

MCMP 442

MEDICINAL CHEMISTRY AND PHARMACOLOGY IV: Chemotherapy of Infectious and Neoplastic Diseases

Course Syllabus Spring 2010

Sem 2, Class 3, credits 3, **Prerequisites:** MCMP 407 and MCMP 441

The focus of this course is the molecular principles of drug action for agents used in the treatment of infectious diseases and cancer. The source, physical and chemical properties of representative drug classes are related to the pharmacodynamic, and pharmacokinetic parameters governing their efficacy. These principles are applied to the clinical context of diagnosis, therapy selection and monitoring.

Instructors

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I. Objectives

A. General

A common thread to the subject areas is the use of chemical agents as selective cellular toxins. This class will focus on the pharmacodynamics that govern the molecular basis for selectivity in drug action. Conceptual and integrative competence of the material presented in the basic pharmaceutical science courses is a major emphasis guiding the curriculum. This course aims to integrate the biological and chemical principles underlying the specific mechanisms and modes of action within each drug class. It is anticipated that the major concepts should be derived from first principles and reviewed in a concise manner. The principles of drug action covered in MCMP 407 and MCMP 441 will be reiterated in the discussion of each drug class. Student review of materials from previous courses will be expected to enhance the integrative learning. Coverage of significant background material central to understanding cancer and infectious diseases will rely on material from MCMP 440 (Pathophysiology), MCMP 422 (Immunology and Biologics) and the integrated laboratory exercises. A review of microbiology in the context of the major course topics will be used to enhance the level of understanding regarding mechanisms of drug action and the appropriate selection of chemotherapy.

B. Physicochemical Principles of Chemotherapy

1. Chemical and Physical Properties of Drugs as Cellular Toxins
 - a. solubility in water and lipids and their relationship to cellular penetration
 - b. use of prodrugs as chemical precursors to control pharmacokinetics
 - c. use of prodrugs to enhance target selectivity
 - d. salt forms to effect changes in properties
 - e. derivatization to alter reactivity toward hydrolysis and oxidation
 - f. structure-activity relationships for reactive functional groups
 - g. identification of chemical structures and associated generic and proprietary names
 - h. relationship of dosage forms to physical and chemical properties
 - i. basic pharmacokinetic properties of the specific drug classes

2. Chemical Sources and Discovery of Chemotherapeutic Agents
 - a. natural sources of selective cell toxins
 - b. role of fermentation and isolation technology in production
 - c. role of chemical diversity in resistance management
 - d. susceptibility assays in diagnosis, drug discovery, therapy selection
- C. Pharmacological Principles of Chemotherapy of Infectious Diseases
1. Infectious Diseases: Host-Microbe Relationships
 - a. Biological niches for organism dictate nature of disease
 - b. Opportunistic infections and essential role of chemotherapy
 - c. Site of infection and selection of drugs
 - d. Host factors dictating drug selection
 - e. Bacteriocidal versus bacteriostatic drug therapies
 2. Epidemiology, Nosocomial Infections and Mechanisms of Resistance
 - a. Modes of transmission and frequency of disease occurrence
 - b. Resistance as a selection process
 - c. Plasmid and chromosomal mutations lead to resistance
 - d. Management of resistance through judicious practice
 3. Diagnosis and Susceptibility as a Basis for Drug Selection
 - a. Cellular barriers to drug entry are dependent upon target organism
 - b. Biochemical markers for diagnostic tests and basic methods
 4. Pharmacodynamics of Chemotherapy
 - a. Role of time course of drug action in disease management
 - b. Physiological factors dictating localization of drugs to target sites
 - c. Selective toxicity based upon drug targets
 - d. Unique biological roles for drug targets that govern efficacy
 - e. Routes of administration and therapeutic applications
 - f. General basis for side effects associated with a given drug class
 5. Viruses, Fungi, and Protozoa Present Unique Problems in Chemotherapy
 - a. Life cycles of nonbacterial pathogens
 - b. Viral infections are distinct from other pathogens: markers of disease progression, latency of viral infection, transformation and integration of genetic material
 - c. Molecular targets that offer selectivity for chemotherapy
 - d. Rate of resistance emergence is different for each pathogen
 - e. Curative versus maintenance therapy
 - f. Fungi are eucaryotic organisms and present challenges for selectivity
- D. Pharmacologic Principles of Cancer Chemotherapy
1. Drug Selectivity
 - a. Cell kinetics
 - b. Cellular pharmacokinetics
 - c. Tumor heterogeneity

- d. Resistance
 - 2. Mechanisms of Growth Inhibition and Cell Kill
 - a. DNA synthesis
 - b. DNA damage and repair
 - c. Inhibition of metabolism
 - d. Inhibition of tubulin polymerization and depolymerization
 - 3. Role of Drugs in Cancer Treatment – “The Clinical Problem”
 - a. Combination chemotherapy
 - b. Adjuvant chemotherapy
 - c. New approaches
- E. School of Pharmacy and Pharmaceutical Sciences Outcome Objectives to be addressed with this course.
- 1. General Outcome Abilities
 - a. Conceptual competence
 - b. Scientific comprehension
 - c. Integrative competence
 - d. Critical thinking and decision making abilities
 - e. Communication abilities
 - f. Self-learning abilities and habits
 - 2. Professional Outcome Abilities
 - a. MCMP 442 is a foundation course
 - (i) Goal 1: evaluate patient data, scientific literature and pharmaceutical products.
 - (ii) Goal 4: ability to make specific, sound recommendations
 - (iii) Goal 5 provide understandable, appropriate and effective education

II. Grading

The course grade will be determined from the scores of four one-hour examinations (worth 100 points each) and a comprehensive final examination (worth 150 points). Final grades will be based upon an absolute scale of 100%-90% = A, 89%-88% = B⁺, 87%-83% = B, 82%-80% = B⁻, 79%-78% = C⁺, 77%-73% = C, 72%-70% = C⁻, and below 70% will constitute a failing grade. The faculty will reserve the right to provide for bonus exercises in the form of written reports or in-class quizzes or take-home problems. There are no makeup exams. All absences from examinations must be excused by the Course Director or the Associate Dean for Professional Programs to qualify for compensation through examination. An unexcused absence from the final exam will result in a grade of incomplete for the course.

Examinations will be structured to assess your mastery of factual information (50%), integration of scientific concepts (25%) and problem solving skills (25%). Each of the 1 hour exams will be composed of matching and multiple choice questions (50%), short answer and discussion type questions.

III. Textbooks

Foye's Medicinal Chemistry, D. A. Williams, and T. L. Lemke, 6th Ed., Lippincott Williams, Wilkins Philadelphia, PA., 2008.

Basic and Clinical Pharmacology, B.G. Katzung, 11th Ed., Lange Medical Books/McGraw-Hill, New York, 2009.

References

In addition, there are a number of sources of supplementary material that will be useful for this course. Several of these references are textbooks from your previous courses in microbiology, biochemistry, and pathophysiology that should prove particularly valuable for your review.

Basic Pathology, Kumar, Abbas, Fausto, Mitchell, 8th Ed., 2007, W. B. Saunders.

Immunology: A Short Course, Coico, Sunshine, Benjamini, 6th Ed., 2009, Wiley.
Microbiology: Principles and Applications, Black, 7th Ed., 2008, Wiley.
Biochemistry with Clinical Correlations, Devlin, 6th Ed., 2005, Wiley.
The Sanford Guide to Antimicrobial Therapy, Gilbert, Moellering, Sande, 39th Ed., 2009.
The Pharmacological Basis of Therapeutics, Goodman and Gilman, 11th Ed., McGraw Hill, 2006.
Physician's Desk Reference, 64th Ed., Thompson, 2010.
Principles of Infectious Diseases Vol 1 and Vol 2, Mandell, Bennett, Dolan; 7th Ed., Elsevier, 2010.
Antimicrobial Therapy and Vaccines, Yu, Weber, Raoult; 2nd Ed., Apple Trees, 2002.
Brody's Human Pharmacology: Molecular to Clinical, Brody, Lerner, Minneman; 5th Ed., Mosby, 2010.
Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Block, Beale, 11th Ed., Lippincott Williams and Wilkins, 2004.
The Immune System, Parham, 3rd Ed., Garland Science Publishing, 2009.

IV. Class Notes

There is a web-based component of this course. You can download the class notes, course information, and assignments from the MCMP 442 YACS site at <https://courses.pnhs.purdue.edu/mcmp442/>. Students will be responsible for downloading and printing their own copies of the notes.

Your review of the note contents before attending lecture will be important for enhancing your opportunities to learn more during the lecture periods.

Not all material provided in the lecture notes will be discussed during lecture. However, all the lecture notes and the assigned reading will be material suitable for formulating exam questions.

V. Academic Dishonesty

Academic dishonesty (cheating) in any form (such as the use of cribs, altering examinations for regrade, copying from others during examinations, plagiarism of homework assignments, and in any way representing the work of others as your own) will not be tolerated. Any such behavior will result in a failing grade in this course. A witness to an act of academic dishonesty that goes unreported will also be considered an accomplice. In addition, all such incidents are reported to the Dean's Office and the University's Office of Student Affairs where further disciplinary actions may ensue.

VI. Copyrights and Note Taking Services

All handouts given in this course are considered as copyrighted materials and cannot be reproduced and distributed for profit. The organization, selection of topics, and collection of facts, in the preparation and presentation of an academic lecture, requires considerable time, expertise, skill, educational background, and training on the part of your professor. The sale of distributed course notes (hardcopy or electronic), for profit, by note-taking services violates all rules regarding the protection of intellectual creativity.

VII. Campus Emergencies

In the event of a major campus emergency, course requirements, deadlines and grading percentages are subject to changes that may be necessitated by a revised semester calendar or other circumstances. If a major campus emergency occurs, you should consult the course web page (<https://courses.pnhs.purdue.edu/mcmp442/>) to get information about changes in this course. Information about campus emergency preparedness can be found at http://www.purdue.edu/emergency_preparedness/. Most of this information will only be helpful if you read it before a campus emergency happens.