

July, 2008 Summary of
Pharmaceutics II Laboratory – PHAR 513 (1 semester credit hour)
Bernard J. Dunn School of Pharmacy • Shenandoah University
Winchester, VA 22601

Course Description

Pharmaceutics II laboratory emphasizes (1) pharmaceutical compounding calculations and judgment, blending and measurement skills, and terminology; and (2) interpretation and application of physical and chemical properties and theories related to biopharmaceutical performance and chemical stability of drugs.

Learning Goals

1. Safely, accurately, and precisely measure and weigh fluids and solids.
2. Identify and explain relevant physical and chemical principles, such as acid-base properties and reactions, diffusion, dissolution, chemical stability reactions, solubility factors, and stability kinetics, in relation to the *in vitro* and *in vivo* performance of pharmaceutical products.
3. Demonstrate proper pharmaceutical *secundum artem*, SA, and correct mathematical problem-solving required for safe, accurate prescription compounding and dispensing.
4. Write clear and accurate reports of each course exercise.

Textbook

L.V. Allen, Jr., N.G. Popovich, and H.C. Ansel. *Pharmaceutical Dosage Forms and Drug Delivery Systems*, Eight Edition, Lippincott Williams & Wilkins; 2005 (ISBN 0-7817-4612-4).

Reference Documents Linked to the Course Homepage (Reference documents by course instructors)

- Measurement Statistics: Accuracy and Precision, Mean and Standard Deviation
- Accuracy Limits of Measuring Devices
- Making Double Dilutions with Graduated Cylinders (Three Bottle Problems)
- Compounding Hard Gelatin Capsules from Bulk Drugs and Excipients
- Compounding Hard Gelatin Capsules from Manufactured Capsules and Tablets
- Compounding Oral Fluids from Manufactured Capsules and Tablets
- Torsion Mechanism Double Pan Prescription (Rx) Balances

Course Grading

Attendance

Each unexcused absence will result in a deduction of 5% from the final course grade. Students must obtain excused absence from the Associate Dean for Students. Make-up opportunities for excused absences will depend on the mutual availability of the instructor, students, and materials.

Weighting of Final Grades

| Type of Graded Work | Percent of Final Grade |
|---|------------------------|
| Attendance and submission of written reports of exercises | 80 |
| Practical skills examination on capsules and dye dilution | 10 |
| Final written examination | 10 |

Requirements for Written Reports of Laboratory Exercises

1. Completed reports must be submitted by the date and time announced by the course instructor.
2. Reports must be hand written or printed legibly in blue or black ink, or dark pencil directly by the student whose name is on the report.
3. Photocopies of completed reports will **NOT** be accepted.

Grading Basis for Written Reports of Laboratory Exercises

Reports will be evaluated for neatness, correctness, completeness, and clarity. In particular, the following characteristics will be judged:

1. Correct selection and use of pharmaceutical measuring and mixing devices, ingredients, and *secundum artem*, SA, procedures.
2. Correct explanations of physical and chemical phenomena, and visual descriptions of preparations.
3. Not less than 95% accuracy of all weight and volume measurements of ingredients.

The instructor will assign a grade of 1 to 5 to submitted reports, where 5 is best. The grading judgment is guided by the extent to which students' reports contain legible writing, correct information, and clear and complete explanations.

Table 1. Pharmaceutical principles and performance activities of the laboratory exercises.

| Exercise # | Principles and Performance Activities* |
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| 1 | <ul style="list-style-type: none">◆ Correct use of toploading electronic balance and graduated cylinders◆ Accuracy and precision of weight and volume measuring with graduated cylinders, teaspoons, beakers, 1-oz plastic dosing cups, and 2-oz plastic Rx ovals◆ Comparison of labeled drug strength with total weight, and weight precision of eight manufactured capsule and tablet products◆ USP percent content ranges of selected active drugs and their dosage forms◆ Accuracy of two dilutions, or “three bottles,” of Patent Blue Violet (PBV) Dye measured spectrophotometrically |
| 2 | <ul style="list-style-type: none">◆ Sodium Fluoride Capsules: Minimum Accurately Weighable Quantity, MAWQ or 95% accuracy limit of balance◆ Compounding <i>secundum artem</i> (SA) skills: geometric trituration of active drug and excipient, and accurate punch-filling of capsules |
| 3 | <p>Disintegration and Exposure of Selected Oral Drugs</p> <ul style="list-style-type: none">◆ <i>in vitro</i> demonstration with 12 types of capsules and tablets in 0.15 N HCl and pH 7.4 buffer at 40°C◆ simulated local vs systemic drug action: presence and lack of green (pH 4) to blue (pH 7) color change of PBV dye solution with an antacid tablet vs Pepcid AC tablet◆ effect of low, medium, and high viscosity fluid (water, water:corn syrup 2:1, and water corn syrup 1:1) on disintegration time of uncoated drug tablets◆ questions about USP dissolution tolerances of oral phenytoin dosage forms; enteric, film, and sugar coatings; and controlled release mechanisms |
| 4 | <p>Ointments and Creams: Levigating Solids and Geometrically Blending Ingredients</p> <ul style="list-style-type: none">◆ prepare four ingredients in Aquabase and Dermabase (bases donated by Paddock Labs.) |

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| | <ul style="list-style-type: none"> ◆ questions on differentiating topical base or vehicle types (absorption [w/o emulsion], cream, oleaginous); effect of drug dissolution in dosage form on drug diffusion; effect of occlusion on drug absorption; ingredients and properties of coal tar solution, USP |
| Practical Exam | <ul style="list-style-type: none"> ◆ Fill one capsule containing two active drugs – one drug source is a bulk or “pure” powder, and the other drug source is a manufactured tablet. ◆ Make a double dilution (“three bottles”) of a known strength stock solution diluted to a specific strength and volume of final (“patient’s”) strength of PBV dye |
| 5 | <p>Oral Fluid Dosage Form Compounded from Unformulated Drug and Manufactured Tablet</p> <ul style="list-style-type: none"> ◆ use one of three different suspension vehicles donated by Paddock Labs., plus four other excipients ◆ questions on correct measurement of ingredients |
| 6 | <p>Drug Solubility Examples</p> <ul style="list-style-type: none"> ◆ Based on visual observations, describe the effect on drug solubility of: (a) ionized (salt) vs non-ionized form, (b) water-miscible “GRAS” alcohols, (c) pH change, (d) surfactant micelles; and (e) charge induction complexation. ◆ questions on water-alcohol intermolecular H bonding; endothermic dissolution of mannitol, pH dependent calcium phosphates solubility; solubility in relation to specific solute-solvent intermolecular forces; |
| 7 | <p>“Surprise” Theoretical Capsule Rx Compounded from Manufactured Drug Tablets</p> <ul style="list-style-type: none"> ◆ Correctly interpret and calculate an Rx for compounded capsules using a manufactured drug tablet as the source of active drug ingredients – students must weigh tablets and provide correct calculations for the Rx, but not actually make it. |
| 8 | <p>Pharmaceutics Smorgasbord</p> <p>All samples result in visible changes within 2-3 weeks of preparation; thus, 2-3 weeks elapse between Exercise 8A the preparation and Exercise 8B the discussion by the class group that made them. Each example below of a stability problem is accompanied by a few pertinent questions.</p> <ul style="list-style-type: none"> ◆ Compatibility and solubility of phenytoin sodium and diphenhydramine HCl solutions in relation to pH and extent of dilution ◆ Phenytoin sodium and diphenhydramine HCl adsorption to activated charcoal and PeptoBismol ◆ Ampicillin stability to hydrolysis in different solvents (D5W, NS, pH buffers) at room and refrigeration temperature evaluated by the of starch-iodine test (hydrolyzed ampicillin results in at least one aldehyde product that reduces iodine to I⁻, and I⁻ does not darken starch as does iodine) ◆ Stability of tetracycline HCl different topical vehicles with and without water ◆ Water-dispersibility of phenytoin in capsules with and without sodium lauryl sulfate ◆ Stability of IV fat emulsion with various TPN ingredients ◆ Calcium phosphate solubility in TPN-like mixtures containing different amounts of 50% dextrose and 8.5% or 10% amino acids ◆ Dopamine stability to oxidation in different pH buffers |
| 9 | <p>Chemical Stability Kinetics: Color Loss Reaction of PBV Dye</p> <ul style="list-style-type: none"> ◆ Differentiate reversible vs irreversible reactions: conversion of PBV from blue to |

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| | green/yellow by adding a few drops of 1 <i>N</i> HCl and back to blue by a few drops of 1 <i>N</i> NaOH vs permanent addition of OH to PBV at pH 13 and 14 (0.1 <i>N</i> and 1 <i>N</i> NaOH) |
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| | ◆ Compare effect of pH 13 and 14, temperature of 25° C and 50° C on the rate of color loss or fading of PBV dye |
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| *Exercises require from 1-3 hours, with a mean ~ 2 hours, for 35-40 students per section. | |
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