

PHM 381M – PHARMACEUTICAL BIOCHEMISTRY
STATEMENT OF COURSE POLICY
FALL 2016 (#59055)

TIME AND LOCATION PHR 2.110, 11:00-12:30, TTh
 PHR 3.106, Wed 1-2, Optional Review Session (starts 8/31)

FACULTY Dr. Chris Whitman, BME 6.202A
 (512-471-6198, whitman@austin.utexas.edu)

The BME building is on the southeast corner of Dean Keeton and University (across the street from the Student Services building!). You enter the building on Dean Keeton on the 3rd floor. Take the elevator (or the stairs) to the 6th floor. Get out of the elevator, turn left, and go through the double doors.

OFFICE HOURS M 11-12 and Th 1-2. Wed. office hour (1-2) is in PHR 3.106.
Office hours are subject to change (I'll give you advanced notice)
Students can meet with me by appointment and email me anytime!

GENERAL TOPICS Structure and Function of Proteins (8 lectures)
 Enzymes (5 lectures)
 Vitamins (4 lectures)
 Vitamins, Carbohydrates, and Metabolism (8 lectures)
 Lipids, Membranes, and Lipid Metabolism (3 lectures)

TEXT Biochemistry (7th Edition) by Mary K. Campbell and Shawn O. Farrell (we'll discuss!)

WEB RESOURCES The Canvas® **web site** for this course is located at:

<http://courses.utexas.edu/>

On login (with your UTEID) you will see a list of Canvas® websites for your current courses. Click on *Pharmaceutical Biochemistry I* to access the site. Messages sent to you via the Canvas® Website (Email and Notifications) are **official** mechanisms for communication in this course; be sure you understand the College Email policies. Handouts and class notes will be available on this website.

In addition, there will be audio and visual recordings of the lectures and all that is shown on the doc cam. This class takes part in lecture capturing (now called lectures online). The audio and visual materials presented in class will be recorded and made available to you for review via Canvas. It is my understanding that links for the recordings will appear on the Canvas page for this class.

Issues might arise that could prevent material from being made available in a timely fashion or at all. Although every effort will be taken to keep the system running, UT and I do not guarantee the availability of these recordings. Attending class is the only way to know for certain that you will see my presentations. You can find additional information (and more instructions) about the lecture capture system at: <http://sites.la.utexas.edu/lecturesonline/>

EXAMINATIONS

Exam 1 - Thur., Sept 22, PHR 2.108/3.106, 7-9 PM

Exam 2 - Thur., Oct 27, PHR 2.108/3.106, 7-9 PM

Exam 3 - Thurs., Dec 1, GAR 0.102, 7-9 PM

Final Exam – Date during Finals week, Dec. 8-14th

Exams (including the final) are worth 100 points each!!!

Exam Rooms are subject to change!!!

Exams will consist of True/False, Multiple/Multiple Choice, and short answer questions. *Students must arrive on time for examinations.* All instructions and corrections will be made at the beginning of the examination period and will not be repeated. Exams will begin promptly at the indicated hour and will be picked up after 2 hrs. The final examination is 3 hrs. Students arriving after any student has completed the exam and left the room may not be allowed to sit for the exam and may receive a score of zero.

No allowances will be made for an exam being missed, other than documented illness or an emergency. Students must contact Dr. Whitman for confirmation *prior to the exam.* If permission is granted to delay the exam, it is the student's responsibility to complete the College Form titled "Student Request for Alternate Exam Time" for consideration and *final approval* by Dr. Whitman. In this event, the nature of the make-up exam will be at my discretion (oral, written, increased weighting of the relevant section on the final, etc.). An unexcused absence from an exam may result in a grade of "zero" for that exam.

Return of Exams and Posting Class Scores & Keys

Exams will be returned to the students within a reasonable time after taking the exam. After grading the exams, they will be available for pick-up in the LRC. Grades and an exam key will be posted on Canvas. **The Final Exam is not returned.**

Post-Exam Remarks and Reconsideration Requests

If there is a disagreement over the answer to a specific question, the student should present his/her exam plus a written explanation (with appropriate documentation) to the instructor within 72 hours of the posting of exam results & key as described above. Documentation may include statements from textbooks, handouts, packets, or current scientific reprints; your lecture notes are *not* authoritative documentation. The explanation must be clear, rational, and concise. (This policy does not apply to addition or other grading errors). We are instructed to wait until after the deadline has passed before responding to specific reconsideration requests, so be patient!

Final Exam Re-Examination Policy

The re-examination policy for this course will follow the General Information Catalog (GIC) policy for the University, which reads as follows: "Only a student who has a grade average of at least a C on all class work and lab work submitted before the final exam may request a temporary delay of the final course grade because he or she failed the final examination, which is the examination given during the final exam period as printed in the official examination schedule. If Dr. Whitman denies the petition, the student's final course grade will remain as originally determined. If the petition is granted by the instructor (i.e., course coordinator), the grade on the reexamination will be **substituted** for the grade on the original exam in determining the student's final course grade, provided the student earns at least a C on the reexamination. **If the grade on the reexamination is less than a C, a final course grade of F must be recorded.**"

Course Grading

A Range:	A = 100%-93%	A- = 92%-90%	
B Range:	B+ = 89%-87%	B = 86%-83%	B- = 82%-80%
C Range:	C+ = 79%-77%	C = 76%-73%	C- = 72%-70%
D Range:	D+ = 69%-67%	D = 66%-65%	
F =	Below 65%		

This scale may be curved more leniently in the final analysis of grades at Dr. Whitman's discretion.

Academic Dishonesty

The "Statement on Scholastic Dishonesty of the College of Pharmacy" reads as follows: "Pharmacy practitioners enjoy a special trust and authority based upon the profession's commitment to a code of ethical behavior in its management of client affairs. The inculcation of a sense of responsible professional behavior is a critical component of professional education, and high standards of ethical conduct are expected of pharmacy students. Students who violate University rules on scholastic dishonesty are subject to disciplinary penalties, including failure of the course involved and dismissal from the college and/or the University. Since dishonesty harms the individual, fellow students, and the integrity of the University and the College of Pharmacy, policies of scholastic dishonesty will be strictly enforced in this class".

Students are expected to work independently on all examinations. Any student caught cheating will be given a "zero" on the assignment (minimum). Any student suspected of dishonesty will be reported to the Dean of the College of Pharmacy and to the Dean of Students, as per University regulations. Students are expected to have read and understood the current issue of the General Information Catalog published by the Registrar's Office for information about procedures and about what constitutes scholastic dishonesty. Students are also expected to be familiar with and abide by the College Honor Code, and will be expected to sign the Honors Statement at the end of each examination.

Students with Disabilities

The University of Texas at Austin provides upon request appropriate academic accommodations for qualified students with disabilities. All University rules concerning accommodations must be followed, including the student arranging for special accommodations *prior to each* examination. In the absence of such *prearrangement*, the student will be expected to take the exam with the rest of the class at the regularly scheduled exam time. For more information, contact the Office of the Dean of Students at 471-6259, 471-4641 TTY.

Campus Carry

Students should familiarize themselves with the information provided by the University regarding the implementation of "Campus Carry" legislation. You will find an information sheet specifically for students (as well as sheets for parents, visitors, faculty, and staff) at <http://campuscarry.utexas.edu/info-sheets>.

Pharmaceutical Biochemistry
PHM 381M
Approximate Course Outline
Fall 2016

- I. Biochemistry and the Organization of Cells (Ch. 1)
- II. Water: The Solvent for Biochemical Reactions (Ch. 2)
- III. Amino Acids and Peptides (Ch. 3)
- IV. The Three-Dimensional Structure of Proteins (Ch. 4)
- V. Protein Purification and Characterization Techniques (Ch. 5)

EXAMINATION #1 (Thurs., Sept 22, 7-9 PM)

- I. The Behavior of Proteins: Enzymes (Ch. 6)
- II. The Behavior of Proteins: Enzymes, Mechanisms, and Control (Ch. 7)
- III. Vitamins and Coenzymes (Ch 7.8 and Table 7.1 with associated sections, Ch. 8.7, and pp. 661-664, 671, and 682 for folate, sulfa drugs, and thymidylate synthase)

EXAMINATION #2 (Thurs., Oct 27, 7-9 PM)

- I. Carbohydrates (Ch. 16)
- II. Importance of Energy Changes and Electron Transfer in Metabolism (Ch. 15)
- III. Glycolysis (Ch. 17)
- IV. The Citric Acid Cycle (Ch. 19)
- V. Storage Mechanisms and Control of Carbohydrate Metabolism (Ch. 18)

EXAMINATION #3 (Thurs., Dec 1, 7-9 PM)

- I. Lipids and Proteins and Biological Membranes (Ch. 8)
- II. Lipid Metabolism (Ch. 21)
- III. Electron Transport and Oxidative Phosphorylation (Ch. 20)

CUMULATIVE FINAL (EXAMS 1-3 and material from the last weeks of class as announced)

Pharmaceutical Biochemistry
PHM 381M
Detailed (and Approximate) Lecture Schedule
Fall 2016

Lecture #1

- I. Biochemistry and the Organization of Cells (Ch. 1)
- II. Water: The Solvent for Biochemical Reactions (Ch. 2)
Acids, Bases, Buffers, and the Henderson-Hasselbalch Equation
The Bicarbonate Buffering System

Lecture #2

- III. Amino Acids and Peptides (Ch. 3)
General Structure and Properties
Structure and Properties of the Individual Amino Acids
Modified Amino Acids

Lecture #3

- Titration Curves (pK_a , and the isoelectric point known as pI)
Peptides and the Peptide Bond

Lecture #4

- More Peptides and Peptides of Physiological Interest - aspartame and glutathione, enkephalins, cyclosporin A, oxytocin, vasopressin, insulin

Lectures #5-6

- IV. The Three-Dimensional Structure of Proteins (Ch. 4)
Levels of structure
Characterization of levels of structure
Globular/Fibrous Proteins and Collagen triple helix– relationship between structure/function
Folding
Examples of medically relevant proteins - Botox, EPO, and more on insulin

Lectures #7-8

- V. Myoglobin and Hemoglobin – emphasizing structure and function
Oxygen binding to myoglobin and hemoglobin
Implications for Oxygen Transport
Allosteric regulators
2,3-bisphospho-D-glycerate
The Bohr Effect
Carbon Dioxide
Sickle Cell Anemia

Examination #1 (Approximate!!!)

Lecture #9-10

- I. The Behavior of Proteins: Enzymes
General Concepts and Enzyme Kinetics

Lecture #11-12

- I. Enzyme Inhibition

Reversible Inhibition – Competitive/Non-Competitive Inhibition with examples
Irreversible Inhibition – Penicillin and others

Lectures #13-15

- II. The Behavior of Proteins: Enzymes, Mechanisms, and Control (Ch. 7)
Proteases - Catalytic Strategies
Serine Proteases and Hydrolases (elastase, acetylcholinesterase, and β -lactamases)
Cysteine Proteases
Metalloproteases (Angiotensin Converting Enzyme)
Aspartic Proteases (HIV protease)
Zymogen Activation (Digestive enzymes and blood clotting)
Protease Inhibitors (α -antitrypsin and emphysema)

Lectures #15-17

- III. Vitamins and Coenzymes
(Tables 24.1 and 24.2, pp. 690-691; Table 7.1, pp. 187-188; Table 8.3, pp. 214-219, pp. 661-664, 671, and 682 for folate, sulfa drugs, and thymidylate synthase)
Water-Soluble Vitamins - properties and roles
The Lipid-Soluble Vitamins - properties and roles

Examination #2 (Approximate!!!)

Lecture #18-19

- IV. Carbohydrates (Ch. 16)
Monosaccharides
Reducing Sugars
Reaction of Glucose with Proteins
Disaccharides
The glycosidic bond, Lactose Intolerance (p. 467), Sucralose (p. 465)
Glycoconjugates

Lectures #20-21

- II. Glycolysis (Ch. 17)
The Reactions of Glycolysis
Mechanism of aldolase and glyceraldehyde 3-phosphate dehydrogenase
Alternate fates of pyruvate
Energy Yield (aerobic vs anaerobic)
Regulation of Glycolysis (control points)

Lectures #22-23

- III. The Citric Acid Cycle (Ch. 19)
Location and Pyruvate Dehydrogenase
The Reactions of the Citric Acid Cycle
Mechanisms (Citrate Synthase, Aconitase, and Isocitrate Dehydrogenase)
Energy Production
Citric Acid Cycle in Catabolism and Anabolism
Regulation of the Citric Acid Cycle

Lectures #24-25

- IV. Storage Mechanisms and Control of Carbohydrate Metabolism (Ch. 18)
Glycogen – structure, production, degradation, and regulation

Gluconeogenesis
Cori Cycle – connecting glycolysis to gluconeogenesis
More regulation
Pentose phosphate pathway

Examination #3 (Approximate!!!)

Lectures #25

- I. Structures of Lipids and Membranes (Ch. 8)
 - Introduction – what are lipids?
 - Classes, biological roles, and chemical features of lipids
 - Biological Membranes
 - Lipid Metabolism (Ch. 21)
 - Fatty acid oxidation (even- and odd-carbon fatty acids)

Lectures #26-27

- II. Ketone Bodies, ketosis, and diabetes mellitus
 - Steroid Biosynthesis
 - Fatty Acid Biosynthesis
 - Fuel Metabolism, Metabolic Stress, and Cancer
 - The Warburg effect (Role in cancer and diagnosis)

Lectures #28

- III. Electron Transport and Oxidative Phosphorylation (Ch. 20)
 - Introduction – Role of electron transport in metabolism
 - Organization of the electron transport complexes
 - Connection between electron transport and phosphorylation
 - Mechanism of coupling of electron transport and ATP synthesis
 - Mitochondrial Diseases

The Final!!!

Pharmaceutical Biochemistry
PHM 381M
Learning Objectives
Fall 2016

At the end of each of lecture (and after doing the assigned problems), you should know or have an understanding of the following concepts and the ability to do the following objectives. The content of each lecture is approximate.

Lecture #1

Define Biochemistry and its relationship to Pharmacy.

Know the common functional groups, the structure and properties of water, covalent/non-covalent interactions (types and relative strengths), and be able to use this knowledge correctly.

Know and/or understand the meaning of acid/base, strong vs weak acid, conjugate acid/base (examples and recognize/identify them when you see them!) pH, pK_a , the Henderson/Hasselbalch equation, calculations using the Henderson/Hasselbalch equation, determination of the pK_a , titration curves and interpretation; buffers and buffer capacity, and the carbon dioxide/bicarbonate buffering system as well as acidosis and alkalosis (respiratory and metabolic) and interpretation.

Lecture #2

Name and recognize the general structure and properties of an amino acid and the 20 common amino acids. Recognize and use the three letter codes, and be able to identify the various acid/conjugate base pairs for the common amino acids. Know the important structural features, as indicated in class...

Lecture #3

...(continuing from above) Know the general properties of the amino acids including the approximate pK_a values, titration curves and their interpretation, whether they are charged or not charged at different pH values and how the charges and/or properties of the side chains are important to the structure of a protein/enzyme, the pI (and implications), and how modified amino acids change these properties (with examples).

Recognize the peptide bond (and conventional representation), its characteristics, and some common biochemically/pharmaceutically relevant peptides (aspartame, glutathione) ...

Lecture #4

...(continuing from above) more examples (enkephalins, Cyclosporin A, oxytocin, vasopressin, insulin).

Lectures #5-6

Define proteins and their importance and relevance. Distinguish among and recognize the four levels of protein structure, and denatured vs native structure (and relevance). Recognize and use conventional representation of α -helices and β -sheets. Know the characteristics of each level of protein structure, and how the structural elements interact and are responsible for the properties of a protein. Distinguish among and recognize globular vs fibrous proteins and the collagen triple helix (with an emphasis on the relationship between structure/function). Describe folding and unfolding and be able to use and interpret

ribbon diagrams. Be familiar with biochemically/pharmaceutically relevant proteins (Botox and EPO) and relevance and implications of pI on insulin.

Lectures #7-8

Describe the role of hemoglobin in oxygen delivery, waste removal, and buffering. Describe the structure and properties of myoglobin and hemoglobin and differences, the composition of the heme ring, and the behavior of iron with oxygen (puckered vs planar). Be able to interpret oxygen binding curves, the implications of the curves and properties of myoglobin and hemoglobin for oxygen transport, cooperativity, and structural basis for cooperativity (T and R states). Define the role, and effects of allosteric regulators, (e.g., 2,3-bisphospho-D-glycerate, protons, carbon dioxide), on adult and fetal hemoglobin and structural basis for the effects. Know the structures as described in class. Describe the Bohr effect, the molecular basis for it, and the implications. Describe sickle cell anemia, the molecular basis, and the implications.

Examination #1 (Approximate!!!)

Lecture #9-10

Define and correctly use the terms enzyme, substrate, active site, rate enhancement, substrate specificity, cofactor, coenzyme, and transition state. Know the importance of enzymes to drug design and action. Describe the basics of enzymatic catalysis, general concepts and key features of active sites, terminology, and properties of enzymes, specificity, and how enzymes work (in general).

Define and correctly use the Michaelis-Menten equation and the kinetic parameters (K_m , k_{cat} , k_{cat}/K_m). Understand the basics and importance of enzyme kinetics. Explain the Michaelis-Menten equation, the terms, implications, general observations (on the plot), how it is a model for enzyme catalysis, and the importance and relevance. Interpret the equation (under the two limiting cases) and explain the terminology.

Lecture #11-12

Define an enzyme inhibitor and its role and importance. Define and understand the difference between reversible and irreversible inhibitors, competitive and non-competitive inhibition, and the meaning and relevance of K_i . Interpret Lineweaver-Burke plots and the difference in the Lineweaver-Burke plots for the different types of inhibitors. Describe the mechanism of penicillin.

Lectures #13-15

Describe what a protease does and the importance of proteases and other enzymes to pharmacy. Describe the physiological roles of proteases and hydrolases, and their properties. Describe with appropriate diagrams or sketches the mechanisms (arrow pushing) of serine proteases and hydrolases (acetylcholinesterase and β -lactamases), cysteine proteases, metalloproteases (angiotensin converting enzyme), and aspartic proteases (HIV protease). Distinguish among the four types of proteases. Describe the structural basis for specificity of proteases and the mechanism of inhibition of DIPP, nerve gases, augmentin, captopril/ACE inhibitors, and HIV protease inhibitors. For all, describe the relevance and importance to pharmacy.

Lecture #15

Describe the importance and significance of regulatory strategies and key strategies (phosphorylation, zymogen activation) and examples (digestive enzymes and blood clotting). Describe the role of protease inhibitors (also a regulatory strategy) and examples (α -antitrypsin and emphysema).

Lectures #15-18

Distinguish between the two classes of vitamins (water-soluble vs lipid soluble) and their properties.

For the water-soluble vitamins, describe the vitamin, coenzyme (if relevant), potential disease (if deficient and relevant), biochemical role and mechanism of action for this role (if relevant). Thiamine, riboflavin, niacin, pantothenic acid, pyridoxine, B₁₂, and folic acid will be covered. Know the important structural features, as indicated in class. Know the relationship between B₁₂ and folate, the mechanism of action of sulfa drugs, and involvement in cancer chemotherapy.

For the lipid-soluble vitamins know the vitamin, coenzyme (if relevant), potential disease (if deficient and relevant), biochemical role and mechanism of action for this role (if relevant). The lipid-soluble vitamins might not be covered. Know the important structural features, as indicated in class.

Examination #2 (Approximate!!!)

Lecture #19-20

Define and correctly use the terms aldose, ketose, pyranose, and furanose. Explain the classification, nomenclature, and chemistry of mono-, di-, and polysaccharides. Explain what is meant by the term reducing sugar and distinguish between the reducing and non-reducing end of a sugar. Describe the reaction of glucose with proteins (Amadori rearrangement and advanced glycation products). Describe a glycosidic bond. Describe the basis for lactose intolerance, and know how the structure of sucralose (Splenda) relates to its function. For all, know the important structural features, as indicated in class. Describe how elevated blood sugar can lead to hemoglobin glycosylation, and how HbA_{1c} is used in following the effectiveness of the treatment of diabetes.

Lectures #20-21

Know the structures of ATP and other phosphorylated compounds (if covered) and the electron carriers, NAD⁺ and FAD, as indicated in class. Understand the structural basis for the hydrolysis of ATP and importance of ATP and phosphorylated compounds.

Describe the overall purpose of glycolysis, its reactants and products, cellular localization, and tissue distribution. Define and use correctly the terms glycolysis, aerobic vs. anaerobic metabolism, hexokinase, phosphofructokinase, pyruvate kinase, and lactate dehydrogenase. Diagram the glycolytic pathway and describe how it can be divided into 3 stages. List the 10 reactions of glycolysis in order (and their location), the key features of each reaction, and understand the overall logic and relevance to various conditions/diseases. Note where ATP is consumed and produced (by substrate-level phosphorylation). Describe the role and fates of NADH produced in glycolysis. Know the mechanism of aldolase and the mechanism and importance of the glyceraldehyde 3-phosphate dehydrogenase reaction, the alternate fates of pyruvate, the energy yield (aerobic vs anaerobic) and the implications of the yield for various diseases/conditions and drug design. Know the important structural features of the glycolytic intermediates, as indicated in class. Explain how glycolysis is regulated - Note the enzymes that catalyze irreversible steps and how control is carried out at the enzyme and hormonal levels.

Lecture #22-23

Describe the pyruvate dehydrogenase reaction (and relationship to α -ketoglutarate dehydrogenase complex), the composition, and significance. Describe the overall purpose of the citric acid cycle, its cellular location, and tissue distribution. Describe the eight reactions of the Citric Acid Cycle (or Krebs Cycle), their location, significance, the mechanism and importance of citrate synthase, aconitase, and isocitrate dehydrogenase, and the regulation of the cycle. Diagram the cycle and know the metabolic intermediates. Know the importance of the cycle in terms of energy production, catabolism, and the production of biosynthetic precursors. Know how the cycle fits into the overall scheme of metabolism (including oxidative phosphorylation).

Lectures #24-25

Describe the overall purpose of glycogenesis and glycogenolysis, their reactants and products, cellular localization, and tissue distribution. Define and use correctly the terms glycogen, glycogenolysis, glycogen synthase, gluconeogenesis, and the Cori cycle. Describe the functions of glycogenolysis, glycogen synthesis, and gluconeogenesis. Note the important precursors and organs/tissues and intracellular locations for each. Describe the regulation for each and the key enzymes, activators, and inhibitors involved. Describe the linkages among these processes. Describe the role of the pentose phosphate pathway.

Examination #3 (Approximate!!!)

Lecture #25

Define and use correctly the terms for the different types of lipids (fatty acids, triacylglycerols, phosphoacylglycerols, waxes, sphingolipids, glycolipids, and steroids), use proper chemical nomenclature to describe them, recognize structures as indicated, and be able to relate structure to physical behavior. Define and understand properties of biological membranes, lipid bilayers, know the types of proteins that interact with membranes, how they function and interact with lipid bilayer.

Lecture #26-27

Define and use correctly the following terms: acyl carrier protein, acetyl CoA, β -oxidation, ketone bodies, fatty acid synthase, malonyl CoA, acetyl CoA carboxylase, and hydroxymethylglutaryl-CoA (HMG-CoA), and recognize structures, as appropriate. Recognize the structures of carnitine and its role. Describe the β -oxidation pathway for fatty acids as well as how the cell breaks down fatty acids with an odd number of carbons. Explain the formation of ketone bodies and identify the physiological and pathological roles. Describe how fatty acids are synthesized. Describe the stages of cholesterol synthesis and role of HMG-CoA reductase. List the biochemical roles for cholesterol. Understand fuel metabolism, the role of insulin and glucagon, the Warburg effect and its role in cancer and diagnosis, starvation, and diabetes.

Lectures #28

Define and use correctly the following terms: electron transport chain, respiratory complex, proton pump, oxidative phosphorylation, heme, nonheme iron, iron-sulfur complexes, cytochromes, ATP synthase, chemiosmotic model, conformational coupling, proton gradient, the P/O ratio, and respiratory inhibitors and uncoupling agents. List the respiratory complexes in the appropriate order and their roles. Explain the chemiosmotic model of oxidative phosphorylation. Understand what mitochondrial diseases are.