FACULTY OF MEDICINE

SCHOOL OF MEDICAL SCIENCES

DEPARTMENT OF PHARMACOLOGY

PHAR3306

PHARMACOLOGY FOR OPTOMETRY

COURSE OUTLINE

Session 2, 2010

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I. PHAR3306 COURSE INFORMATION

UNITS OF CREDIT (UOC)

Pharmacology for Optometry is a 3rd year Science Course with 6 Units of Credit (UOC).

PREREQUISITES

VISN2111 Vision Science 2A

PHSL2101 Physiology 1A

PHSL2201 Physiology 1B

VISN2231 Introduction to Ocular Disease

OBJECTIVES OF THE COURSE

The aims of the course are to provide optometry students with

- a strong knowledge base in pharmacology and therapeutics that will benefit you in your future optometric practice
- the essential knowledge of the mechanisms of action of pharmacological agents and their therapeutic use in the treatment of systemic and ocular diseases, with emphasis on the agents that optometrists are licensed to prescribe (see appendix 1)
- basic principles of drug action, pharmacokinetics, pharmacodynamics, autonomic pharmacology, major drugs used in the management of cardiovascular, central nervous system, endocrine and inflammatory disorders and infection, drugs for eye diseases, side effects and contraindications of commonly used therapeutic agents

COURSE CO-ORDINATORS

Course Coordinator:

Dr. Lu Liu
Room 209a, Wallace Wurth Building
Phone: 9385 8762
Email: Lu.Liu@unsw.edu.au
Consultation times: by email arrangement

Co-coordinator:

Dr. Nicole Jones
Room M205, Wallace Wurth Building
Phone: 9385 2568
Email: N.Jones@unsw.edu.au
Consultation times: by email arrangement

LECTURERS IN THIS COURSE

Dr. T. Binder W.Binder@unsw.edu.au
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COURSE STRUCTURE AND TEACHING STRATEGIES

This 6 UOC course consists of

- 3 lectures per week
- tutorials and practical classes at alternative weeks, up to 3 hours

Lectures: Wednesday 1-2 pm, Thursday 4-5 pm and Thursday 5-6 pm. **Week 1-12**

Tutorials; Monday 3-4 pm. From Week 2, even weeks

Practicals: Monday 3-6 pm. From Week 3, odd weeks

You are expected to attend all scheduled activities for the full duration. You are reminded that UNSW recommends that a 6 units-of-credit course should involve about 125-150 hrs of study and learning activities. Apart from the formal learning activities you are strongly recommended to do your own studies throughout the semester.

Lectures will provide you with the concepts and theory essential for understanding basic pharmacology. To assist in the development of research and analytical skills practical classes and tutorials will be held. These classes and tutorials allow you to engage in a more interactive form of learning than is possible in the lectures. The skills you will learn in practical classes are relevant to your professional development.

APPROACH TO LEARNING AND TEACHING

The learning and teaching philosophy underpinning this course is centred on student learning and aims to create an environment, which interests, challenges, and enthuses students. The teaching is designed to be relevant and engaging in order to prepare students for future careers.

The primary source of information for this course is the lecture material, and the tutorials and practical classes will be directly related to the lectures. Nevertheless, effective learning can also be enhanced through self directed use of other resources such as textbooks, literature references and web based sources. Your practical classes will be directly related to the lectures and you are advised to prepare for practical classes before attendance. It is up to you to ensure you perform well in each part of the course; preparing for classes; studying for exams and seeking assistance to clarify your understanding.

STUDENT LEARNING OUTCOMES

PHAR3306 will develop those attributes that the Faculty of Science has identified as important for a Science Graduate to attain. These include; skills, qualities, understanding and attitudes that promote lifelong learning that you should acquire during your university experience.

Graduate Attributes

A. Research, inquiry and analytical thinking abilities
B. The capability and motivation for intellectual development
C. Ethical, social and professional understanding
D. Effective communication
E. Teamwork, collaborative and management skills
F. Information Literacy – the skills to locate, evaluate and use relevant information.

On completion of this course you should:

1. have developed an understanding of the concepts of pharmacology
2. be able to apply pharmacological approaches to problem solving
3. be able to identify areas in the knowledge of pharmacology that could be improved, and carry out the research necessary to "fill the gaps"
4. be able to organise scientific information into a clear report
5. be able to demonstrate ability to work in teams and communicate scientific information effectively

ASSESSMENT PROCEDURES

	% total mark
Mid session test (50 min duration)	**20%**
Practical assessment (2 short reports, 5% each)	**10%**
Group Assignment	**10%**
Final exam (2 hours duration)	**60%**

Mid session test format: multiple choice questions (MCQs).

Final exam format: multiple choice questions, short and long answer questions

Practicals and tutorials

The practicals and tutorials are provided to support lecture material and practise analytical skills. The practical classes and tutorials help you to develop graduate attributes A, C, D, E & F. During the practical course students will be required to submit written reports for two of the practical sessions. The report itself should be in the form of a scientific communication comprising aims, results and discussion. Answers to questions must also be included. Reports must be legible and as concise as possible. The electronic version of the prac report must be submitted via Blackboard **on the same day as the prac**. No hardcopy is required. There will be a "10% mark deduction per day penalty" for late submission unless in the case of documented illness or family emergency or by pre-arrangement with the course coordinator.

Group Assignment

You will work in teams to research new approaches/developments in ocular pharmacology and a written report to summarise your findings is required. This assessment task will allow you to develop your research, information literacy, communication and time management skills, as well as allowing them to demonstrate the ability to work in a team and collaborate successfully (Graduate attributes A, C, D, E & F). The electronic version of the assignment must be submitted **via Blackboard through Turnitin**, and the hardcopy of the assignment accompanied by a signed plagiarism form must be placed in the locked box in room MG14, Wallace Wurth Building **before 5 pm, Friday, 24th September**. There will be a "10% mark deduction per day penalty" for late submission unless in the case of documented illness or family emergency or by pre-arrangement with the course coordinator. The topics, instructions and marking criteria for the group assignment will be handed to you on the first tutorial class.

Mid session test and final exam

The mid session test will be held during the session on the **2nd of September**. The format is MCQs.

The end of session examination will be held during the official examination period, and the format will be MCQs, and short/long answer questions.

The exam questions will mainly be based on the material covered in the lectures; however the material pertaining to the tutorials and practical classes will also be examinable.

The mid and end of session examinations will address graduate attributes A, B and F and give you feedback on how you are succeeding in the course.

TEXTBOOKS

Prescribed textbook:

- Rang and Dale's pharmacology. 6th ed. Churchill Livingstone/Elsevier. c2007.

Recommended textbooks:

- Goodman and Gilman's the pharmacological basis of therapeutics. 11th ed. McGraw-Hill, Medical Pub. Division, c2006. (available as an e-book from the UNSW Library: http://info.library.unsw.edu.au/cgi-bin/local/access/access.cgi?url=http://www.accessmedicine.com/textbooks.aspx)

- Clinical Ocular Pharmacology. 5th ed. Oxford: Butterworth-Heinemann. c2008.

These textbooks are available in the library. They are also available from the Medical Society Bookshop located in the Old Morgue Building, Prince of Wales Hospital, Barker Street Randwick. The opening hours of the Bookshop are: Mon, Tues, and Thurs. 11:00am-2:30pm, Wed 3:00-7:00pm and Fri 1:00-5:00pm.

National Prescribing Service (NPS) is a member-based organisation providing accurate, balanced, evidence-based information and services to health professionals and the community on Quality Use of Medicines (QUM). You are strongly encouraged to use this service: http://www.nps.org.au/

COURSE EVALUATION AND DEVELOPMENT

Each year feedback is sought from students about the courses offered in the Department of Pharmacology and continual improvements are made based on this feedback. The Course and Teaching Evaluation and Improvement [CATEI] Process of the UNSW is the way in which student feedback is evaluated and significant changes to the course will be communicated to subsequent cohorts of students. Also a staff-student liaison group will be set up and students will be invited to become class representatives to seek feedback from their colleagues and meet with academic staff to discuss any issues that arise. Improvements to PHAR3306 have been made based on feedback given in last year, including increases of practical laboratory and modifications of lecture contents.

GENERAL INFORMATION

The Department of Pharmacology is part of the School of Medical Sciences and is within the Faculty of Medicine. It is located on the lower ground, ground, 2nd and 3rd floors of the Wallace Wurth building. General inquiries can be made at the School of Medical Sciences Student enquires counter, located on the Ground Floor of the Biosciences building (G27). Office hours are 9.00 am - 5:00 pm.

Professor Margaret Morris is Head of Department and appointments may be made through her Administrative officer Chris Riordan (c.riordan@unsw.edu.au) in Room MG14.

There is an **honours** program conducted by the School. The Honours program is co-ordinated by Dr Patsie Polly, Room 508, Wallace Wurth building (ph: 9385 2924; email patsie.polly@unsw.edu.au). Any students considering an Honours year should discuss the requirements with the co-ordinator. Medical students may take a year out of the medical course to undertake an Honours program. This is normally done between the 3rd and 4th year of the course. Outstanding students may be considered for scholarships offered by the University and School and these are offered annually.

Postgraduate research degrees: The Department of Pharmacology offers students the opportunity to enter into **Doctorate** (**Ph.D).** For further information contact the co-ordinator, Dr Pascal Carrive (p.carrive@unsw.edu.au)

School Vacation Scholarships: School of Medical Sciences supports several summer vacation scholarships each year to enable good students to undertake short research projects within the department. For further details contact the Administrative Officer.

Student Advisor: The School Student Advisor Ms Carmen Robinson (9385 2464) is able to provide additional information on any courses offered by the School. Email: Carmen.Robinson@unsw.edu.au

OFFICIAL COMMUNICATION BY EMAIL

All students in the course PHAR3306 are advised that email is now the official means by which the School of Medical Sciences will communicate with you. All email messages will be sent to your official UNSW e-mail address (e.g. z1234567@student.unsw.edu.au) and, if you do not wish to use the University email system, you MUST arrange for your official mail to be forwarded to your chosen address. The University recommends that you check your mail at least every other day. Facilities for checking e-mail are available in the School of Medical Sciences and in the University library. Further information and assistance is available from IT Service Centre, ph. 9385 1333. http://www.it.unsw.edu.au/index.html.

ATTENDANCE REQUIREMENTS

Attendance at practical classes/demonstrations is compulsory, and must be recorded in the class roll ON THE DAY OF THE CLASS. It is your responsibility to ensure that the demonstrator records your attendance and no discussions will be entered into after the completion of the class. Satisfactory completion of the work set for each class is essential. It should be noted that non attendance for other than documented medical or other serious reasons, or unsatisfactory performance, **for more than 1 practical class during the session** may result in ineligibility to pass the course.

BEHAVIOUR AND SAFETY IN PRACTICAL CLASSES

The practical class is an opportunity for students to develop graduate attribute C by behaving in an ethical, socially responsible and professional manner within the practical class.

- Punctual arrival is expected.
- Turn off mobile phones before entering the class.
- Lab coat and enclosed shoes are compulsory in week 9 Human Pharmacology practical class.

Information on relevant Occupational Health and Safety policies and expectations will be provided in the practical notes, as outlined at:
http://www.hr.unsw.edu.au/ohswc/ohs/ohs_policies.html.

Students must take due care with biological and hazardous material and make sure all equipment is left clean and functional. Those who don't adhere to these basic laboratory rules will be marked absent. Special attention should be paid to any precautionary measures recommended in the notes. If any accidents or incidents occur they should be reported immediately to the demonstrator in charge of the class who will record the incident and recommend what further action is required.

NOTICEBOARDS

Noticeboards for this course can be found on the 2nd floor of the Wallace Wurth building. Current timetables and information relevant to you will be displayed here and on the course page on Blackboard. It is your responsibility to check these regularly.

WWW TEACHING RESOURCES

The Department of Pharmacology has chosen to use the University's central Blackboard service to provide teaching materials for all of its courses.

- To access these materials, either point your browser to the TeLT gateway (http://telt.unsw.edu.au/) or go to the School's home page at: http://medicalsciences.med.unsw.edu.au/ then select "Current Students" from the menu bar and click on UNSW Blackboard Learning, under "Quicklinks" in the left column.
- Log in using your zPass (zStudentNo. and password).
- After logging on to Blackboard, look for the course PHAR3306. You should have access to it if you are properly enrolled.

You can make use of Lectopia (formerly ilectures) recordings taken of the lectures that are available on Blackboard. Lecture notes will also be made available on Blackboard before each lecture. It is recommended that students print these out and bring them to the lecture, so they can annotate them and make their additional own notes during the lecture.

HANDWRITING

Students whose writing is difficult to understand will disadvantage themselves in their written assessment. Make every effort to write clearly and legibly. Do not use your own abbreviations.

STUDENT RIGHTS AND RESPONSIBILITIES

Refer to Student Central @:
https://my.unsw.edu.au/student/academiclife/StudentCentralKensington.html.
Student equity and diversity issues can be addressed via Student Equity Officers (Disability) in the Student Equity and Diversity Unit (9385 4734).

SPECIAL CONSIDERATION

Please note the following Statement regarding Special Consideration.

If you believe that your performance in a course, either during session or in an examination, has been adversely affected by sickness or for any other reason, you should notify the Registrar and ask for special consideration in the determination of your results. Such requests should be made as soon as practicable after the problem occurs. ***Applications made more than three days after an examination in a course will only be considered in exceptional circumstances****.*

*When submitting a request for special consideration you should provide all possible supporting evidence (eg medical certificates) together with your registration number and enrolment details. Consideration request forms are available from Student Central. In exceptional circumstances further assessment may be given****. If you believe you might be eligible for further assessment on these grounds, you should contact the Course Coordinator as soon as possible.***

MISSED ASSESSMENT ITEMS

If in any circumstances you unavoidably miss the final exam, mid session test or cannot hand in an assessment task on time, **you must inform the course coordinator and you must lodge a special consideration request**, supported by a medical certificate or other documentation to Student Central (see web address above) within **3 DAYS**.

Your request for consideration will be assessed and a deferred exam may be granted. You cannot assume you will be granted supplementary assessment.

If necessary, a supplementary final examination will be held **in the week starting 6th December 2010**.

Normally, if you miss an exam (without valid reasons) you will be given an absent fail. If you arrive late for an exam no time extension will be granted. It is your responsibility to check timetables and ensure that you arrive with sufficient time.

MISSED PRACTICAL CLASSES

Students who miss practical classes due to illness or for other reasons must submit a copy of medical certificates or other acceptable documentation to the course coordinator in Room M206. **Certificates should be lodged no more than 3 days after an absence.**

MEDICAL CERTIFICATES

Students who miss practical classes due to illness or for other reasons must submit a copy of medical certificates or other acceptable documentation to the course co-ordinator in Room 209a. **Certificates should be lodged no more than 7 days after an absence. Certificates lodged after 7 days will not be accepted**. The following details must be attached: Name, Subject number, Group number, Date of the class, Name of class/es missed.

REPEATING STUDENTS

Practical class exemptions may be granted to repeat students but students **must** check with the course co-ordinator whether they have exemption **prior** to their first practical class. All students must be familiar with the material covered in the practical classes.

STUDENT SUPPORT SERVICES

Those students who have a disability that requires some adjustment in their teaching or learning environment are encouraged to discuss their study needs with the course coordinator prior to, or at the commencement of, their course. Issues to be discussed may include access to materials, signers or note-takers, the provision of services and additional exam and assessment arrangements. Early notification is essential to enable any necessary adjustments to be made. Further information for students with disabilities is available at http://www.studentequity.unsw.edu.au/disabil.html.

APPEAL PROCEDURES

Refer to Student Central @:
https://my.unsw.edu.au/student/academiclife/StudentCentralKensington.html

GRIEVANCE RESOLUTION OFFICER

In case you have any problems or grievances about the course, you should try to resolve it with the Course Organizer (Dr. Lu Liu ph:9385 8762) or the Head of Department (Prof Margaret Morris ph: 9385 1560). If the grievance cannot be resolved in this way, you should contact the School of Medical Sciences Grievance Officer, Dr P.Pandey (9385 2483, P.Pandey@unsw.edu.au).

PLAGIARISM

The School of Medical Sciences will not tolerate plagiarism in submitted written work. The University regards this as academic misconduct. Evidence of plagiarism in submitted assignments, etc. will be thoroughly investigated and may be penalised by the award of a score of zero for the assessable work. Evidence of plagiarism may result in a record being

made in the Central Plagiarism Register and the Faculty Students Ethics Officer being notified.

What is Plagiarism?
Plagiarism is the presentation of the thoughts or work of another as one's own.[1] Examples include:

- direct duplication of the thoughts or work of another, including by copying material, ideas or concepts from a book, article, report or other written document (whether published or unpublished), composition, artwork, design, drawing, circuitry, computer program or software, web site, Internet, other electronic resource, or another person's assignment without appropriate acknowledgement;
- paraphrasing another person's work with very minor changes keeping the meaning, form and/or progression of ideas of the original;
- piecing together sections of the work of others into a new whole;
- presenting an assessment item as independent work when it has been produced in whole or part in collusion with other people, for example, another student or a tutor; and
- claiming credit for a proportion a work contributed to a group assessment item that is greater than that actually contributed.[2]
- For the purposes of this policy, submitting an assessment item that has already been submitted for academic credit elsewhere may be considered plagiarism.
- Knowingly permitting your work to be copied by another student may also be considered to be plagiarism.
- Note that an assessment item produced in oral, not written, form, or involving live presentation, may similarly contain plagiarised material.
- The inclusion of the thoughts or work of another with attribution appropriate to the academic discipline does *not* amount to plagiarism.
- The Learning Centre website is the main repository for resources for staff and students on plagiarism and academic honesty. These resources can be located via: www.lc.unsw.edu.au/plagiarism

The Learning Centre also provides substantial educational written materials, workshops, and tutorials to aid students, for example, in:

- correct referencing practices;
- paraphrasing, summarising, essay writing, and time management;
- appropriate use of, and attribution for, a range of materials including text, images, formulae and concepts.

Individual assistance is available on request from The Learning Centre.

Students are also reminded that careful time management is an important part of study and one of the identified causes of plagiarism is poor time management. Students should allow sufficient time for research, drafting, and the proper referencing of sources in preparing all assessment items.

[1] Based on a document proposed to the University of Newcastle by the St James Ethics Centre. Used with kind permission from the University of Newcastle.

[2] Adapted with kind permission from the University of Melbourne.

II. LECTURE OUTLINES

The course **timetable** is appended at the end of this book (**Appendix II**) and can also be found on Blackboard.

Pharmacodynamics - Sites of drug action
This lecture provides an introduction to pharmacodynamics – what the drug does to the body; it includes: receptors, affinity and efficacy, side effects, desensitisation, up and down regulation, quantitation of drug-receptor interactions, dose-response curves, ED50, and spare receptors.

Pharmacodynamics - Agonist and antagonist activity
Competitive antagonism, irreversible antagonism, functional (physiological) antagonism, chemical antagonism, concept of tone, potentiation, partial agonist, quantitative response, quantal response, therapeutic ratio, indirectly acting drugs.

Pharmacokinetics - Drug absorption and distribution
Pharmacokinetic parameters, half-life, volume of distribution and clearance. Relationship between lipid solubility and drug absorption, distribution, excretion: drug dosage forms, advantages and disadvantages. Renal filtration, reabsorption and secretion. Renal dysfunction and elimination.

Pharmacokinetics - Drug metabolism
Pathways of metabolism of drugs including phase I and phase II metabolism. Hepatic and extrarenal metabolism, genetic polymorphisms and their effects on duration of drug action. Important pathways of ocular drug metabolism. Pharmacokinetic formulae and calculations.

Autonomic nervous system - Cholinergic mechanisms
Introduction to the autonomic nervous system (ANS) and the parasympathetic nervous system (PNS). Synaptic release of acetylcholine and cholinergic transmission. Cholinergic receptor classifications and distributions.

Introduction to 3 classes of cholinergic agents: Muscarinics, Nicotinics and Anticholinesterases. Representative agents of each class, mechanisms of action, clinical uses, side effects and contraindications.

Autonomic nervous system - Adrenergic mechanisms
Catecholamines. synthesis and metabolism of catecholamines. Adrenergic receptors. Alpha-1 adrenergic agonists and antagonists. Alpha-2 adrenergic agonists and antagonists. Beta adrenergic agonists and antagonists. Indirectly acting sympathomimetic amines. Examples of use of these classes of drugs in the eye will be given through out the lectures.

Autonomic control of the eye and autonomic ocular drugs
Commonly used autonomic drugs as cycloplegics, miotics, mydriatics, including. Parasympathomimetics: carbachol and pilocarpine; Parasympatholytics: atropine, tropicamide and cyclopentolate; Sympathomimetics: phenylephrine and dipivefrine; Sympatholytics: brimonidine and timolol. Mechanisms of action, side effects and contraindications.

Anaesthetics
Definition of local anaesthesia. Structure activity relationships. Mode of action, metabolism. Commonly used agents. Therapeutic applications. Toxicity.

Antiepileptic drugs/sedatives/hypnotics
Different types of epilepsy. Anticonvulsant drugs and how they work: (clonazepam, valproate, vigabatrin, phenobarbitone, primidone, phenytoin, carbamazepine, ethosuximide, trimethadione); adverse effects on CNS, blood and other tissues. Desirable properties of sedatives and hypnotics. Mechanism of action of benzodiazepines and barbiturates.

Pharmacology of benzodiazepines. Advantages of benzodiazepines over barbiturates. Zopiclone, a new hypnosedative. Indications for use.

Antidepressants
Monoamine theory of depression; pharmacology of antidepressant drugs. Tricyclic antidepressants, possible modes of action, side effects, overdose. MAO inhibitors: side effects including food interactions (hypertensive crisis) of non-specific MAO inhibitors. Specific MAO inhibitors (moclobemide). SSRI's (fluoxetine as prototype). Li^+ for bipolar depression.

VEGF and angiogenesis in eye disease
Vascular endothelial growth factor A (VEGF-A) is a central mediator in blood vessel growth (angiogenesis) in the eye. "Wet AMD" is a particular form of age-related macular degeneration caused by abnormal growth of blood vessels under the macula. Currently available antiangiogenesis drugs for the treatment of wet AMD will be presented.

Drugs to treat thrombosis
Review of the mechanism of thrombosis formation. The mechanism of actions of (i) Anti-platelet drugs, (ii) Anti-coagulation drugs and (iii) Thrombolytic drugs. By the end of the lecture students should be able to (i).Describe how aspirin prevents platelet activation; (ii) Identify drugs which prevent thrombosis formation versus drugs which remove thrombosis (iii) Describe the mechanisms of action of warfarin and heparin.

Opioid analgesics
Historical introduction. The opioid receptors. The chemistry of the opioids: naturally occurring, semisynthetic, synthetic. Commonly used agents: morphine, codeine, pethidine, methadone, dextropropoxyphene, fentanyl, oxycodone, naloxone, bupremorphine. The assessment of analgesic activity and pain management. Adverse effects of the opioids.

Drugs acting on the cardiovascular system - Antihypertensives
Rationale for treating hypertension, the place of drug therapy, major classes of antihypertensive drugs - ACE inhibitors, calcium antagonists, diuretics, beta-blockers, alpha blockers; commonly used examples from each class; review of basic pharmacology/mechanisms of action; adverse effects and contraindications.

Drugs acting on the kidney - Diuretic agents
Brief review of renal physiology. Diuretic drugs: acetazolamide, furosemide (frusemide) and loop diuretics, chlorothiazide and distal tubule acting diuretics. Potassium sparing diuretics, amiloride, triamterene and spironolactone. Actions, interactions and side effects of the diuretics will be covered, and their clinical uses.

Drugs used to treat asthma
Treatments for asthma and associated pharmacology. Bronchial asthma, inflammatory cells and mediators, commonly used anti-asthmatic drugs [ß-adrenergic agonists, xanthines, glucocorticoids, oral steroids]. Asthma management, treatment of severe acute asthma, viral infections, novel treatments for asthma

Diseases of the human ocular surface
This lecturer will cover the pathogenesis of common and rare diseases of the human ocular surface with particular focus on the impact of ultraviolet radiation exposure. Other topics covered will include ocular surface stem cells and techniques used to treat patients with stem cell failure.

Endocrine drugs- thyroid drugs
Drugs used to treat deficiencies or overactivity in thyroid secretion: thyroxine, triiodothyronine, propylthiouracil, carbimazole, radioactive iodine, high dose iodine, ß blockers.

Endocrine drugs- antidiabetic drugs
Improving glycaemic control using orally active agents, incorporating mechanism of action, clinical use, side effects of the following drugs: Sulphonylureas; metformin, tolbutamide, chlorpropamide, glibenclamide. The insulin sensitising agents.

Anti-inflammatory drugs-NSAIDs
Gross effects, therapeutic uses (including ocular) and side effects of non-steroidal anti-inflammatory drugs. Relationships of effects of NSAIDs to inhibition of cyclooxygenase, analgesia, anti-inflammatory, antipyresis, anti-platelet effects, effects on uterus, gastrointestinal tract. Selective COX-2 inhibitors.

Anti-inflammatory drugs-steroids
Inappropriate inflammatory or immune reactions are involved in many disease processes. Antiinflammatory drugs have been either glucocorticosteroids (GCS), or non-steroidal agents (NSAIDs). The pathway of synthesis of the prostaglandins and their major actions. The gross effects (including the anti-inflammatory effects) of the GCS. Dose forms of eye drops and ointments. Additives to eye drops of GCS.

Antiglaucoma
Brief introduction to the pathology of glaucoma and ocular hypertension. Rationale for the use of directly acting cholinomimetics, acetylcholine esterase inhibitors, adrenergics, carbonic anhydride inhibitors, etc, in treatment. Comparison of pharmacokinetics, routes of administration, contraindications and side effects.

Antihistamine and mast cell stabilizers
History. synthesis & storage. Histamine release. Metabolism. Effects of histamine with focus on allergic reaction and gastric acid secretion. The “triple response”. Histamine H_1 and H_2 receptors. Anti-histamines: actions & clinical uses. Commonly used mast cell stabilizers and how mast cell stabilizers work to prevent or control allergic disorders.

Antibiotics
Mechanisms of action of antibiotics and antimicrobial agents, including inhibitors of DNA synthesis (inhibitors of DNA gyrase and folic acid biochemistry), cell wall synthesis (inhibitors of peptido-glycan synthesis), and the various steps in protein synthesis.

Dry eyes and treatment
The tear film, functions of the tear film and teal secretion; Causes and pathyphisology of dry eye; Management and pharmacology treatment of dry eye

Antiviral and antifungal agents
Pathogenic viruses, viral life cycles, virus-specific targets, DNA polymerase inhibitors, reverse transcriptase inhibitors, protease inhibitors, inhibitors of virus attachment. Pathogenic fungi, sites for chemotherapeutic intervention, antifungal antibiotics including amphoteracin and nystatin, antifungal drugs including flucytosine, azoles such as ketoconazole and clotrimazole.

Adverse drug effects
Epidemiology, severity, most common drugs; type A reactions, dose dependent, related to usual actions of drug; type B reactions, not dose dependent, not related to usual actions of drug. Adverse ocular and systemic effects of drugs administered in eye drops. Adverse ocular effects of drugs administered orally or by injection.

Development of new drugs
There is a need for the development of new drugs because of side effects, tolerance, resistance, and other problems encountered by existing drugs to treat eye diseases. This lecture will present an overview over modern methods of drug discovery, design and development.

III. INFORMATION ABOUT GROUP ASSIGNMENTS

Graduate Attributes will be assessed in this group project are:

- Research, inquiry and analytical thinking abilities
- Effective communication
- Teamwork, collaborative and management skills
- Information Literacy – the skills to locate, evaluate and use relevant information

Aims:

The aims of the group project are:

- To develop your basic and clinical science skills by researching a topic related to eye diseases
- To update your knowledge of recent developments in the treatment of eye diseases
- To develop your skill in collaborative learning (teamwork)

Number of students per group: 4
Each group will be allocated a topic to research and present the information in the form of an assignment.

Task description:

- Research recent advances in the treatment (or potential therapeutic) of your assigned eye disease
- All members should receive a fair amount of task. The group should produce an integrated assignment with a word limit of 3000 words (excluding tables, figures, figure legends and references)
- A hard copy of the assignment must be accompanied by a signed plagiarism form (signed by each member of the group) and placed in the locked box in room MG14. An electronic version must also be submitted via Blackboard.
- The assignment is to be submitted by **5pm on the 24th of September 2010**. A penalty will apply for late submissions.
- Each member should used the "Group Members – Evaluation Form" (see attached) to evaluate the members of your group, including yourself. The form should be submitted individually via Blackboard.

Assessment:

- The assignment will be worth 10% of your total grade.
- The assignment will be assessed by one of the members of the PHAR3306 lecturing staff.

Group Assignment Topics on Ocular Pharmacology

Novel therapeutic approaches to treat:

1. Eye infection
2. Eye inflammation
3. Glaucoma
4. Allergic eye disease
5. Age-related macular degeneration
6. AIDs-related vision impairment
7. Eye cancer
8. Dry eyes
9. Diabetes-related eye disease
10. Corneal angiogenesis
11. Retinitis pigmentosa
12. Giant cell arteritis
13. Hypertensive retinopathy
14. Ocular manifestations of inflammatory bowel disease

Group Assignment Marking Criteria

PHAR3306 S2, 2010

Student names:

Assignment Topics:

SECTION	COMPONENT PARTS	*COMMENTS*
Preliminaries	**Title page** Assignment title, students' names and numbers; Course name & number, date **1**	
Introduction		
The introduction gives an overview of the whole paper	Introduce the topic area; state clearly the purpose of the assignment article; give the reader an indication of what to expect. **5**	
Body of Essay		
Background information	Clearly discuss and introduce the pathophysiological and pharmacological issues related to your topic; outline your main argument **30**	
Evaluation of the issues identified from the sources	**Critical evaluation** of the issues identified and supported by your chosen sources. A balanced and logical presentation that explores the strengths and weaknesses of your issue **30**	
End of Essay		
Conclusion	**Re-state key findings** and state position/argument about the identified issue **4**	

Writing Checklist	Writing Conventions	*Comments*
	Overall readability-Sentence structure-correct grammar and word usage. Sentence and paragraphs well connected. Question clearly answered. Topic sentences, supporting and concluding sentences **5**	
	Appropriate written expression Discipline specific – appropriate vocabulary-use of formal not oral language. Has been proof read. **4**	
	Support –sources-evidence *BJP** **– in-text citations** (4) **and reference list** (4**) follow conventions relevant information selected.** **8**	
	Word Limit- 3000 words **1**	
	Assignment Presentation -Neat, margins, 1.5 spacing, 12 point font. Simple staple. Page numbering **2**	

**: Reference follows the style of British Journal of Pharmacology*

Content & structure: /70

Writing Conventions: /20

Peer/Self evaluations: /10

Total: /100 FINAL /10%

Additional comments:

Group Members - Evaluation Form

Group number _____ **Student name:** _____

Instructions: Use this form to evaluate the members of your group. Write the name of each group member, including yourself, on top of one of the columns, then assign a score of 0 to 10 (0 being the lowest grade, 10 the highest) to each group member for each criterion. Because each group member has different strengths and weaknesses, the scores you assign will differ. At the bottom of this sheet, write down any comments you wish to make.

Criteria	**Group Members**			
Regularly attends meetings				
Is prepared at meetings				
Meets deadlines				
Contributes good ideas				
Effort given to researching subject				
Submits high-quality work				
Listens to other members				
Gives constructive feedback				
Responds to feedback				
Overall assessment of this person's contribution				
Total (/100)				

Comments:

IV. SELECTED PAST EXAM QUESTIONS

SHORT ANSWER QUESTIONS (5 MIN)

1. 5 mg of a drug that occupies a single compartment is administered by i.v. injection. The initial plasma concentration of the drug is 55µg/L and its clearance is 1.5 L/hr. Calculate the elimination rate constant (Ke) and half life ($t_{1/2}$) for this drug.

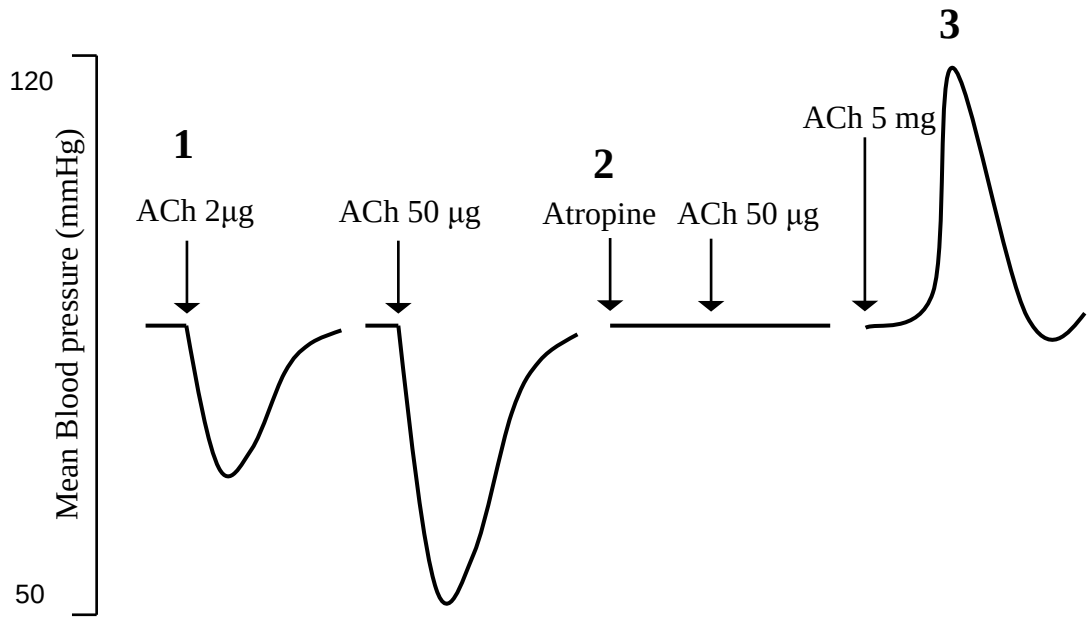
2. Define Phase I and Phase II drug metabolism and give 3 examples each of an inducer & inhibitor of a CYP450 enzyme.

3. Oxybutynin hydrochloride is a non-selective muscarinic receptor antagonist used to treat bladder overactivity.

   a). A contraindication for use of oxybutynin is Glaucoma. Explain what effect oxybutynin could have on a glaucoma patient?

   b). How does oxybutynin cause the side effect of blurred vision?

4. Below is a blood pressure trace from an experiment done in the early 20th Century where acetylcholine was infused into a cat and the blood pressure monitored.



   Describe what receptors are involved in the effects of acetylcholine on blood pressure at points: **1.** **2.** **3.**

5. What are the principal opthalmic applications of adrenergic drugs, and what physiological mechanisms are involved?

6. Some antidepressant agents modulate noradrenergic transmission as part of their mechanism of action. Describe the mechanism of action of agents such as fluoxetine and the monoamine oxidase inhibitors. What are their adverse effects?

7. Describe the differences in the mode of action of β_2 adrenoceptor agonists and glucocorticoids in the treatment of asthma; include examples in your answer.

8. Describe the cellular actions of opioids. How do they produce analgesia?

9. What are the major causes of peptic ulcers? Explain why histamine H_2 receptor antagonists can be used to treat peptic ulcer disease.

10. Discuss antiviral chemotherapy, focusing on the main drugs used to treat virus infections in the eye.

11. Describe the mechanisms of action of the main classes of antibiotics giving and example in each class.

12. What is the effect of ibuprofen on the responses to preformed prostaglandins? Explain briefly.

13. Why are corticosteroids used as eye drops when they are present in the eye after systemic administration?

14. What are the potential (if any) systemic adverse effects of the following drugs after their application to the eye:

    Timolol

    Chloramphenicol

    Pilocarpine Cyclopentolate

15. What are the potential adverse effects of fluorescein packaged in multi-dose eye drops?

LONG ANSWER QUESTIONS (15 MIN)

1. ACE inhibitors and diuretic drugs are widely used in the treatment of hypertension. Discuss the mechanisms of action of these drugs and comment on their adverse effects. What are the applications of diuretics in ocular disease?

2. Improving blood glucose control is of paramount importance in both type 1 and type 2 diabetes. Using examples, contrast the ways in which the different agents used to treat type 1 and type 2 diabetes exert their effects.

3. How do the non-steroidal anti-inflammatory drugs produce their multiple pharmacological effects? Outline the differences between the two major classes of non-steroidal anti-inflammatory drugs. How does their anti-inflammatory activity compare with that of the glucocorticosteroids?

4. Describe the mechanisms of action of antibacterial antibiotics, giving named examples of drug classes.

5. Describe the major classes of drugs used in the treatment of glaucoma. Give an example of each class and discuss their mechanisms of action.

6. Drugs A, B & C were administrated to three patients.

   The following results occurred:
   Drug A caused a reduction in blood pressure
   Drug B caused an increase in blood pressure
   Drug C caused a decrease in blood pressure

   Drug A regulates part of the cholinergic system. Drugs B & C regulate part of the adrenergic system.

	Drug A	**Drug B**	**Drug C**
	Cholinergic system	Adrenergic System	Cholinergic System
Give an example of a drug that would cause the effect seen above?			
What receptor (subtype) does this drug act on?			
What is the mechanism of action of this drug?			
What are the side effects or contraindications of this drug?			
What disease state or ophthalmologic procedure is this drug used in?			

FACULTY OF MEDICINE

SCHOOL OF MEDICAL SCIENCES

DEPARTMENT OF PHARMACOLOGY

PHAR3306

PHARMACOLOGY FOR OPTOMETRY

Practical Class Experimental Procedures

SESSION 2, 2010

1. CONCENTRATION RESPONSE CURVES

Learning objectives

To determine how the agonists, carbachol and histamine respond in the presence of the antagonists, atropine and mepyramine.

Introduction

The guinea-pig ileum is a smooth muscle preparation which also contains parasympathetic ganglion cells and postganglionic parasympathetic nerves. On the smooth muscle fibres are many receptors that control muscle contraction; these include receptors for acetylcholine (muscarinic receptors) and histamine (H_1 receptors). Nicotinic receptors are found on the ganglion cells.

An explanation of the relationship between concentration and response involves the concept of receptors. The magnitude of the response is thought to be proportional to the number of receptors occupied.

In the presence of an antagonist (i.e. a drug which has affinity but no intrinsic activity) the response to a fixed concentration of agonist is decreased. If the concentration-response curve of the agonist in the presence of the antagonist is now plotted and there is a parallel displacement of the concentration-response curve to the right without a shift in the maximum response, then the antagonist is said to act competitively.

Methods

A.THE EXPERIMENTAL PREPARATION

You will be using a computer program which simulates the responses of an isolated guinea-pig ileum preparation to a range of agonists and antagonist.

2 cm of guinea pig ileum is suspended in an organ bath by attaching one end of the ileum to the wire strut and the other end to a length of cotton which will be attached to the force transducer (see Figure 1). This attachment is made to the ileum by pushing the needle and cotton through the muscle wall on one side so as to leave the lumen open. The reservoir is filled with Krebs solution. The solution runs through to the organ bath by opening the clamp situated next to the organ bath. Carbogen is used for aeration of the tissue and the temperature of the bath is maintained at 32°C. Drugs are added to the bath fluid by pipette and the responses of the ileum are recorded by means of a force transducer connected to a chart recorder. After the action of the drug has been noted it is washed out thoroughly until resting baseline activity is reached.

Choose "**Virtual Organ bath**" from the Class Menu. This opens the computer simulation.

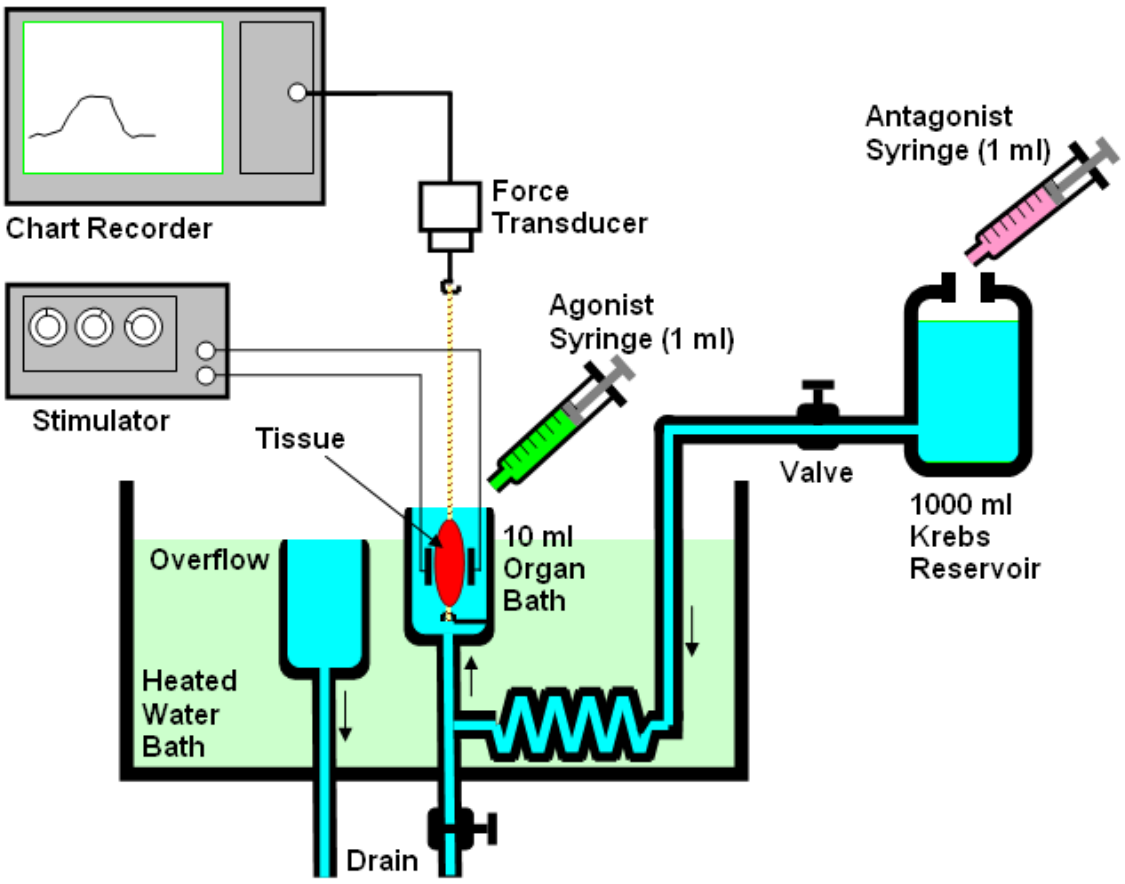


Figure 1. The setup of guinea-pig ileum organ bath

Note: it is important that you don't close down the program before you finish all parts of the practical (A- E) as this will give you a new piece of "ileum" and your results will be slightly different, just as they are when you change real preparations.

B. DILUTIONS

1. Calculate the volume and stock concentration you need to achieve each of the final bath concentrations listed in Table 1 & 2.

The volume of the organ bath is 10 ml and in order to avoid changes in the composition of the bath fluid and to simplify calculation, drugs should be added in volumes of 0.1ml to 1ml.

The final bath concentration, in Molar (M) is related to the stock solution concentration (M), the volume of stock added to the bath (in ml) and the tissue bath volume (ml) by the formula:

Stock Concentration x volume to be added to bath = Final bath concentration x volume of bath

For example:, in order to expose the tissue to a concentration of 1×10^{-7} M it is necessary to add 0.1ml of a $1x\ 10^{-5}$ M (1E-5M) solution

Table 1: Carbachol

Bath Concentration (M)	Volume Added (ml)	Stock Concentration (M)	Response (g)	% Maximum Response
1×10^{-10}				
1×10^{-9}				
3×10^{-9}				
1×10^{-8}				
3×10^{-8}				
1×10^{-7}				
3×10^{-7}				
1×10^{-6}				
3×10^{-6}				
1×10^{-5}				
3×10^{-5}				

Table 2: Histamine

Bath Concentration (M)	Volume Added (ml)	Stock Concentration (M)	Response (g)	% Maximum Response
$1x\ 10^{-9}$				
3×10^{-9}				
1×10^{-8}				
3×10^{-8}				
1×10^{-7}				
3×10^{-7}				
1×10^{-6}				
3×10^{-6}				
1×10^{-5}				
3×10^{-5}				
1×10^{-4}				

C. AGONIST CONCENTRATION - RESPONSE CURVES

CARBACHOL

1. Click on the “record” button to start the chart before adding the drug
2. Select carbachol from the list of available agonists
3. Select the stock concentration you require for $10x10^{-10}$ M (note $x10^{-10}$ can also be written as E-10), as per Table 1.
4. Enter the volume (between 0.1 and 1ml) of the stock solution to be applied into the Volume box, as per Table 1.
5. Click the “Add to Organ Bath” button to pipette the selected volume of the stock solution of carbachol into the organ bath.
6. When the tissue response on the chart recording reaches a steady state (or after 30 seconds if no response has occurred) click the “Flush Reservoir to Bath” button to wash out the carbachol from the organ bath.
7. When the preparation has returned to baseline add the next concentration of carbachol by repeating steps 3-6.
8. Continue adding increasing concentrations (by repeating steps 3) until a maximal response is achieved
9. Click the “Stop” button to stop recording.
10. Using the scroll bar at the bottom of the chart recorder display, select a section of the recording containing the tissue contraction to be measured.
11. Drag the measurement cursor on the chart display to the plateau of agonist response. The contractile force at the cursor point (in units of gms.) is displayed below the cursor. Record the force of contraction in grams (gms) in Table 1.

HISTAMINE

12. Repeat Steps 1-11 for Histamine (remember to change the agonist to histamine) and record your data in Table 2.

Data Analysis

13. Calculate and record in Table 1 & 2 the percent maximum response for your data using the formula: % Maximum Response = (response/ maximum response) x 100
14. Plot the percent maximum response data on the semi-log graph paper provided. The CONCENTRATION is on the logarithmic scale and RESPONSE on the linear scale.
15. From the curve determine the EC_{50}. Enter this data in Table 3.
16. Calculate the volume and stock concentration you need to achieve the EC_{50} as the bath concentration for each agonist.

Table 3

	EC_{50} (M) (Bath Concentration)	***Volume Added (mL)***	***Stock Concentration (M)***
Carbachol			
Histamine			

D. EFFECT OF ANTAGONISTS

ATROPINE AND MEPYRAMINE

1. Click on the "record" button to start the chart before adding the drug
2. Select carbachol from the list of available agonists
3. Select the stock concentration you require for the EC_{50} concentration, as per Table 3
4. Enter the volume (between 0.1 and 1ml) of the stock solution to be applied into the Volume box, as per Table 3
5. Click the "Add to Organ Bath" button to add the selected volume of the stock solution of carbachol into the organ bath.
6. When the tissue response on the chart recording reaches a steady state click the "Flush Reservoir to Bath" button to wash out the carbachol from the bath.
7. When the preparation has returned to baseline repeat steps 1-6 for the histamine EC_{50} concentration
8. Add 10nM of the antagonist atropine to the 1L reservoir
    a) Select atropine from the list of available antagonists.
    b) Select a stock concentration of 1E-5M
    c) Enter 1ml in the volume box
    d) Select "to reservoir" from the "Add to" pull down menu.
    e) Click the "Add to" button
9. Add atropine to the bath by clicking the "flush the reservoir to the bath" button.
10. Add the EC_{50} concentration for carbachol to the bath by repeating steps 1-6
11. Add the EC_{50} concentration for histamine to the bath by repeating steps 1-6
12. Remove atropine from the bath and reservoir by clicking the "Fresh Reservoir" button followed by the "Flush Reservoir to Bath" button.
13. Add 1nM of the antagonist mepyramine to the 1L reservoir
    a) Select mepyramine from the list of available antagonists.
    b) Select a stock concentration of 1E-6M
    c) Enter 1ml in the volume box
    d) Select "to reservoir" from the "Add to" pull down menu.
    e) Click "Add to" button
14. Add mepyramine to the bath by clicking the "flush the reservoir to the bath".
15. Add the EC_{50} concentration for carbachol to the bath by repeating steps 1-6.
16. Add the EC_{50} concentration for histamine to the bath by repeating steps 1-6.
17. Remove atropine from the bath and reservoir by clicking the "Fresh Reservoir" button followed by the Flush Reservoir to Bath" button.
18. Click the "Stop" button to stop recording.
19. Using the scroll bar at the bottom of the chart recorder display, select a section of the recording containing the tissue contraction to be measured.
20. Measure the plateau of each agonist response. Record the force of contraction in grams (g) in Table 4. Calculate the change in response for each agonist in the presence of antagonist

Table 4

Agonist	Size of contraction (g) to agonist				
	Before adding antagonist	In the presence of 10nM atropine	Change in response (+ or – g)	In the presence of 1nM mepyramine	Change in response (+ or – g)
Carbachol					
Histamine					

E. CONCENTRATION RESPONSE CURVE IN THE PRESENCE OF ANTAGONISTS

CARBACHOL

Repeat the carbachol concentration response curve in the presence of the antagonist which produced a reduction in the carbachol response in Table 4. Use the same antagonist concentration as those used in Part D.

1. Click on the "record" button to start the chart
2. Add the antagonist to the 1L reservoir
   a) Select the antagonist from the list of available antagonists.
   b) Select a stock concentration needed
   c) Enter the volume in the volume box
   d) Select "to reservoir" from the "Add to" pull down menu.
   e) Click "Add to" button
3. Add the antagonist to the bath by clicking the "flush the reservoir to the bath" button
4. Select carbachol from the list of available agonists
5. Select the stock concentration you require for $10x10^{-10}$ M
6. Enter the volume (between 0.1 and 1ml) of the stock solution to be applied into the Volume box
7. Click the "Add to Organ Bath" button to pipette the selected volume of the stock solution of carbachol into the organ bath.
8. When the tissue response on the chart recording reaches a steady state (or after 30 seconds if no response has occurred) click the "Flush Reservoir to Bath" button to wash out the carbachol from the organ bath.
9. When the preparation has returned to baseline add the next concentration of carbachol by repeating steps 3-6.
10. Continue adding increasing concentrations (by repeating steps 3) until a maximal response is achieved
11. Remove the antagonist from the bath and reservoir by clicking the "Fresh Reservoir" button followed by the Flush Reservoir to Bath" button.
12. Click the "Stop" button to stop recording.
13. Drag the measurement cursor on the chart display to the plateau of agonist response. Record the force of contraction in grams (gms) in Table 4.

HISTAMINE

Repeat the histamine concentration response curve in the presence of the antagonist which produced a reduction in the histamine response in Table 4. Use the same antagonist concentration as those used in Part D.

14. Repeat Steps 1-13 for Histamine and record your data in Table 5.

Data Analysis

15. Calculate and record in Tables 4 & 5 the percent maximum response for your data using the formula: % Maximum Response = (response/ maximum response) x 100
16. Plot the percent maximum response data on the same graph as the agonist only curve.

Table 4: Carbachol + _____ (Antagonist)

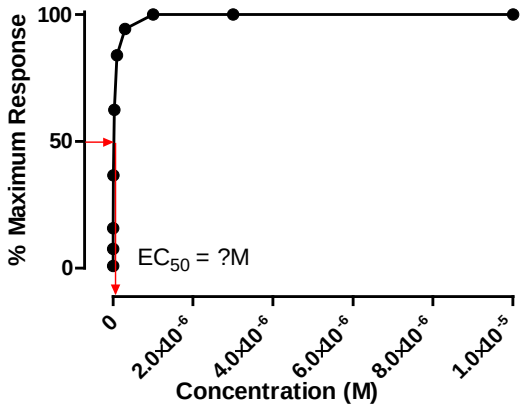
Bath Concentration (M)	Volume Added (ml)	Stock Concentration (M)	Response (g)	% Maximum Response
1×10^{-10}				
1×10^{-9}				
3×10^{-9}				
1×10^{-8}				
3×10^{-8}				
1×10^{-7}				
3×10^{-7}				
1×10^{-6}				
3×10^{-6}				
1×10^{-5}				
3×10^{-5}				
1×10^{-4}				

Table 5: Histamine + _____ (Antagonist)

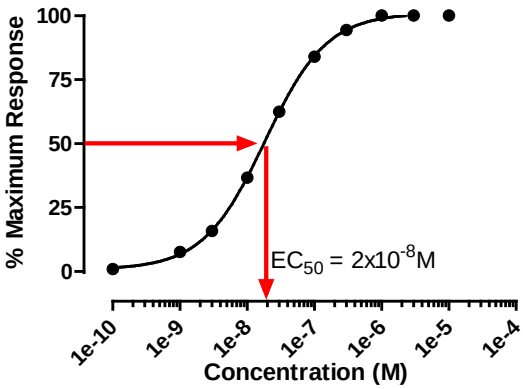
Bath Concentration (M)	Volume Added (ml)	Stock Concentration (M)	Response (g)	% Maximum Response
$1x\ 10^{-9}$				
3×10^{-9}				
1×10^{-8}				
3×10^{-8}				
1×10^{-7}				
3×10^{-7}				
1×10^{-6}				
3×10^{-6}				
1×10^{-5}				
3×10^{-5}				
1×10^{-4}				
3×10^{-4}				

Use of Semi-logarithmic Graph Paper

Linear Graph

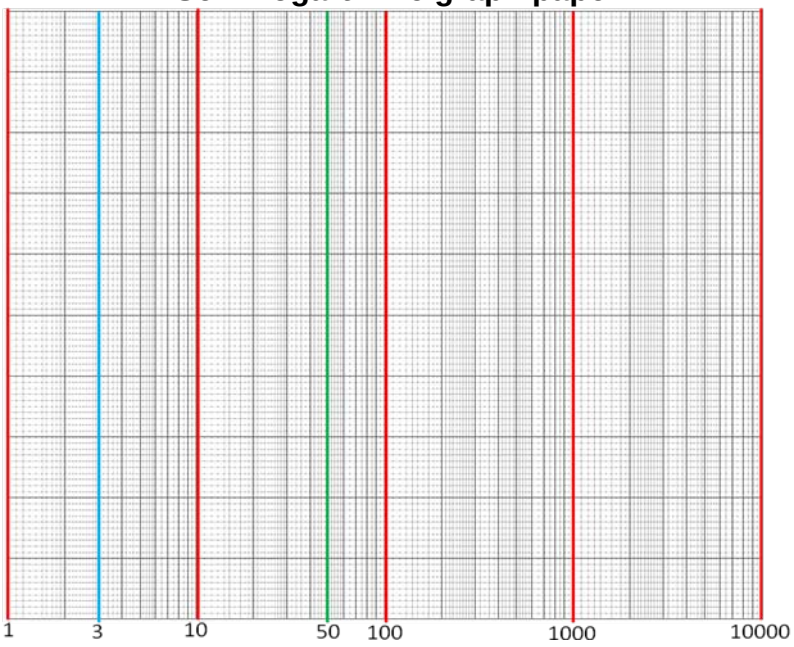


Semi-logarithmic Graph

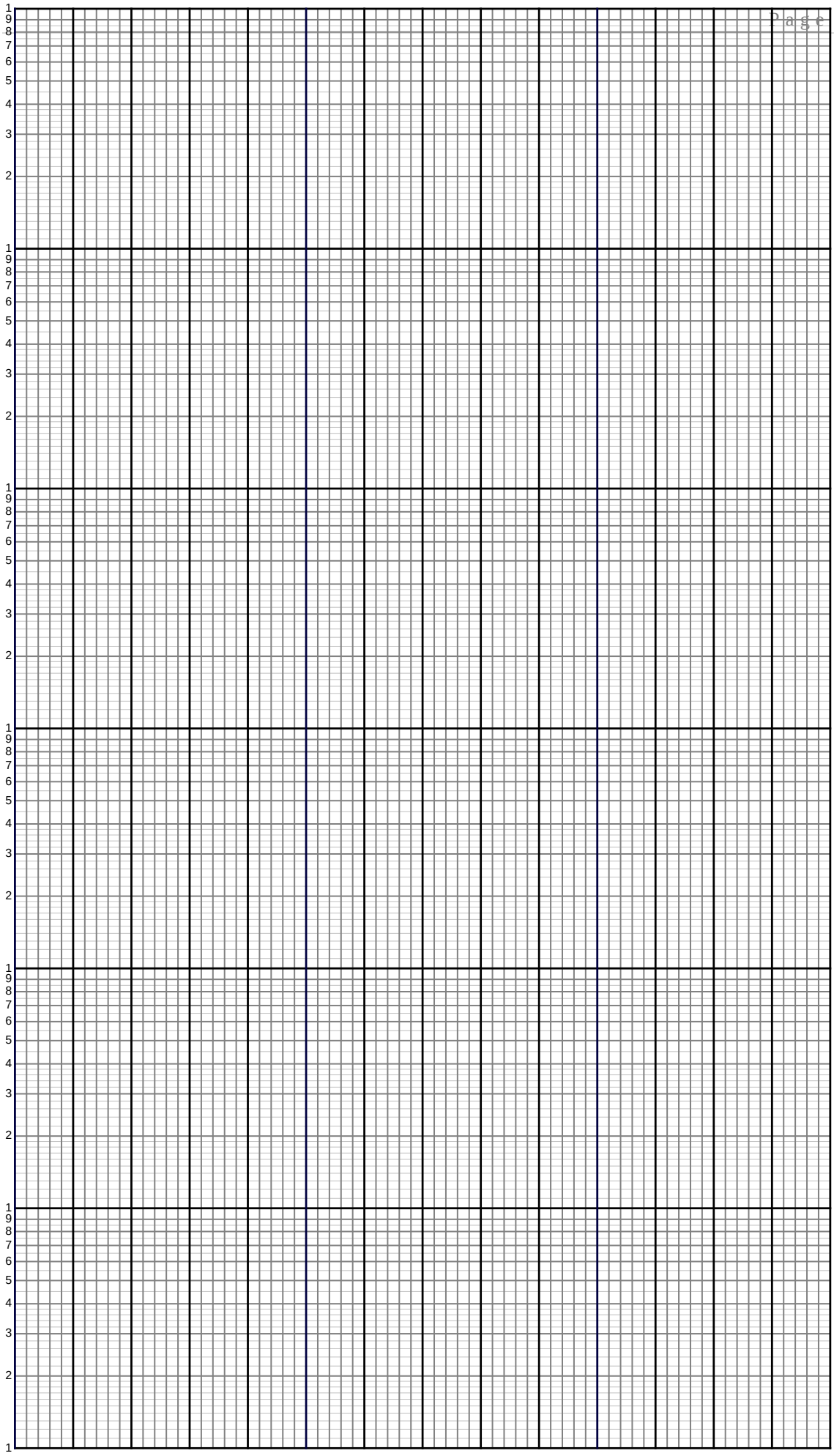


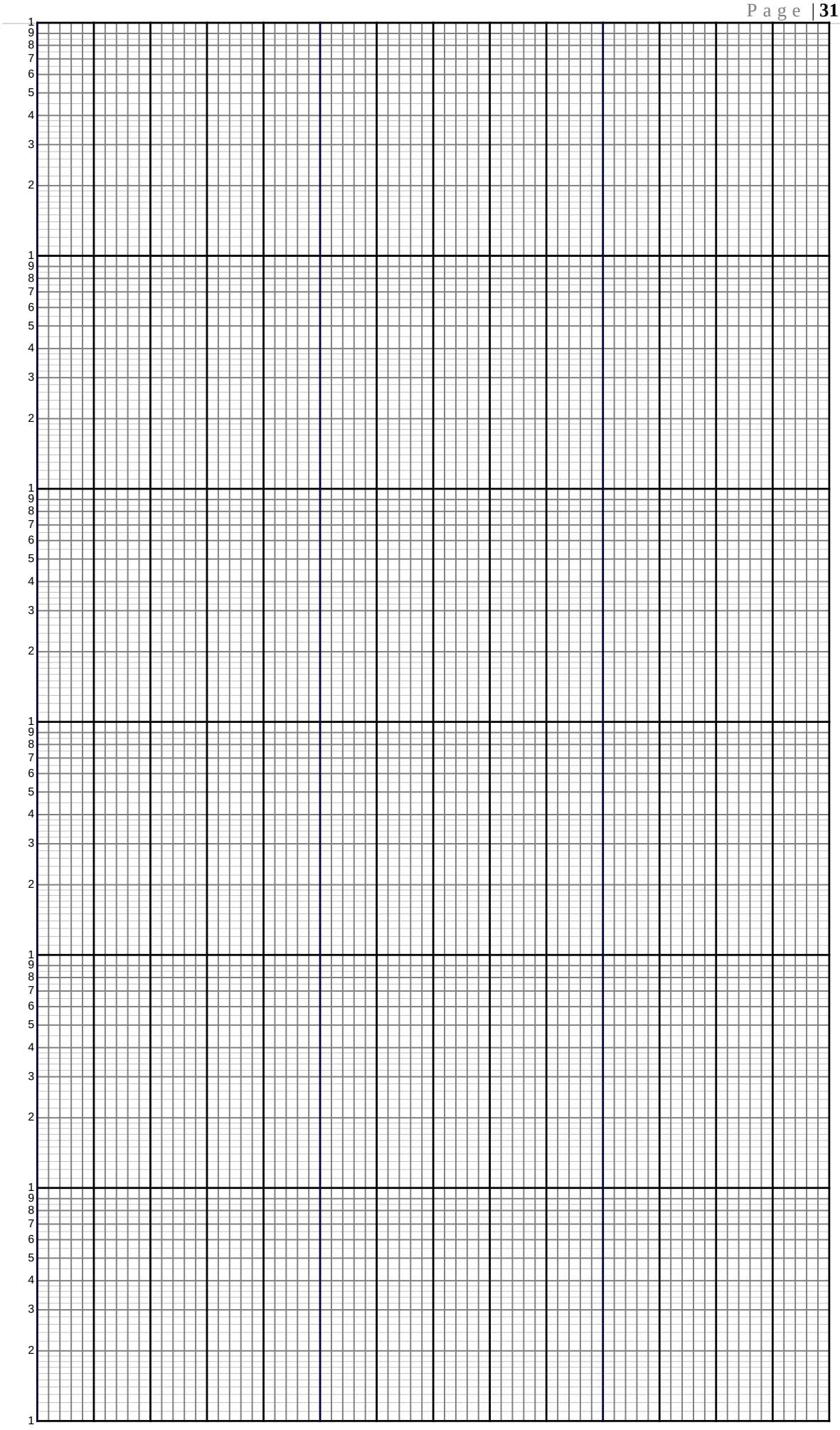
If concentration-response data is plotted with concentration on a linear scale a hyperbolic curve results, when the same data is plotted with concentration on a logarithmic scale (ie the abscissa is log) a sigmoidal curve results. This results in the linear portion of the curve falling between 25-75% of the maximum response thus allowing the EC_{50} to be easily determined. By using semi-logarithmic graph paper we eliminate the need for calculating the logarithmic values of the concentrations. It also allows the data to be displayed as the actual concentration and not the log concentration.

Semi-logarthmic graph paper



To use semi-logarthmic paper to plot concetration response data; plot the x-axis on the logarithmic scale and the y-axis on the linear scale. The divisions on the abscissa (x-axis) of semi-logarthmic graph paper run from the biggest divisions to smallest divisions for each cycle (eg 1-10). For example 3 is mid-way between 1 and 10 while 50 is closer to 100 than it is to 10. This is important to note when orientating your graph paper as the logarthmic scale is sometimes printed on the "top" of the graph.





2. PHARMACOKINETICS

Learning Objectives

To gain an understanding of key pharmacokinetic parameters and their significance in pharmacology.

Instructions

1. Each student will be given a set of plasma drug concentrations from a timed experiment of drug clearance over time.

1. Plot the data on the semi-logarithmic graph paper provided (you will need to include this graph in your prac report).
    a. Calculate the half-life ($t_{1/2}$) from your graph (and compare this to the calculated value below)

3. Using the computer program provided calculate and record the following pharmacokinetic parameters for the drug you have been assigned:
    b. half-life ($t_{1/2}$)
    c. clearance (Cl)
    d. volume of distribution (Vd)

You MUST check that your answers are correct with a demonstrator.

Using the Computer program for AUC and half-life

A computer program is available to calculate the area under the curve using the trapezoidal rule.

To access this program go to **Class programs** → Pharmacology → Pharmacokinetics and enter your data, leaving 0,0 as the first data point.

- You need to specify the route of administration.
- You also must identify the number of points that lie on the terminal **linear phase** of your semi-log graph and enter this number in “number of points to regress”.
- The computer will determine the line of best fit for your data and also calculate the slope of the line or **ke** (the elimination rate constant).
- The program will also calculate the terminal **half-life** from this data and the total **area under the curve** (AUC) which can then be used to calculate **clearance** and hence **volume of distribution**.

Pharmacokinetic parameters

Half-life (t½)

= the time taken for the plasma concentration to fall by half.

This parameter can be obtained directly from the semi-logarithmic plot of the plasma concentration-time data, read off the log-linear phase of the graph.

Elimination rate constant (k)

The elimination rate constant k = the slope of the log-linear phase of the semi-logarithmic plot of the plasma concentration-time data. If the half-life (t½) is known then: $k = 0.693/ t_{½}$

Area under the plasma concentration-time curve (AUC)

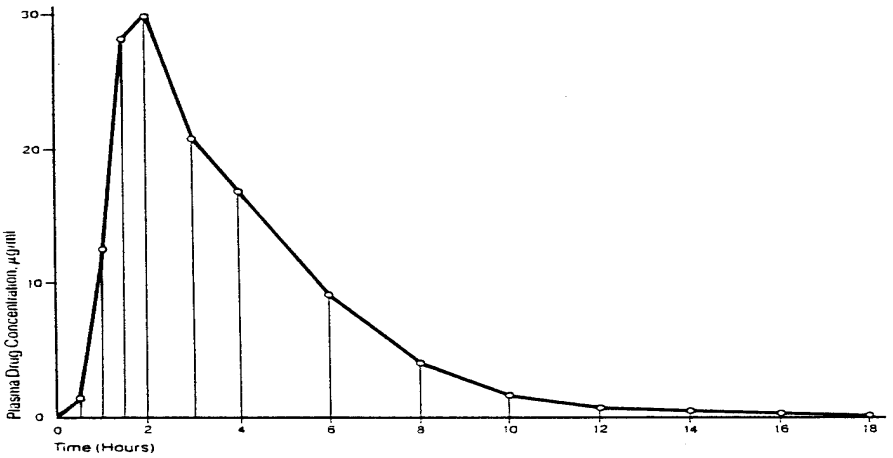


Figure 1. Area under the drug concentration Vs Time curve represented by a series of trapezoids

According to the **trapezoidal rule**, the area under a drug concentration-time curve can be estimated by assuming that the area can be represented by a series of trapezoids (Figure 1).

The total area will be the sum of the areas of the individual trapezoids.

i.e. $AUC = ½(C_0+C_1)(t_1-t_0) + ½(C_1+C_2)(t_2-t_1) + \ldots\ldots + ½(C_{n-1}+C_n)(t_n-t_{n-1})$

where C_n and t_n are drug concentrations and time, respectively.

This method allows for the determination of the AUC to the last concentration-time point. To determine the remaining area the last concentration point is divided by the elimination rate constant i.e. $AUC_{(Cn-\infty)} = C_n/ke$

Note

For intravenous dosage *the concentration at zero time needs to be estimated. This is achieved by extrapolating the distributional phase of the semi-logarithmic plot of the plasma concentration-time data back to the y-axis and reading off the concentration.*

For oral dosage *the first concentration and time point is 0, 0.*

Clearance (CL)

The clearance of the drug can be calculated using the following equation:

$CL = F \times dose/AUC$

where F = the fraction of the dose absorbed.
For intravenous dosage F = 1.

Units for clearance are **ml/min**.

Volume of distribution (Vd)

The volume of distribution of the drug can be calculated using the following equation:

$Vd = t_{½} \times CL/0.693$

Units for volume of distribution are **litres**.

Bioavailability (F)

In some exercises the fraction of the dose that is absorbed (F) must be calculated.

$$F = \frac{Dose_{IV}}{AUC_{IV}} \times \frac{AUC_{oral}}{Dose_{oral}}$$

or

$$F = \frac{AUC_{oral}}{AUC_{IV}}$$ if oral and IV doses are the same

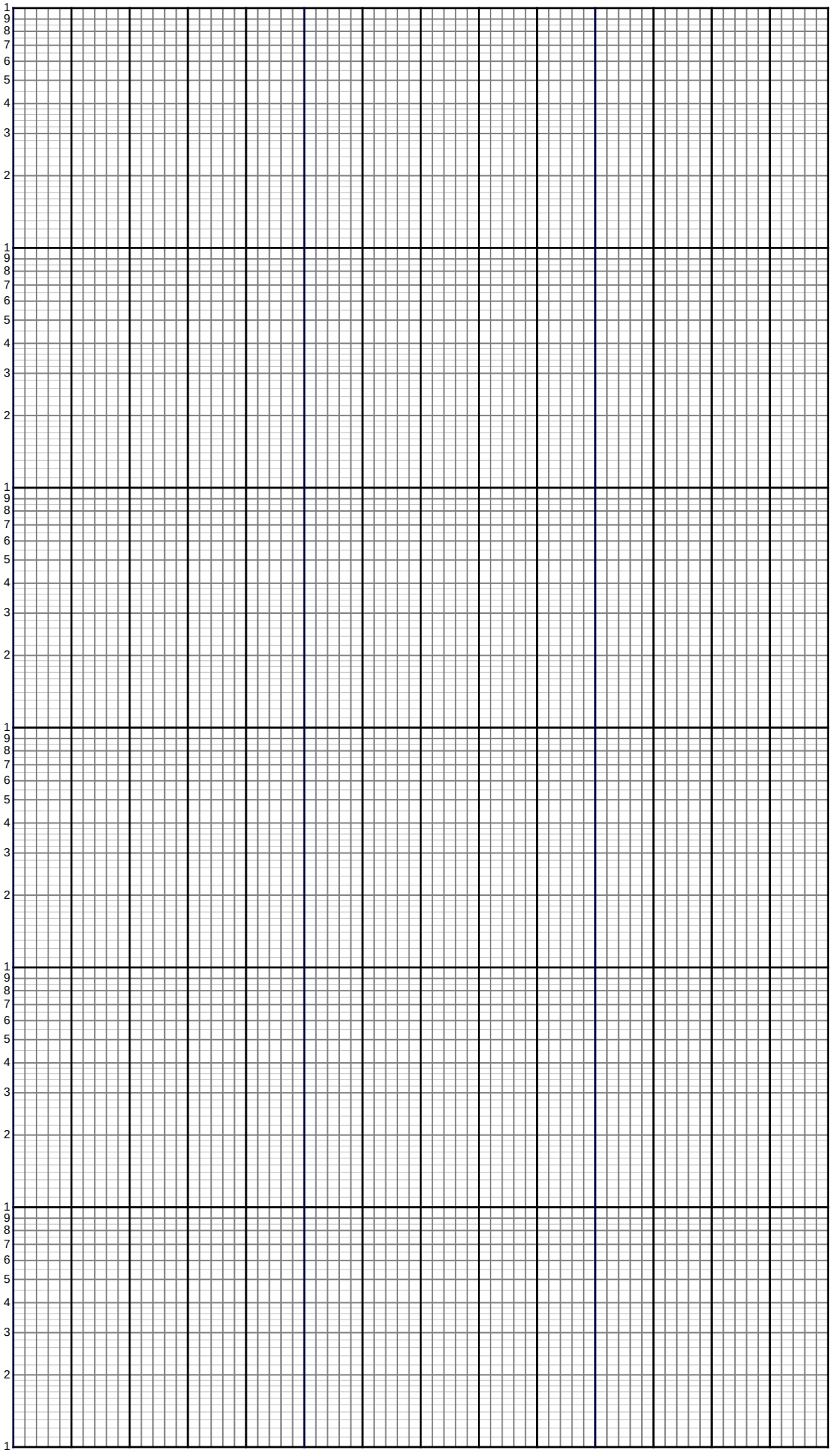
Answer the following questions

1. Plot the time course of plasma concentrations of the drug on the attached semi-logarithmic paper.

2. Compare the parameters obtained from the computer program with those estimated from your plot.

3. What parameters (if any) may be changed in disease states or by dosage with other drugs?

4. How do the pharmacokinetic parameters affect the dosage regimen of the particular drug?



3. BEHAVIOURAL SCREENING OF CNS DRUGS

Learning Objectives

To observe and evaluate behavioural responses of animals to various pharmacological agents.

Introduction

A behavioural screening test is usually applied to new compounds to determine preliminary information on their activities and toxicities, and provide clues for their classification. Most screening tests are performed on animals, usually mice and rats, since it would be unethical to test drugs with potentially adverse side-effects on human beings. After drug administration, the animals are carefully monitored for various parameters, such as awareness, mood, motor activity, central nervous system excitation, muscle tone, reflexes etc., and scored on a numerical scale. From the scores given to the observations, tentative conclusions can be made about the pharmacology of the compound.

Behavioural screening studies are important in ensuring that pharmacologists are aware of the distinctive effects, efficacies and toxicities of the drugs. However, such studies require large quantities of animals, which cause financial and animal ethical concerns. Hence, the development of alternative approaches for teaching and researching behavioural pharmacology has become a worldwide issue.

In this practical you will be introduced to an alternative approach to teaching behavioural pharmacology, involving the use of pre-recorded video to demonstrate drug screening procedures in live animals. With the use of video sequences within the program, together with tutorial style questions, you will have a store of visual information available regarding the appropriate behavioural effects of some drugs, such as CNS stimulants, sedatives and narcotic analgesics.

Methods

PART 1. Observation of behaviour responses to pharmacological agents

Students will observe computer-based demonstrations and recordings of the actions of various CNS active agents and the responses of animals to these agents, and will be asked to comment upon and evaluate these during the class.

Make sure you read the **definitions** of various behaviours that may be observed in the tests before the class starts.

Use the multimedia CD-ROM to observe the behavioural effects of the following agents:

a) **Hypnotics/Sedatives:** Barbiturates//Benzodiazepines

b) **Opioids**: Morphine

c) **Stimulants**: Amphetamine/Cocaine/Picrotoxin

Definitions of behaviours

Ataxia - loss of the ability to coordinate muscular movement.

Clonic convulsion - uncontrollable contractions of muscles marked by alternating contraction and relaxation of the muscles.

Corneal reflex - reaction of the eye to changes in light (change in the size of the pupil)

Dyspnoea - difficult or laboured breathing.

Hypertonia - excessive tone of the skeletal muscle.

Hypotonia -diminished tone of skeletal muscle.

Miosis - contraction of the pupil.

Mydriasis - dilation of the pupil.

Opisthotonus - a form of spasm consisting of extreme hypertension of the body.

Piloerection - erection of hair.

Ptosis - drooping or closure of the eyelids.

Salivation - secretion of clear alkaline from mouth.

Sedation - defined as the act or process of calm.

Spasms - sudden violent involuntary contraction of muscle.

Stereotypies – persistent repetition of stereotyped behavior, eg, preening and sniffing the floor.

Straub tail - raising the tail in the air.

Wet-dog shakes - twisting & shaking of the head and neck.

Use the following table to indicate the type(s) of behaviours you observe for each of the agents tested.

Behaviour	Hexobarbital	Morphine	Amphetamine	Picrotoxin
Ataxia				
Corneal reflex				
Clonic convulsion				
Dyspnoea				
Hypertonia				
Hypotonia				
Miosis				
Opisthotonus				
Piloerection				
Ptosis				
Respiratory depression				
Salivation				
Sedation				
Spasms				
Stereotypies				
Straub tail				
Wet dog shaking				

PART 2. ELEVATED PLUS MAZE

The elevated plus maze is a common behavioural test used to assess fear and anxiety in rats and mice. The equipment used for this test is an elevated 4 armed maze, 2 of the arms are completely open, while the other 2 arms have enclosed / raised sides. This test is used to determine whether drugs / treatments have potential anxiolytic (reduce anxiety) or anxiogenic (increase anxiety) actions.

Students will observe the behaviour of two rats on the elevated plus maze. Each rat has been injected with a drug and has been placed in the centre of the elevated plus maze. Each CD will contain 10 min video recordings from 2 individual rats. You will receive a short demonstration of how to measure the behaviour using the elevated plus maze.

For each rat your group will need to note down and measure:
a) Rat ID
b) Total time spent in the open arms (using timer)
c) The number of entries into the open or the closed arm of the maze.
Note: each entry is counted as when the whole of the rat's body has entered an arm of the maze.

You should express your results according to the table below. Once you have filled in the table provided – add your results to the class data

Rat ID	**# entries open**	**# entries closed**	**# entries total**	**% open entries / Total**	**Time spent in open arms (sec)**

When all of the class data has been collected and the codes for the treatment groups have been revealed:

- Calculate the mean and standard deviation (% open entries) for both control and diazepam treated groups:

1. Open GraphPad Prism via the following path: Class programs \ Physiology and Pharmacology \ Utilities and Office applications \ Graph Pad Prism
2. Select "start with an empty data table", Choose Graph "Column bar graph, vertical", choose to plot "mean with SD"
3. Enter control values (% open entries) in column "A" and diazepam values (% open entries) in column "B"
4. Click on the "analyse" button, Under "column analyses, select t-test (and non-parametric tests)
5. Select "paired test", two-tailed, and use 95% confidence intervals
6. Click "OK" and your Prism will perform the t-test
7. Click on "Graph" to view your bar graph

8. Label each axis. “X” = Treatment, “Y” = % open entries

- Calculate the mean and standard deviation (Time spent in open arms) for both control and diazepam treated groups.

  Repeat steps 1-8 (above), but use class data for Time Spent in open arms and label your “Y” axis on the graph accordingly.

4. HUMAN AUTONOMIC PHARMACOLOGY

SAFETY INSTRUCTIONS

When handling saliva other than your own you must wear disposable gloves.

Saliva contaminated measuring cylinders must be placed in the hypochlorite solution provided.

Risks

This class involves the administration of injections.
As with all injections there are potential problems such as:

- infection - disposable sterile apparatus is used and scrupulous technique is demonstrated to the students.
- drug reactions - the dosages are routine and widely used clinically – the risks are minimal.

Students acting as subjects in the class are required to sign a consent form.

This practical class involves contact with human body fluids and injection of a subcutaneous drug. For these reasons the following precautions must be taken.

i) No eating, drinking or smoking in practical class area.
ii) If you have a past history of hepatitis or if you have a current infection do not volunteer as an experimental subject.
iii) Avoid contact with blood.
iv) Avoid spilling or splashing samples.
v) Do not resheathe any used needles. Place all needles, swabs, syringes or disposable containers in appropriate containers which have been provided.
vi) If you accidentally prick yourself with a dirty needle then report to the demonstrator in charge of class.

Learning Objectives

To examine the pharmacological responses produced by a subcutaneous injection of atropine in human subjects.

Introduction

This class will examine some of the actions of atropine in humans.
The experiments will be done in groups of four or five. One subject from each group will receive the atropine. The other members of the group will act as recorders.

Methods

In each group one subject will receive a subcutaneous injection of 1.2 mg atropine, administered by a medically qualified demonstrator using disposable single use syringes and vials.

All injections will be given by a medical qualified demonstrator.

Observations

For these to be of any value they must be made under standard conditions THROUGHOUT THE EXPERIMENT i.e. with the subject LYING DOWN, relaxed and in constant illumination.

Three sets of control responses are recorded initially at 5 minute intervals before the injection is administered. After the injection, observations are made at 5, 10, 20, 30, 45 and 60 minutes.

Record

1. Pulse rate - the radial pulse is counted for 30 seconds and the results recorded as pulse rate per minute.
2. Blood pressure - measure with a sphygmomanometer.
3. Pupil size - measure in millimetres using the ruler provided.
4. Near point - estimate by moving a piece of typed paper towards the eye until the subject can no longer focus on the type. The distance between the eye and the paper is then measured.
5. Salivary secretion - the subject should swallow all resting saliva. Four drops of 3% solution of citric acid are then dropped on the tongue and held in the mouth for 30 seconds. At the end of this time 4 ml of water are taken into the mouth and swilled around for a further 15 seconds. GREAT CARE SHOULD BE TAKEN NOT TO SWALLOW.

   The mixture of saliva and water is now ejected carefully into a 10 ml measuring cylinder with the aid of a funnel. The volume minus 4 ml gives the amount of saliva produced during the test. Record negative values as zero.

Tabulate all your results and the mean results for the class.

Data Recording

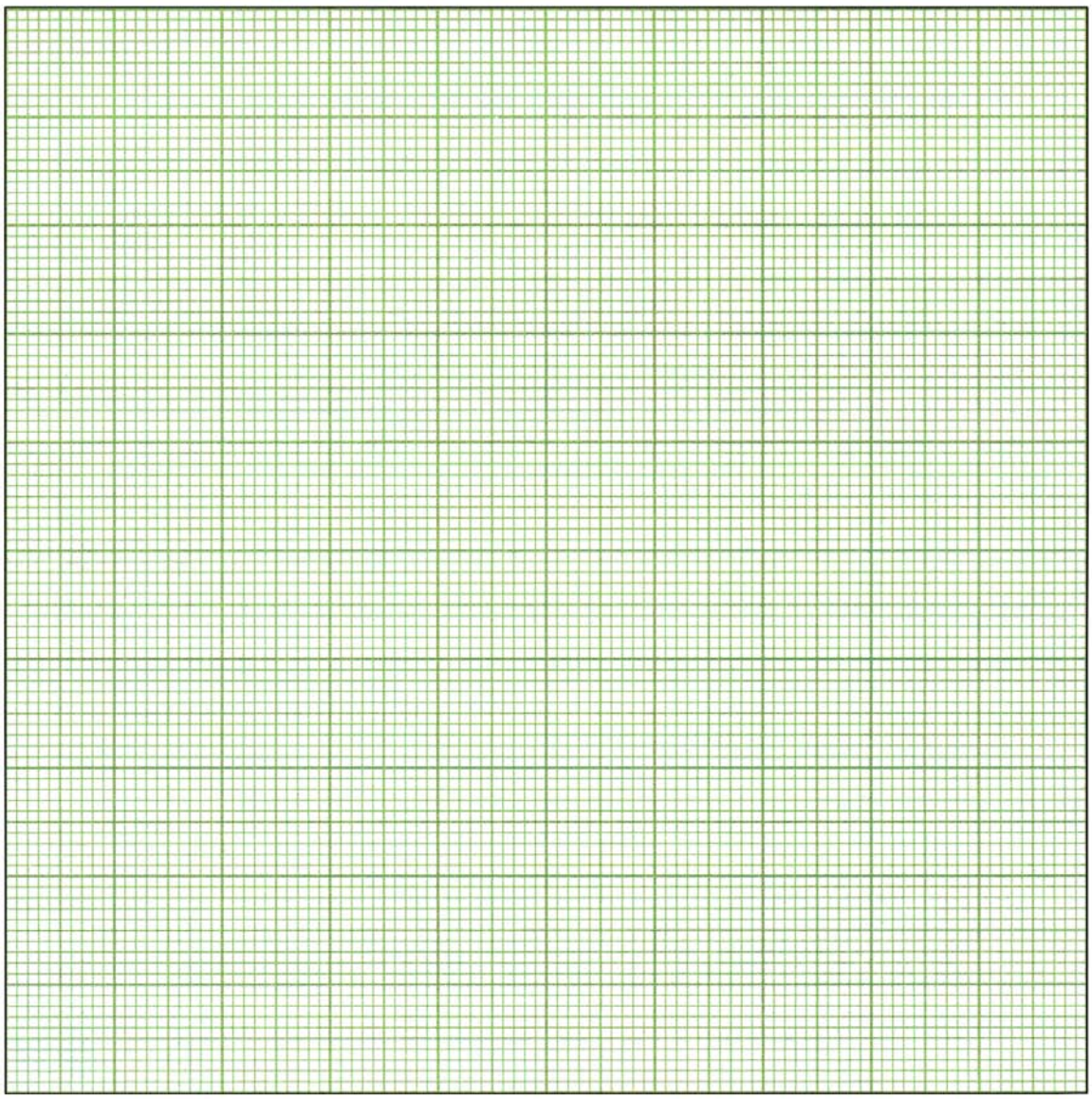
Parameters	Control			5 min	10 min	20 min	30 min	45 min	60 min
	1	2	3						
Pulse Rate (b/m)									
Blood Pressure (mm Hg) Systolic Diastolic									
Pupil Size (mm)									
Near Point (mm)									
Salivary Secretion (ml)									

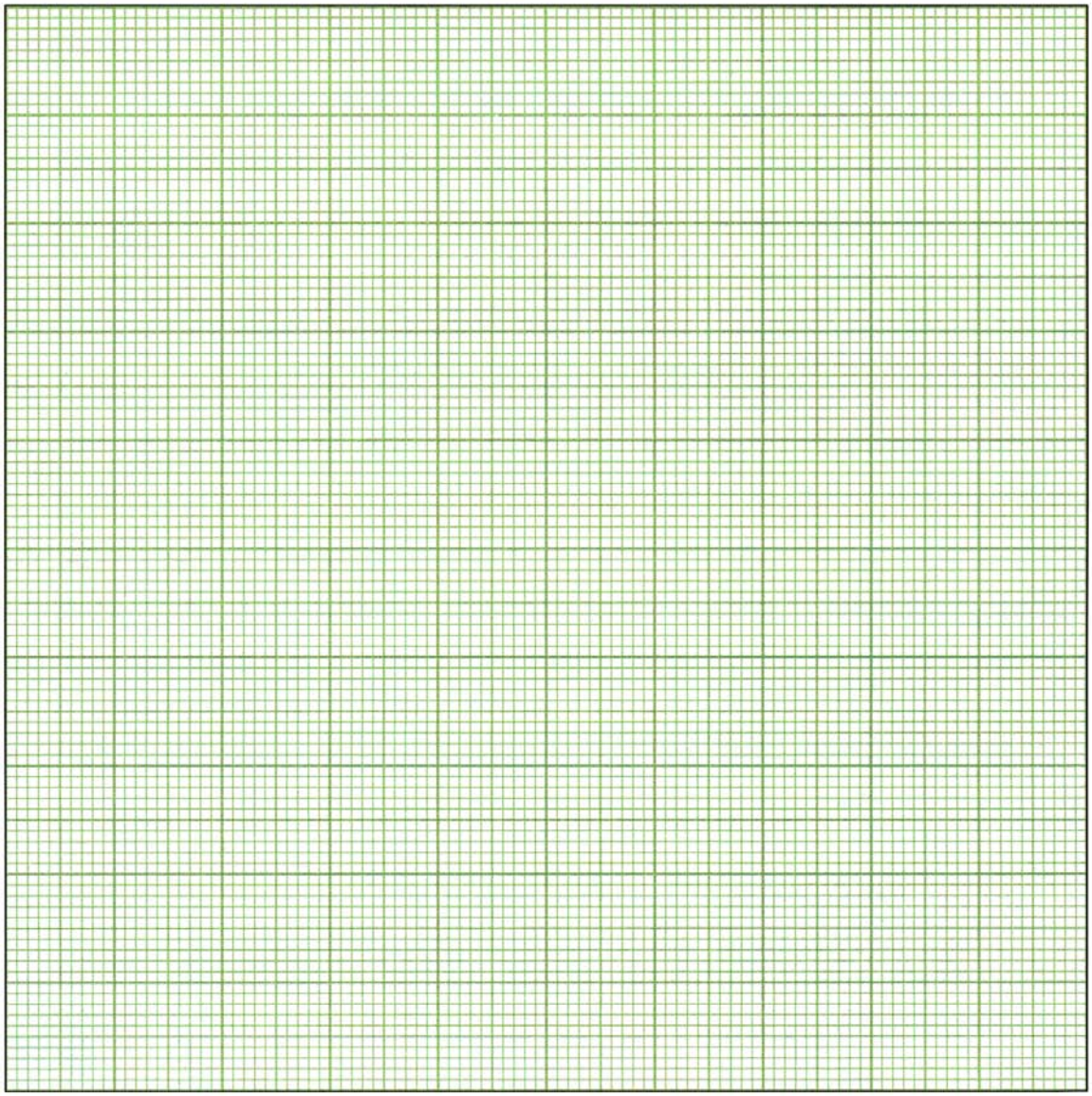
Questions

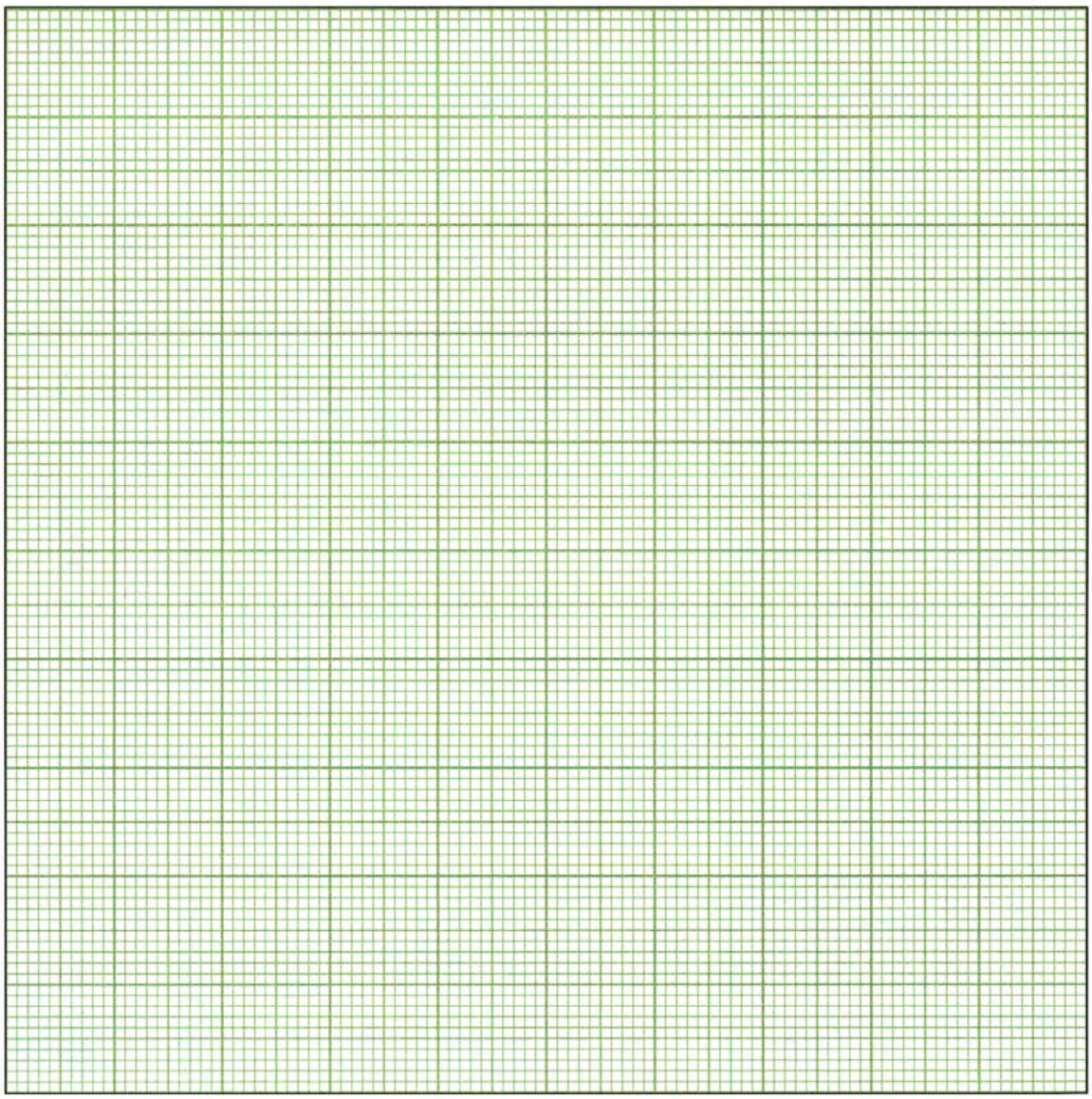
1. Plot the time course vs the class mean data of each parameter on the attached linear graph papers or using Excel or Prism.

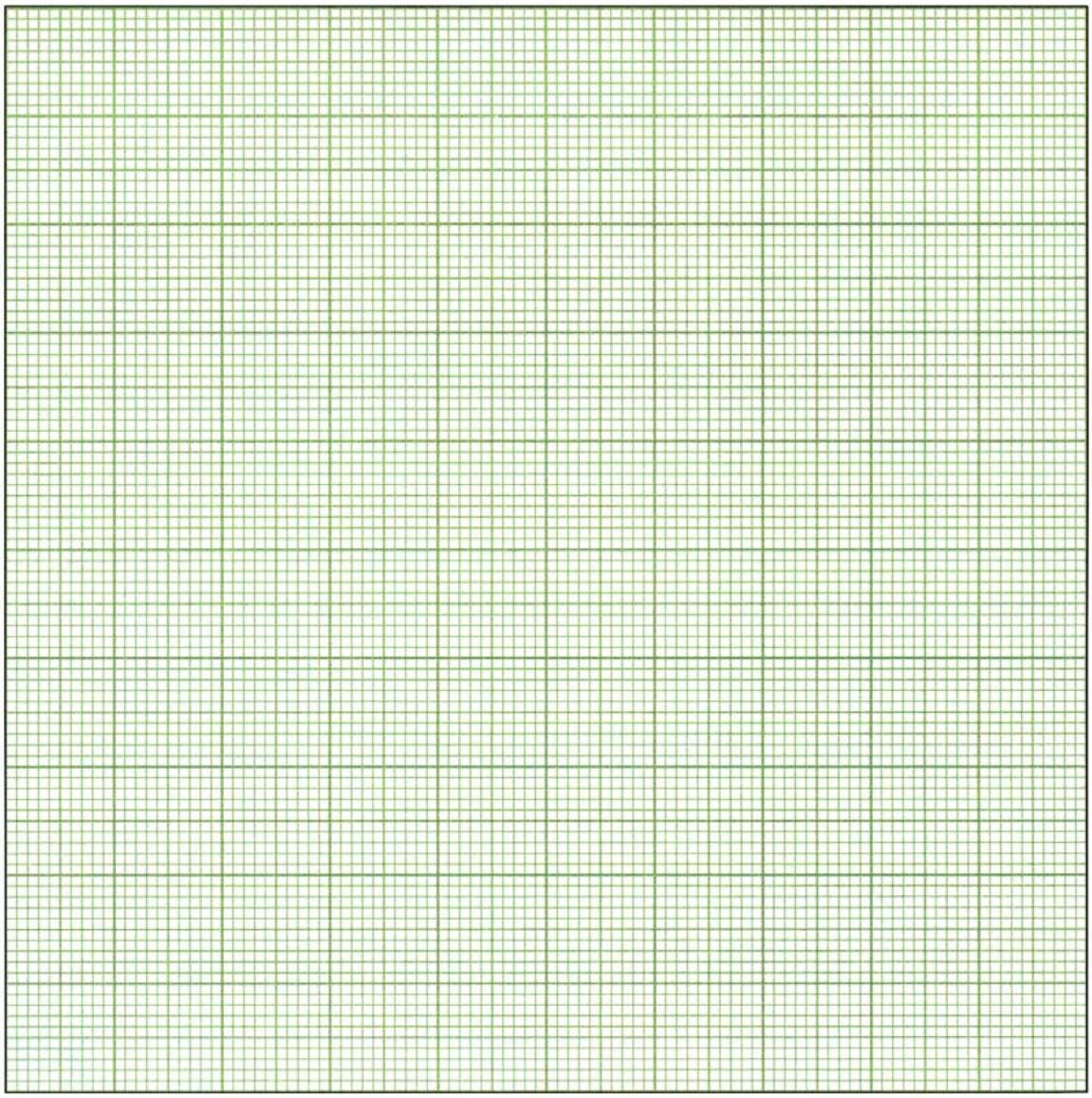
2. Explain the results that you observed. Would the effects to the eye by s.c. injection of atropine be the same if atropine were administered directly into the eye?

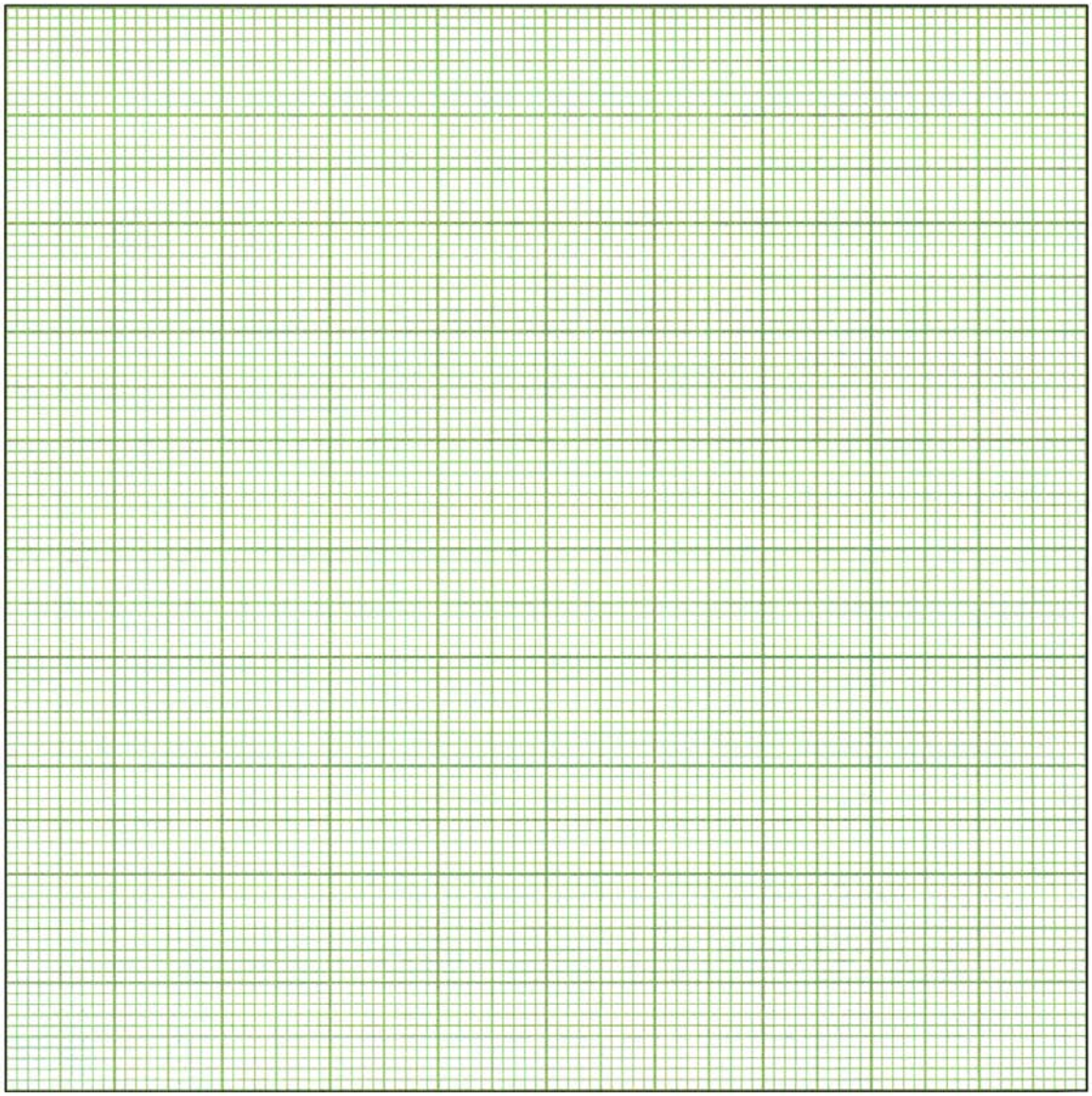
3. Describe clinical uses of atropine, its side effects and contraindications.











5. AUTONOMIC DRUGS ON THE EYE

Learning Objectives

To promote an understanding of the autonomic control of pupil diameter and the pharmacology of the autonomic nervous system.

To begin the exercise, locate **START** on your computer screen. Click on **Class Software (main)** and go to the page of **PHYSIOLOGY & PHARMACOLOGY**

Click on **PHARMACOLOGY** and then **AUTONOMIC PHARMACOLOGY**

For all patients: Mr. Brown, Mrs Jone, Mr. Black and Mr Mulligan: Describe (1) what symptoms or problems you have observed; (2) which eye you think to be the problem; (3) which nervous system (parasympathetic or sympathetic, preganglionic or postganglionic) might be involved in causing the problem; (4) your final diagnosis and what evidence support your diagnosis.

Appendix 1.

THE USE OF OCULAR THERAPEUTIC DRUGS IN NEW SOUTH WALES[3]

Introduction

The competency standards that an optometrist must achieve in order to be granted a drug authority are the therapeutic competencies that were developed by the Optometrists Association Australia. The criteria to ascertain whether an optometrist meets those competency standards is through the optometrist's provision of evidence of successful completion of an educational course or program which addresses the adopted competencies, that is recognised by the New South Wales Optometrists Registration Board for this purpose and which has been accredited by the Optometry Council of Australia and New Zealand.

The following qualifications are recognised by the Board on the recommendation of the Optometry Council of Australia and New Zealand:

Graduate Certificate in Ocular Therapeutics	University of New South Wales
Postgraduate Certificate in Ocular Therapeutics	University of Melbourne
Graduate Certificate in Ocular Therapeutics	Queensland University of Technology
The Auckland Programme in Ocular Therapeutics	University of Auckland
Bachelor of Optometry	University of Melbourne, conferred in 2007 and thereafter
Bachelor of Optometry	University of Auckland, conferred in 2007 and thereafter

The Ocular Conditions that an Authorised Optometrist may treat

An optometrist granted a drug authority in New South Wales shall be permitted to use, supply or prescribe topical preparations in the following circumstances:

- For dry eye and related conditions;
- As an anti-infective prophylaxis after foreign body removal;
- As an adjunct to co-management of surgical cases with an attending ophthalmic surgeon;
- For non-vision threatening inflammatory diseases of the anterior segment, and
- For infectious and inflammatory disease of the anterior eye, with the exception of uveitis and herpetic conditions.

[3] from http://www.optomreg.health.nsw.gov.au/optom_ocular.htm

LIST OF APPROVED SCHEDULE 4 REGISTERED RESTRICTED DRUGS FOR TOPICAL USE IN NSW AS AT 20 JULY 2005

a. ***Group 1 - Anti-infective agents***
   i. Chloramphenicol
   ii. Framycetin
   iii. Gramicidin
   iv. Neomycin
   v. Polymyxin
   vi. Tetracycline

b. ***Group 2 - Decongestants & anti-allergic agents***
   i. Ketotifen
   ii. Levocabastine
   iii. Lodoxamide
   iv. Olopatadine
   v. Sodium cromoglycate

c. ***Group 3 - NSAIDS***
   i. Diclofenac
   ii. Flurbiprofen
   iii. Ketorolac

d. ***Group 4 –Topical Ocular Steroids***
   i. Fluorometholone
   ii. Hydrocortisone

e. ***Group 5 - Glaucoma medications*** (subject to the development of appropriate clinical pathways and protocols)
   i. Apraclonidine
   ii. Betaxolol
   iii. Bimatoprost
   iv. Brimonidine
   v. Brinzolamide
   vi. Carbachol
   vii. Dipivefrin
   viii. Dorzolamide
   ix. Latanoprost
   x. Levobunolol
   xi. Pilocarpine
   xii. Timolol
   xiii. Travoprost

f. Group 6 – Mydriatics & Cycloplegics

i. Atropine
ii. Cyclopentolate
iii. Homatropine
iv. Phenylephrine
v. Tropicamide

g. Group 7 – Local Anaesthetics

i. Amethocaine
ii. Oxybuprocaine
iii. Proxymetacaine

NB. There are certain medications that optometrists in NSW will **not** be permitted to use or prescribe. These are:

- Fluoroquinolones (ciprofloxacin, ofloxacin)
- Anti-virals (aciclovir)
- Deep-penetrating steroids (prednisolone, dexamethasone)

Appendix II. Timetable - PHAR3306 Pharmacology for Optometry, S2, 2010

Wk	TUTORIALS AND PRACTICAL CLASSES			LECTURES				
	Date	Time	Tutorial (T)/Practical (P)	Date	Time	Theatre	Lecture title	Lecturer
1				July 21, Wed	1-2 pm	WW LG 02	Welcome & Introduction. Sites of drug action	Liu / Binder
				July 22, Thur	4-5 pm	WW LG 02	Pharmacodynamics: agonist and antagonist activity	T. Binder
				July 22, Thur	5-6 pm	WW LG 02	Pharmacokinetics-Drug absorption and distribution	R. Griffith
2	July 26, Mon	3-4 am	Group project instructions **(T)**	July 28, Wed	1-2 pm	WW LG 02	Pharmacokinetics-Drug metabolism	R. Griffith
			WW LG 02	July 29, Thur	4-5 pm	WW LG 02	Pharmacokinetic formulae and calculations	R. Griffith
			L. Liu	July 29, Thur	5-6 pm	WW LG 02	Autonomic nervous system-Introduction/Cholinergic	L. Liu
3	Aug 2, Mon	3-6pm	Dose-response **(P)**	Aug 4, Wed	1-2 pm	WW LG 02	Autonomic Nervous System-Cholinergic	L. Liu
			WW 106/108/109/110	Aug 5, Thur	4-5 pm	WW LG 02	Autonomic Nervous System-Adrenergic	L. Wakelin
			R. Griffith & L. Wakelin	Aug 5, Thur	5-6 pm	WW LG 02	Autonomic Nervous System-Adrenergic	L. Wakelin
4	Aug 9, Mon	3-4 am	Cholinergic **(T)**	Aug 11, Wed	1-2 pm	WW LG 02	ANS control of the eye/cycloplegics, miotics, mydriatics	L. Liu
			WW LG 02	Aug 12, Thur	4-5 pm	WW LG 02	Anaesthetics	L. Wakelin
			L. Liu	Aug 12, Thur	5-6 pm	WW LG 02	CNS- Antiepileptic drugs/Sedatives /Hypnotics	N. Jones
5	Aug 16, Mon	3-6pm	Pharmacokinetics **(P)**	Aug 18, Wed	1-2 pm	WW LG 02	CNS-Antidepressants	N. Jones
			WW 106/108/109/110	Aug 19, Thur	4-5 pm	WW LG 02	VEGF and angiogenesis in eye disease	R. Griffith
			R. Grant & R. Griffith	Aug 19, Thur	5-6 pm	WW LG 02	Drugs to treat thrombosis	N. Jones
6	Aug 23, Mon	3-4 am	Adrenergic (**T**)	Aug 25, Wed	1-2 pm	WW LG 02	Opioids	T. Binder
			WW LG 02	Aug 26, Thur	4-5 pm	WW LG 02	Antihypertensives	M. Morris
			L. Wakelin	Aug 26, Thur	5-6 pm	WW LG 02	Drugs acting on renal system - Diuretic agents	M. Morris
7	Aug 30, Mon	3-6pm	CNS drugs (**P**)	Sept 1, Wed	1-2 pm	WW LG 02	Drugs used to treat asthma	T. Binder
			WW 106/108/109/110	Sept 2, Thur	4-5 pm	WW LG 02		
			N. Jones	Sept 2, Thur	5-6 pm	WW LG 02	**Mid session test (50 min)**	N. Jones
Mid-semester break (6 Sept - 12 Sept)								
8	Sept 13, Mon		Work on Group project	Sept 15, Wed	1-2 pm	WW LG 02	Ocular surface disease	N. Di Girolamo
			(Due 5 pm, Fri, Sept 24)	Sept 16, Thur	4-5 pm	WW LG 02	Endocrine drugs - Thyroid drugs	M.Morris
				Sept 16, Thur	5-6 pm	WW LG 02	Endocrine drugs - Antidiabetic drugs	M.Morris
9	Sept 20, Mon	3-6 am	Human Pharmacology (**P**)	Sept 22, Wed	1-2 pm	WW LG 02	Anti-inflammatory drugs-NSAIDs	T. Binder
			WW 204	Sept 23, Thur	4-5 pm	WW LG 02	Anti-inflammatory drugs-Steroids	J. Langlands
			L. Liu & N. Jones	Sept 23, Thur	5-6 pm	WW LG 02	Anti-glaucoma drugs	R. Lim
10	Sept 27, Mon	3-4 pm	Antiinflammatory (**T**)	Sept 29, Wed	1-2 pm	WW LG 02	Antihistamine/mast cell stabilizers	L. Liu
			WW LG 02	Sept 30, Thur	4-5 pm	WW LG 02	Antibiotics 1	L. Wakelin
			T. Binder	Sept 30, Thur	5-6 pm	WW LG 02	Antibiotics 2	L. Wakelin
11	Oct 4, Mon		Public Holiday	Oct 6, Wed	1-2 pm	WW LG 02	Dry eyes and treatment	D. Wakefield
				Oct 7, Thur	4-5 pm	WW LG 02	Antiviral and antifungal agents	L. Wakelin
				Oct 7, Thur	5-6 pm	WW LG 02	Antimicrobial chemotherapy for ocular infection	L. Wakelin
12	Oct 11, Mon	3-6 pm	Autonomic drugs on eye (**P**)	Oct 13, Wed	1-2 pm	WW LG 02	Ocular side effects of systemic drugs	G. Graham
			WW 106/108/109/110	Oct 14, Thur	4-5 pm	WW LG 02	Development of new drugs	L Wakelin
			L. Liu & N. Jones	Oct 14, Thur	5-6 pm	WW LG 02	Revision	L. Liu