Tuesday, April 28, 9am, Science Student Centre, E7A. It must be accompanied with the assignment cover sheet provided on the web site. The oral defence time will be advised following consultation with the unit convenor, being ~1-2 weeks after submission of the written report.

On successful completion you will be able to:

- Define the major biological targets for drugs and how these drugs achieve their pharmacological effect
- Define where new drugs come from
- Describe qualitatively and quantitatively the relationship between structure and biological

activity of drugs
- Describe qualitatively and quantitatively the factors affecting drug absorption, distribution and metabolism
- Use the chemical literature to find suitable methods to make new compounds
- Explain medicinal chemistry concepts clearly in the classes and in written format in exams, tests and laboratory reports

## Spot Test

Due: **Undated**
Weighting: **2%**

Spot tests may be conducted at any stage within the lectures. They are to encourage continuous learning of the lecture material without the stress of a significant assessment component.

On successful completion you will be able to:
- Define the major biological targets for drugs and how these drugs achieve their pharmacological effect
- Describe qualitatively and quantitatively the relationship between structure and biological activity of drugs
- Describe qualitatively and quantitatively the factors affecting drug absorption, distribution and metabolism
- Explain medicinal chemistry concepts clearly in the classes and in written format in exams, tests and laboratory reports

## Workshop

Due: **Week 12**
Weighting: **15%**

The computational chemistry component will include your satisfactory completion of the workshop tasks and your comprehension of those plus a written assignment that will allow assessment of your integration of the skills you have learnt in a contemporary context and the application of these to the design of sulfonamide antibiotics.  Assignment 2 is due at the end of the semester (by Week 12, Friday June 6 to Prof Karuso, F7B232). Late reports will not be marked. All assignments must be accompanied with the assignment cover sheet provided on the web site.

On successful completion you will be able to:
- be able to build, edit, manipulate and visualise small molecules and proteins using the MOE suite of programs. • understand the concepts of structure based design,

pharmacophore modelling, molecular modelling and simulations, and medicinal chemistry applications as implemented in MOE

- be able to develop a Quantitative Structure Activity Relationship using experimental data

## Final Examination

Due: **TBA**
Weighting: **50%**

the final exam will be 3 hours in length with 10 minutes reading time. It is designed to assess specific understanding and holistic concepts of all the topics presented within the course and an opportunity for you to show what knowledge you have obtained and how you can be apply this to new problems.

On successful completion you will be able to:

- Define medicinal chemistry and what medicinal chemists know
- Define the major biological targets for drugs and how these drugs achieve their pharmacological effect
- Define where new drugs come from
- Describe qualitatively and quantitatively the relationship between structure and biological activity of drugs
- Describe qualitatively and quantitatively the factors affecting drug absorption, distribution and metabolism
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- be able to develop a Quantitative Structure Activity Relationship using experimental data

# Delivery and Resources

CBMS842 is a 4 credit point, half year unit and will require an average of 12 hours of work per week (contact hours plus self study time). For students with weak chemistry backgrounds, more time than the average 12 hours per week will probably be necessary to perform satisfactorily in this unit. CBMS842 is run with three hours of lectures/tutorials per week, along with 4 hour blocks of laboratories/workshops. Additional time (~5 x 4 hr slots) will also be needed to conduct computational chemistry workshops. Students are required to attend all lectures, tutorials, laboratory classes and computational chemistry workshops. Active participation by the students in all of these fora is expected.

- Lectures will be presented as a combination of formal lectures and interactive tutorial sessions. Some lecture material will be available on the unit web site, while other material will be provided in the lecture class. Learning is an active process, and as such,

you must engage with the material. This means reading the textbook (and beyond) before and after lectures and studying the computational chemistry notes after each workshop, attempting the assignment questions and other questions, discussing the concepts with your classmates and lecturers. Do not be afraid to ask questions – everyone benefits from a robust and open discussion of the topics.

- Assignment questions are issued so that you will have the opportunity to use the information provided in the lectures and textbook and to test your degree of understanding of those topics as well as further explore the literature to extend your knowledge in contemporary medicinal chemistry.
- Spot tests and a mid session test will also be run in the lecture session. The spot tests will cover any material prior to that day's lecture, therefore all students are expected to keep up to date with lecture material through revision each week. The spot tests and mid session test are designed to allow you to continuously learn and to identify what you understand and the areas that you need to spend more time on, with minimal assessment penalty.
- The computational chemistry workshops will allow you to develop skills in visualisation and explaining of specific properties of drugs and drug development methods.
- To develop communication skills, a short oral on a research topic related to chemical biology will be assessed. You will also be asked for an oral defence of your first assignment (pharmaceutical agent profile) to both determine your true understanding of specific concepts and to further develop your communication skills.
- All laboratory experiments will be conducted in groups. These have a highly collaborative and investigative approach, where you will be designing and synthesising a series of sulfonamides and subsequently testing them for antibacterial activity to determine the important features for their antibacterial activity. In addition, the program MOE will be used to derive a QSAR relationship for the class results in conjunction with published data on a wide range of sulfonamides. The laboratory work is designed to give real life experiences in research by involving students in the design of the experiments, using literature procedures as a guide, and trouble shooting to identify the best experimental conditions. It will emphasise the importance of being highly prepared for all experiments and being fully aware of all safety procedures, proper recording and reporting of all data and interpreting of all results, and having an analytical and inquisitive approach.

## Unit Web Page

The web page for this unit can be found at ilearn.mq.edu.au. Just login and follow the prompts to CBMS842. You can use any web browser such as Firefox, Internet Explorer or Safari to login. iLearn is the name for Macquarie University's new Learning Management System (LMS). The iLearn online learning environment enables learning, teaching, communication and collaboration. It is used to make lecture notes, laboratory notes, discussion forums, digital lecture recordings and other learning resources available to students online.

## Technology Used

You are expected to access the unit web site frequently  This contains important information including notes on the topics to be covered; the laboratory manual; What You Need to Know Sheets; your marks for practicals, quizzes and the mid-session exam; and past exam papers, including with answers.  Additionally, the web site will also be used to post important messages and links to internet facilities and sites of relevance to the course, downloadable software, and lots of other interesting material. If you do not have your own computer you may wish to access the Medicinal Chemistry web resources on campus using the PC computers in the Library or in the C5C computer laboratories.  To view notes on all the topics and past exams on the unit web site, you will require Adobe Acrobat Reader Version 9 or later to be installed on your computer. Acrobat Reader can be downloaded from the Adobe web site http://get.adobe.com/uk/reader/. If you are using the computers in the library, then Acrobat has already been installed.  Please note information will also be sent by email to your student email account so please look at your email account on a frequent basis. You are expected to access SciFinder Scholar and Reaxys to assist in searching the literature. These are available through the library web site. Hand-held calculators will be occasionally used in tutorials and practicals, for tests and in the final examination. Note that text-retrieval calculators are not allowed in the in-semester tests or final examination.

# Unit Schedule

Lectures/tutorials:

The first 3/4 of CBMS842 will provide an overview of the important concepts in medicinal chemistry and the last 1/4 will concentrate on a series of case studies (e.g. penicillins). CBMS842 has three hours/week allocated to lectures/tutorials. While formal lectures will be presented, discussion sessions will also form a major part of the classes. This will be supplemented by practical classes utilising synthetic chemistry, spectroscopic methods and bioassays and workshops on computational chemistry methods.

The laboratory classes will be run in groups and students are required to, in part, design the experiments, using literature procedures as a guide.  Considerable preparation is therefore needed. Past students have found this a valuable experience as it gives them a realistic

approach to conducting research. The laboratory classes will run every week, Friday 1-5 pm except Good Friday, the mid-session break and week 13.

## Topics Lect/Tut Lecturer

- Overview of Medicinal Chemistry wk 1-2 JJ
- Cellular targets ('receptors') for drug action
- Binding of drugs to 'receptors'
- Interaction of 'receptors' with agonists and antagonists
- Protein structure and function wk 2-3 JJ
- Enzyme kinetics
- Interaction of enzymes with inhibitors (competitive, non-competitive)
- Nucleic acids wk 4 JJ
- Drug discovery from nature wk 4-6 JJ
- Drugs from synthesis
- Optimisation of lead compound, structure-activity relationships
- Physicochemical properties of drugs
- Drug absorption, distribution, metabolism and excretion
- Prodrugs
- Quantitative structure-activity relationships wk 7-10 PK
- Combinatorial synthesis
- Case Studies (G-coupled protein receptors)
- Case studies (e.g. antibacterial agents) wk 10-12 JJ
- Chemoinformatics (Guest lecture)
- Discussion of sulfonamide antibacterial assays and lab report wk 12/13 JJ/PK
- Revision wk 13 JJ/PK

# Learning and Teaching Activities

## Lectures/tutorials

Lectures will be presented as a combination of formal lectures and interactive tutorial sessions.

## Practicals

All laboratory experiments will be conducted in groups using a highly collaborative and investigative approach, where you will be designing and synthesising a series of sulfonamides and subsequently testing them for antibacterial activity to determine the important features for their antibacterial activity.

# Policies and Procedures

Macquarie University policies and procedures are accessible from Policy Central. Students should be aware of the following policies in particular with regard to Learning and Teaching:

Academic Honesty Policy http://mq.edu.au/policy/docs/academic_honesty/policy.html

Assessment Policy http://mq.edu.au/policy/docs/assessment/policy.html

Grading Policy http://mq.edu.au/policy/docs/grading/policy.html

Grade Appeal Policy http://mq.edu.au/policy/docs/gradeappeal/policy.html

Grievance Management Policy http://mq.edu.au/policy/docs/grievance_management/policy.html

Disruption to Studies Policy http://www.mq.edu.au/policy/docs/disruption_studies/policy.html *The Disruption to Studies Policy is effective from March 3 2014 and replaces the Special Consideration Policy.*

In addition, a number of other policies can be found in the Learning and Teaching Category of Policy Central.

## Student Code of Conduct

Macquarie University students have a responsibility to be familiar with the Student Code of Conduct: https://students.mq.edu.au/support/student_conduct/

# Student Support

Macquarie University provides a range of support services for students. For details, visit http://students.mq.edu.au/support/

## Learning Skills

Learning Skills (mq.edu.au/learningskills) provides academic writing resources and study strategies to improve your marks and take control of your study.

- Workshops
- StudyWise
- Academic Integrity Module for Students
- Ask a Learning Adviser

# Student Services and Support

Students with a disability are encouraged to contact the Disability Service who can provide appropriate help with any issues that arise during their studies.

## Student Enquiries

For all student enquiries, visit Student Connect at ask.mq.edu.au

## IT Help

For help with University computer systems and technology, visit http://informatics.mq.edu.au/help/.

When using the University's IT, you must adhere to the Acceptable Use Policy. The policy applies to all who connect to the MQ network including students.

# Graduate Capabilities

## PG - Discipline Knowledge and Skills

Our postgraduates will be able to demonstrate a significantly enhanced depth and breadth of knowledge, scholarly understanding, and specific subject content knowledge in their chosen fields.

This graduate capability is supported by:

### Learning outcomes

- Define medicinal chemistry and what medicinal chemists know
- Define the major biological targets for drugs and how these drugs achieve their pharmacological effect
- Define where new drugs come from
- Describe qualitatively and quantitatively the relationship between structure and biological activity of drugs
- Describe qualitatively and quantitatively the factors affecting drug absorption, distribution and metabolism
- Be able to design experiments to determine the structure-activity relationship within a class of drugs
- Use the chemical literature to find suitable methods to make new compounds
- Use analytical techniques to determine the molecular composition of reaction products
- Analyse experimental results to solve related problems
- Accurately record your laboratory observations in an appropriate scientific manner
- be able to build, edit, manipulate and visualise small molecules and proteins using the MOE suite of programs. • understand the concepts of structure based design, pharmacophore modelling, molecular modelling and simulations, and medicinal chemistry applications as implemented in MOE

## Assessment tasks

- Practical
- Mid Semester Test
- Assignment
- Spot Test
- Final Examination

## Learning and teaching activities

- Lectures will be presented as a combination of formal lectures and interactive tutorial sessions.
- All laboratory experiments will be conducted in groups using a highly collaborative and investigative approach, where you will be designing and synthesising a series of sulfonamides and subsequently testing them for antibacterial activity to determine the important features for their antibacterial activity.

# PG - Critical, Analytical and Integrative Thinking

Our postgraduates will be capable of utilising and reflecting on prior knowledge and experience, of applying higher level critical thinking skills, and of integrating and synthesising learning and knowledge from a range of sources and environments. A characteristic of this form of thinking is the generation of new, professionally oriented knowledge through personal or group-based critique of practice and theory.

This graduate capability is supported by:

## Learning outcomes

- Describe qualitatively and quantitatively the relationship between structure and biological activity of drugs
- Be able to design experiments to determine the structure-activity relationship within a class of drugs
- Analyse experimental results to solve related problems
- be able to develop a Quantitative Structure Activity Relationship using experimental data

## Assessment tasks

- Practical
- Final Examination

## Learning and teaching activities

- Lectures will be presented as a combination of formal lectures and interactive tutorial sessions.

- All laboratory experiments will be conducted in groups using a highly collaborative and investigative approach, where you will be designing and synthesising a series of sulfonamides and subsequently testing them for antibacterial activity to determine the important features for their antibacterial activity.

# PG - Research and Problem Solving Capability

Our postgraduates will be capable of systematic enquiry; able to use research skills to create new knowledge that can be applied to real world issues, or contribute to a field of study or practice to enhance society. They will be capable of creative questioning, problem finding and problem solving.

This graduate capability is supported by:

## Learning outcomes

- Describe qualitatively and quantitatively the factors affecting drug absorption, distribution and metabolism
- Be able to design experiments to determine the structure-activity relationship within a class of drugs
- Use the chemical literature to find suitable methods to make new compounds
- Use analytical techniques to determine the molecular composition of reaction products
- Analyse experimental results to solve related problems
- be able to develop a Quantitative Structure Activity Relationship using experimental data

## Assessment tasks

- Practical
- Mid Semester Test
- Final Examination

## Learning and teaching activities

- Lectures will be presented as a combination of formal lectures and interactive tutorial sessions.
- All laboratory experiments will be conducted in groups using a highly collaborative and investigative approach, where you will be designing and synthesising a series of sulfonamides and subsequently testing them for antibacterial activity to determine the important features for their antibacterial activity.

# PG - Effective Communication

Our postgraduates will be able to communicate effectively and convey their views to different social, cultural, and professional audiences. They will be able to use a variety of technologically supported media to communicate with empathy using a range of written, spoken or visual

formats.

This graduate capability is supported by:

## Learning outcomes

- Accurately record your laboratory observations in an appropriate scientific manner
- Explain medicinal chemistry concepts clearly in the classes and in written format in exams, tests and laboratory reports

## Assessment tasks

- Practical
- Mid Semester Test
- Assignment

## Learning and teaching activities

- Lectures will be presented as a combination of formal lectures and interactive tutorial sessions.

# PG - Engaged and Responsible, Active and Ethical Citizens

Our postgraduates will be ethically aware and capable of confident transformative action in relation to their professional responsibilities and the wider community. They will have a sense of connectedness with others and country and have a sense of mutual obligation. They will be able to appreciate the impact of their professional roles for social justice and inclusion related to national and global issues

This graduate capability is supported by:

## Learning outcomes

- Accurately record your laboratory observations in an appropriate scientific manner
- Work with colleagues to undertake experiments in a safe and harmonious way

## Assessment tasks

- Practical
- Mid Semester Test

## Learning and teaching activities

- All laboratory experiments will be conducted in groups using a highly collaborative and investigative approach, where you will be designing and synthesising a series of sulfonamides and subsequently testing them for antibacterial activity to determine the important features for their antibacterial activity.

## PG - Capable of Professional and Personal Judgment and Initiative

Our postgraduates will demonstrate a high standard of discernment and common sense in their professional and personal judgment. They will have the ability to make informed choices and decisions that reflect both the nature of their professional work and their personal perspectives.

This graduate capability is supported by:

### Learning outcomes

- Work with colleagues to undertake experiments in a safe and harmonious way
- be able to build, edit, manipulate and visualise small molecules and proteins using the MOE suite of programs. • understand the concepts of structure based design, pharmacophore modelling, molecular modelling and simulations, and medicinal chemistry applications as implemented in MOE

### Assessment tasks

- Practical
- Mid Semester Test

### Learning and teaching activities

- All laboratory experiments will be conducted in groups using a highly collaborative and investigative approach, where you will be designing and synthesising a series of sulfonamides and subsequently testing them for antibacterial activity to determine the important features for their antibacterial activity.

# What has changed

This  unit is essentially the same as last year.