Comprehensive Pharmacy Review for NAPLEX

Eighth Edition

Leon Shargel
Alan H. Mutnick
Paul F. Souney
Larry N. Swanson

Wolters Kluwer Health | Lippincott Williams & Wilkins

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Wolters Kluwer | Lippincott Williams & Wilkins
Health

Philadelphia • Baltimore • New York • London
Buenos Aires • Hong Kong • Sydney • Tokyo

Acquisitions Editor: Sirkka Howes
Product Manager: Michael Marino
Marketing Manager: Joy Fisher-Williams
Design Coordinator: Teresa Mallon
Production Services: Absolute Service, Inc.

Eighth Edition

351 West Camden Street
Baltimore, MD 21201

Two Commerce Square
2001 Market Street
Philadelphia, PA 19103

Printed in China

9 8 7 6 5 4 3 2 1

Library of Congress Cataloging-in-Publication Data

Comprehensive pharmacy review for NAPLEX / editors, Leon Shargel ... [et al.]. — 8th ed.
p. ; cm.
Comprehensive pharmacy review for North American Pharmacist Licensure Examination
Includes index.
Rev. ed. of: Comprehensive pharmacy review / editors, Leon Shargel ... [et al.]. 7th ed. c2010.
ISBN 978-1-4511-1704-2 (pbk.)
I. Shargel, Leon, 1941- II. Comprehensive pharmacy review. III. Title: Comprehensive pharmacy review for North American Pharmacist Licensure Examination.
[DNLM: 1. Pharmacy—Examination Questions. QV 18.2]

615'.1076—dc23

2012020144

Preface

This eighth edition of *Comprehensive Pharmacy Review* reflects the continuing evolution of pharmacy practice and educational requirements. The main objective of the book is to provide a comprehensive study guide for pharmacy students and other candidates who are preparing for the North American Pharmacist Licensure Examination (NAPLEX). This volume represents the contributions of more than 50 specialists who provide wide expertise in pharmaceutical science, pharmacy practice, and clinical pharmacy. Their contributions to *Comprehensive Pharmacy Review* assure that this review guide is accurate and current as well as written in a comprehensible manner for students, teachers, and practitioners alike. This review publication, along with the separate booklet of simulated NAPLEX exams (Comprehensive Pharmacy Review Practice Exams, 8th edition), provides both guidance and test practice for NAPLEX candidates.

The current pharmaceutical education provides greater career opportunities for pharmacists than ever before. Pharmaceutical education, including pharmaceutical science and practice, must prepare pharmacy practitioners for the future. Among the many career choices for pharmacists include work in academic pharmacy, community pharmacy, long-term care, and consulting pharmacy, including hospice and home care, pharmaceutical and health care distributors, pharmaceutical industry, professional trade organizations, uniformed (public health) services, federal and state governments, hospital and institutional practice settings, managed care pharmacy, and other settings. Moreover, pharmacists are actively involved in health care. Examples include counseling and medication therapy, disease state management, and screening programs such as diabetes, hypertension, and high cholesterol along with the more traditional role of dispensing medication and educating patients. Many students enroll in pharmaceutical education programs that are combined with a business (MBA), research (PhD), or law (JD) degree to provide opportunities in various pharmacy-related professions and other challenging fields.

Comprehensive Pharmacy Review is principally written for NAPLEX candidates. However, the book is also intended for a broader audience of pharmacy undergraduates and health professionals who seek detailed summaries of pharmacy subjects. A wide range of topics central to the study of pharmacy—chemistry, pharmaceutics, pharmacology, pharmacy practice, drug therapy—is organized to parallel the pharmacy curriculum and presented in outline form for easy use. The *Comprehensive Pharmacy Review* may be used as a quick review (or preview) of essential topics by a diverse group of readers, including

- **Matriculating pharmacy students.** The organization and topical coverage of *Comprehensive Pharmacy Review* are such that many pharmacy students will want to purchase it in their first professional year and use it throughout their pharmacy education to prepare for course examinations.
- **Instructors and preceptors.** *Comprehensive Pharmacy Review* also functions as an instructor's manual and a reference for teachers and tutors in pharmacy schools. Chapter outlines can be used to organize courses and to plan specific lectures.
- **Professional pharmacists.** *Comprehensive Pharmacy Review* offers practitioners a convenient handbook of pharmacy facts. It can be used as a course refresher and as a source of recent information on pharmacy practice. The appendices include prescription dispensing information, common prescription drugs, and general pharmacy references.
- **Foreign pharmacy graduates.** *Comprehensive Pharmacy Review* provides a source of current information on pharmaceutical science, pharmacy practice, and clinical pharmacy for foreign pharmacy graduates who may be candidates for the Foreign Pharmacy Graduate Equivalency Examination (FPGEE). The appendices include prescription dispensing information, common prescription drugs, and general pharmacy references.

WHAT'S NEW IN THIS EDITION

The continuing evolution of pharmacy practice is reflected by the licensure examinations developed by the National Association of Boards of Pharmacy (NABP) to assess the competence of pharmacy candidates. For this reason, we have requested and have been given permission by NABP to reproduce the competency statements for the NABP examination (NAPLEX) in the front matter of this edition of *Comprehensive Pharmacy Review*.

Because of the significant advances in drug therapy since the publication of the last edition, this edition has been revised to reflect the current educational and competency requirements for a successful career in pharmacy. Many of the chapters have been revised to represent the latest understanding of disease and therapeutic management. New chapters, such as Pain Management Including Migraines, Hepatic Disorders, Pediatrics, Geriatrics, Women's Health have been added to reflect the needs of special populations. The addition of the chapter, Biostatistics and Medical Literature Evaluation provides a basis for the evaluation of new therapeutic moieties that will be marketed in the future.

ORGANIZATIONAL PHILOSOPHY AND CHAPTER STRUCTURE

The organization of the eight edition reflects the current undergraduate pharmacy curriculum. Pharmaceutical Sciences (Chapters 1–18), contains subject matter pertaining to the basic science of pharmacy. Pharmacy Practice (Chapters 19–64), contains subject matter for the practice of pharmacy with emphasis on pharmaceutical care. Each chapter of the book contains topic outlines and practice questions according to the pharmacy school curriculum.

At the front matter of this book, you'll find guidelines for taking a test and an introduction to the NAPLEX exam, including the actual NAPLEX blueprint. The appendices of this book are compilations of handy reference tables.

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Taking a Test

One of the least attractive aspects of pursuing an education is the necessity of being examined on the material that has been presented. Instructors do not like to prepare tests, and students do not like to take them.

However, students are required to take many examinations during their learning careers, and little, if any, time is spent acquainting them with the positive aspects of tests and with systematic and successful methods for approaching them. Students perceive tests as punitive and sometimes feel as if they were merely opportunities for the instructor to discover what the student has forgotten or has never learned. Students need to view tests as opportunities to display their knowledge and to use them as tools for developing prescriptions for further study and learning.

While preparing for any exam, class and board exams as well as practice exams, it is important that students learn as much as they can about the subject they will be tested and are prepared to discover just how much they may not know. Students should study to acquire knowledge, not just to prepare for tests. For the well-prepared student, the chances of passing far exceed the chances of failing.

MATERIALS NEEDED FOR TEST PREPARATION

In preparing for a test, most students collect far too much study material, only to find that they simply do not have time to go through all of it. They are defeated before they begin because either they cannot get through all the material, leaving areas unstudied, or they race through the material so quickly that they cannot benefit from the activity.

It is generally more efficient for the student to use materials already at hand—that is, class notes, one good outline to cover and strengthen all areas and to quickly review the whole topic, and one good text as a reference for complex material that requires further explanation.

Also, many students attempt to memorize far too much information, rather than learning and understanding less material and then relying on that learned information to determine the answers to questions at the time of the examination. Relying too heavily on memorized material causes anxiety, and the more anxious students become during a test, the less learned knowledge they are likely to use.

ATTITUDE AND APPROACH

A positive attitude and a realistic approach are essential to successful test taking. If the student concentrates on the negative aspects of tests or on the potential for failure, anxiety increases and performance decreases. A negative attitude generally develops if the student concentrates on "I must pass" rather than on "I can pass." "What if I fail?" becomes the major factor motivating the student to run from failure rather than toward success. This results from placing too much emphasis on scores. The score received is only one aspect of test performance. Test performance also indicates the student's ability to use differential reasoning.

In each question with five alternatives, of which one is correct, there are four alternatives that are incorrect. If deductive reasoning is used, the choices can be viewed as having possibilities of being correct. The elimination of wrong choices increases the odds that a student will be able to recognize the correct choice. Even if the correct choice does not become evident, the probability of guessing correctly increases. Eliminating incorrect choices on a test can result in choosing the correct answer.

Answering questions based on what is incorrect is difficult for many students because they have had nearly 20 years of experience taking tests with the implied assertion that knowledge can be displayed only by knowing what is correct. It must be remembered, however, that students can display knowledge by knowing something is wrong, just as they can display it by knowing something is right.

PREPARING FOR THE EXAMINATION

1. **Study for yourself.** Although some of the material may seem irrelevant, the more you learn now, the less you will have to learn later. Also, do not let the fear of the test rob you of an important part of your education. If you study to learn, the task is less distasteful than studying solely to pass a test.

2. **Review all areas.** You should not be selective by studying perceived weak areas and ignoring perceived strong areas. Cover all of the material, putting added emphasis on weak areas.
3. **Attempt to understand, not just to memorize, the material.** Ask yourself: To whom does the material apply? When does it apply? Where does it apply? How does it apply? Understanding the connections among these points allows for longer retention and aids in those situations when guessing strategies may be needed.
4. **Try to anticipate questions that might appear on the test.** Ask yourself how you might construct a question on a specific topic.
5. **Give yourself a couple days of rest before the test.** Studying up to the last moment will increase your anxiety and cause potential confusion.

TAKING THE EXAMINATION

1. Be sure to pace yourself to use the test time optimally. You should use all of your allotted time; if you finish too early, you probably did so by moving too quickly through the test.
2. Read each question and all the alternatives carefully before you begin to make decisions. Remember, the questions contain clues, as do the answer choices.
3. Read the directions for each question set carefully. You would be amazed at how many students make mistakes in tests simply because they have not paid close attention to the directions.
4. It is not advisable to leave blanks with the intention of coming back to answer questions later. If you feel that you must come back to a question, mark the best choice and place a note in the margin. Generally speaking, it is best not to change answers once you have made a decision. Your considered reaction and first response are correct more often than are changes made out of frustration or anxiety.
5. Do not let anxiety destroy your confidence. If you have prepared conscientiously, you know enough to pass. Use all that you have learned.
6. Do not try to determine how well you are doing as you proceed. You will not be able to make an objective assessment, and your anxiety will increase.
7. Do not become frustrated or angry about what appear to be bad or difficult questions. You simply do not know the answers; you cannot know everything.

SPECIFIC TEST-TAKING STRATEGIES

Read the entire question carefully, regardless of format. Test questions have multiple parts. Concentrate on picking out the pertinent key words that will help you problem-solve. Words such as *always*, *all*, *never*, *mostly*, *primarily*, and so forth play significant roles. In all types of questions, distractors with terms such as *always* or *never* most often are incorrect. Adjectives and adverbs can completely change the meaning of questions—pay close attention to them. The knowledge and application of grammar often are key to dissecting questions.

MULTIPLE CHOICE QUESTIONS

Read the question and the choices carefully to become familiar with the data provided. Remember in multiple choice questions, there is one correct answer and there are four distractors, or incorrect answers. (Distractors are plausible and possibly correct, otherwise they would not be called distractors.) They are generally correct for part of the question but not for the entire question. Dissecting the question into parts helps eliminate distractors.

Many students think that they must always start at option A and make a decision before they move to option B, thus forcing decisions they are not ready to make. Your first decisions should be made on those choices you feel the most confident about.

Compare the choices with each part of the question. To be wrong, a choice needs to be incorrect for only part of the question. To be correct, it must be totally correct. If you believe a choice is partially incorrect, tentatively eliminate that choice. Make notes next to the choices regarding tentative decisions. One method is to place a minus sign next to the choices you are certain are incorrect and a plus sign next to those that potentially are correct. Finally, place a zero next to any choice you do not understand or need to come back to for further inspection. Do not feel that you must make final decisions until you have examined all choices carefully.

When you have eliminated as many choices as you can, decide which of those that remain has the highest probability of being correct. Above all, be honest with yourself. If you do not know the answer, eliminate as many choices as possible and choose reasonably.

Multiple choice questions are not as difficult as some students make them. There are two general types of multiple choice questions, including (1) the more traditional single answer type question in which the candidate must decide one of five choices (a, b, c, d, or e) and (2) the combined response ("K" type) multiple choice question, which is shown next. In this case, these are the questions for which you must select from the following choices:

A if **only I** is correct
B if **only III** is correct
C if **I and II** are correct
D if **II and III** are correct
E if **I, II, and III** are correct

Remember that the name for this type of question is *multiple true–false* and then use this concept. Become familiar with each choice and make notes. Then concentrate on the one choice you feel is definitely incorrect. If you can find one incorrect alternative, you can eliminate three choices immediately and be down to a 50–50 probability of guessing the correct answer. If choice A is incorrect, so are choices C and E; if choice B is incorrect, so are choices D and E. Therefore, you are down to a 50–50 probability of guessing the correct answer.

After eliminating the choices you are sure are incorrect, concentrate on the choice that will make your final decision. For instance, if you discard choice I, you have eliminated alternatives A, C, and E. This leaves B (III) and D (II and III). Concentrate on choice II and decide if it is true or false. (Take the path of least resistance and concentrate on the smallest possible number of items while making a decision.) Obviously, if none of the choices is found to be incorrect, the answer is E (I, II, III).

GUESSING

Nothing takes the place of a firm knowledge base; but having little information to work with, you may find it necessary to guess at the correct answer. A few simple rules can help increase your guessing accuracy. Always guess consistently if you have no idea what is correct—that is, after eliminating all that you can, make the choice that agrees with your intuition or choose the option closest to the top of the list that has not been eliminated as a potential answer.

When guessing at questions that present with choices in numeric form, you will often find the choices listed in an ascending or descending order. It is generally not wise to guess the first or last alternative because these are usually extreme values and are most likely incorrect.

USING A PRACTICE EXAM TO LEARN

All too often, students do not take full advantage of practice exams. There is a tendency to complete the exam, score it, look up the correct answer to those questions missed, and then forget the entire thing.

In fact, great educational benefits could be derived if students would spend more time using practice tests as learning tools. As mentioned previously, incorrect choices in test questions are plausible and partially correct, otherwise they would not fulfill their purpose as distractors. This means that it is just as beneficial to look up the incorrect choices as the correct choices to discover specifically why they are incorrect. In this way, it is possible to learn better test-taking skills as the subtlety of question construction is uncovered.

In addition, it is advisable to go back and attempt to restructure each question to see if all the choices can be made correct by modifying the question. By doing this, you will learn four times as much. By all means, look up the right answer and explanation. Then, focus on each of the other choices, and ask yourself under what conditions, if any, they might be correct.

SUMMARY

Ideally, examinations are designed to determine how much material students have learned and how that material is used in the successful completion of the examination. Students will be successful if these suggestions are followed:

- Develop a positive attitude and maintain that attitude.
- Be realistic in determining the amount of material you attempt to master and in the score you hope to attain.
- Read the directions for each type of question and the questions themselves closely, and follow the directions carefully.
- Bring differential reasoning to each question in the examination.
- Guess intelligently and consistently when guessing strategies must be used.
- Use the test as an opportunity to display your knowledge and as a tool for developing prescriptions for further study and learning.

Board examinations are not easy. They may be almost impossible for those who have unrealistic expectations or for those who allow misinformation concerning the exams to produce anxiety out of proportion to the task at hand. Examinations are manageable if they are approached with a positive attitude and with consistent use of all of the information the student has learned.

Michael J. O'Donnell

Introduction to the NAPLEX

After graduation from an accredited pharmacy program, the prospective pharmacist must demonstrate the competency to practice pharmacy. The standards of competence for the practice of pharmacy are set by each state board of pharmacy. NAPLEX—The North American Pharmacist Licensure Examination—is the principal instrument used by the state board of pharmacy to assess the knowledge and proficiency necessary for a candidate to practice pharmacy. The National Association of Boards of Pharmacy (NABP) is an independent, international, and impartial association that assists member boards and jurisdictions in developing, implementing, and enforcing uniform standards for the purpose of protecting the public health. NABP develops examinations that enable boards of pharmacy to assess the competence of candidates seeking licensure to practice pharmacy. Each state board of pharmacy may impose additional examinations. The two major examinations developed by NABP are

- The North American Pharmacist Licensure Examination (NAPLEX)
- Multistate Pharmacy Jurisprudence Examination (MPJE)

Foreign pharmacy graduates must pass the Foreign Pharmacy Graduate Equivalency Examination (FPGEE) as part of the Foreign Pharmacy Graduate Equivalency Certification process. Foreign-educated pharmacists awarded FPGEC certification is considered to have partially fulfilled eligibility requirements for licensure in those states that accept the certification.

A description of these computerized examinations and registration information may be found on the NABP website online at http://www.nabp.net. Before submitting registration materials, the pharmacy candidate should contact the board of pharmacy for additional information regarding procedures, deadline dates, and required documentation.

The NAPLEX is a computer-adaptive test. These questions measure *the prospective pharmacist's ability to measure pharmacotherapy and therapeutic outcomes, prepare and dispense medications, and implement and evaluate information for optimal health care*. The computer adaptive exam tests a candidate's knowledge and ability by assessing the answers before presenting the next test question. If the answer is correct, the computer will select a more difficult question from the test item pool in an appropriate content area; if the answer is incorrect, an easier question will be selected by the computer. The NAPLEX score is based on the difficulty level of the questions answered correctly.

NAPLEX consists of 185 multiple choice test questions. In the past, 150 questions were used to calculate the test score. The remaining 35 items served as pretest questions and do not affect the NAPLEX score. Pretest questions are administered to evaluate the item's difficulty level for possible inclusion as a scored question in future exams. These pretest questions are dispersed throughout the exam and cannot be identified by the candidate.

A majority of the questions on the NAPLEX are asked in a scenario-based format (i.e., patient profiles with accompanying test questions). To properly analyze and answer the questions presented, the candidate must refer to the information provided in the patient profile. Some questions appear in a stand-alone format and should be answered solely from the information provided in the question.

NAPLEX Blueprint

THE NAPLEX COMPETENCY STATEMENTS

All NAPLEX questions are based on competency statements that are reviewed and revised periodically. The NAPLEX Competency Statements describe the knowledge, judgment, and skills that the candidate is expected to demonstrate as an entry-level pharmacist. A complete description of the NAPLEX Competency Statements is published on the NABP website and is reproduced, with permission of NABP. A strong understanding of the Competency Statements will aid in your preparation to take the examination.

Area 1 Assess Pharmacotherapy to Assure Safe and Effective Therapeutic Outcomes (Approximately 56% of Test)

- **1.1.0** Identify, interpret, and evaluate patient information to determine the presence of a disease or medical condition, assess the need for treatment and/or referral, and identify patient-specific factors that affect health, pharmacotherapy, and/or disease management.
- **1.1.1** Identify and assess patient information including medication, laboratory, and disease state histories.
- **1.1.2** Identify patient-specific assessment and diagnostic methods, instruments, and techniques and interpret their results.
- **1.1.3** Identify and define the etiology, terminology, signs, and symptoms associated with diseases and medical conditions and their causes and determine if medical referral is necessary.
- **1.1.4** Identify and evaluate patient genetic, biosocial factors, and concurrent drug therapy relevant to the maintenance of wellness and the prevention or treatment of a disease or medical condition.
- **1.2.0** Evaluate information about pharmacoeconomic factors, dosing regimen, dosage forms, delivery systems and routes of administration to identify and select optimal pharmacotherapeutic agents for patients.
- **1.2.1** Identify specific uses and indications for drug products and recommend drugs of choice for specific diseases or medical conditions.
- **1.2.2** Identify the chemical/pharmacologic classes of therapeutic agents and describe their known or postulated sites and mechanisms of action.
- **1.2.3** Evaluate drug therapy for the presence of pharmacotherapeutic duplications and interactions with other drugs, food, and diagnostic tests.
- **1.2.4** Identify and evaluate potential contraindications and provide information about warnings and precautions associated with a drug product's active and inactive ingredients.
- **1.2.5** Identify physicochemical properties of drug substances that affect their solubility, pharmacodynamic and pharmacokinetic properties, pharmacologic actions, and stability.
- **1.2.6** Evaluate and interpret pharmacodynamic and pharmacokinetic principles to calculate and determine appropriate drug dosing regimens.
- **1.2.7** Identify appropriate routes of administration, dosage forms, and pharmaceutical characteristics of drug dosage forms and delivery systems to assure bioavailability and enhance therapeutic efficacy.
- **1.3.0** Evaluate and manage drug regimens by monitoring and assessing the patient and/or patient information, collaborating with other health care professionals, and providing patient education to enhance safe, effective, and economic patient outcomes.
- **1.3.1** Identify pharmacotherapeutic outcomes and end points.
- **1.3.2** Evaluate patient signs and symptoms and the findings of monitoring tests and procedures to determine the safety and effectiveness of pharmacotherapy. Recommend needed follow-up evaluations or tests when appropriate.
- **1.3.3** Identify, describe, and provide information regarding the mechanism of adverse reactions, allergies, side effects, iatrogenic, and drug-induced illness, including their management and prevention.

- **1.3.4** Identify, prevent, and address methods to remedy medication nonadherence, misuse, or abuse.
- **1.3.5** Evaluate current drug regimens and recommend pharmacotherapeutic alternatives or modifications.

Area 2 Assess Safe and Accurate Preparation and Dispensing of Medications (Approximately 33% of Test)

- **2.1.0** Demonstrate the ability to perform calculations required to compound, dispense, and administer medication.
- **2.1.1** Calculate the quantity of medication to be compounded or dispensed; reduce and enlarge formulation quantities and calculate the quantity or ingredients needed to compound the proper amount of the preparation.
- **2.1.2** Calculate nutritional needs and the caloric content of nutrient sources.
- **2.1.3** Calculate the rate of drug administration.
- **2.1.4** Calculate or convert drug concentrations, ratio strengths, and/or extent of ionization.
- **2.2.0** Demonstrate the ability to select and dispense medications in a manner that promotes safe and effective use.
- **2.2.1** Identify drug products by their generic, brand, and/or common names.
- **2.2.2** Identify whether a particular drug dosage strength or dosage form is commercially available and whether it is available on a nonprescription basis.
- **2.2.3** Identify commercially available drug products by their characteristic physical attributes.
- **2.2.4** Assess pharmacokinetic parameters and quality assurance data to determine equivalence among manufactured drug products, and identify products for which documented evidence of inequivalence exists.
- **2.2.5** Identify and provide information regarding appropriate packaging, storage, handling, administration, and disposal of medications.
- **2.2.6** Identify and provide information regarding the appropriate use of equipment and apparatus required to administer medications.
- **2.3.0** Demonstrate the knowledge to prepare and compound extemporaneous preparations and sterile products.
- **2.3.1** Identify techniques, procedures, and equipment related to drug preparation, compounding, and quality assurance.
- **2.3.2** Identify the important physicochemical properties of a preparation's active and inactive ingredients.
- **2.3.3** Identify the mechanism of and evidence for the incompatibility or degradation of a product or preparation and methods for achieving its stability.

Area 3 Assess, Recommend, and Provide Health Care Information that Promotes Public Health (Approximately 11% of Test)

- **3.1.0** Identify, evaluate, and apply information to promote optimal health care.
- **3.1.1** Identify the typical content of specific sources of drug and health information for both health care providers and consumers, and recommend appropriate resources to address questions or needs.
- **3.1.2** Evaluate the suitability, accuracy, and reliability of clinical and pharmacoeconomic data by analyzing experimental design, statistical tests, interpreting results, and formulating conclusions.
- **3.2.0** Recommend and provide information to educate the public and health care professionals regarding medical conditions, wellness, dietary supplements, and medical devices.
- **3.2.1** Recommend and provide health care information regarding the prevention and treatment of diseases and medical conditions, including emergency patient care and vaccinations.
- **3.2.2** Recommend and provide health care information regarding nutrition, lifestyle, and other nondrug measures that promote health or prevent the progression of a disease or medical condition.
- **3.2.3** Recommend and provide information regarding the documented uses, adverse effects, and toxicities of dietary supplements.
- **3.2.4** Recommend and provide information regarding the selection, use, and care of medical/surgical appliances and devices, self-care products, and durable medical equipment, as well as products and techniques for self-monitoring of health status and medical conditions.

NABP offers candidates who are preparing for the NAPLEX—the Pre-NAPLEX, which is similar to the actual NAPLEX and allows candidates to gain experience in answering questions before examination day. The Pre-NAPLEX can be accessed via the Internet at the following website: http://www.nabp.net/prenaplex/. For foreign pharmacy graduates, the FPGEE Study Guide is available from NABP and includes information about the blueprint of the FPGEE, sample questions, and a list of textbooks commonly used in United States pharmacy schools.

Pharmaceutical Calculations

ROBERT B. GREENWOOD

I. FUNDAMENTALS OF MEASUREMENT AND CALCULATION.

The pharmacist is often required to perform or evaluate a variety of calculations. Many of these calculations involve the use of direct or inverse proportions. **Dimensional** (or **unit**) **analysis** and **approximation** can be useful in solving these problems. In dimensional analysis, dimensions (or units) are included with each number used in the calculation. Units common to the numerator and denominator may be canceled and the remaining units provide the units for the final answer. In approximation, each number used in the calculation is rounded to a single significant digit. Factors common to the numerator and denominator may be canceled, and the answer to this approximation should be reasonably close to the final exact answer.

A. Ratio and proportion

1. **Ratio**. The relative magnitude of two like quantities is a ratio, which is expressed as a fraction. Certain basic principles apply to the ratio, as they do to all fractions.
   - **a.** When the two terms of a ratio are multiplied or divided by the same number, the value of the ratio is unchanged.

$$\frac{1}{3} \times \frac{2}{2} = \frac{2}{6} = \frac{1}{3}$$

   - **b.** Two ratios with the same value are equivalent. Equivalent ratios have equal cross products and equal reciprocals. For example:

$$\frac{1}{3} = \frac{2}{6}$$

and

$$1 \times 6 = 3 \times 2 = 6$$

If two ratios are equal, then their reciprocals are equal:

$$\text{if } \frac{1}{3} = \frac{2}{6}\text{, then } \frac{3}{1} = \frac{6}{2}$$

2. **Proportion**. The expression of the equality of two ratios is a proportion. The product of the extremes is equal to the product of the means for any proportion. The way to express this, from the example cited, would be 1:3 = 2:6, where the means are 3 and 2, and the extremes are 1 and 6. Furthermore, the numerator of the one fraction equals the product of its denominator and the other fraction (i.e., one missing term can always be found given the other three terms). Most pharmaceutical calculations can be performed by use of proportion.
   - **a. Proper ratios**. Some pharmacists use proper ratios (in which similar units are used in the numerator and denominator of each ratio) in their proportion calculations. Several examples follow:
     - **(1)** If 240 mL of a cough syrup contains 480 mg of dextromethorphan hydrobromide, then what mass of drug is contained in a child's dose, 1 teaspoon (5 mL) of syrup?

$$\frac{240 \text{ mL}}{5 \text{ mL}} = \frac{480 \text{ mg}}{x \text{ mg}}$$

$$x = \frac{480 \times 5}{240} = 10 \text{ mg}$$

(2) If a child's dose (5 mL) of a cough syrup contains 10 mg of dextromethorphan hydrobromide, what mass of drug is contained in 240 mL?

$$\frac{240 \text{ mL}}{5 \text{ mL}} = \frac{x \text{ mg}}{10 \text{ mg}}$$

$$x = \frac{240 \times 10}{5} = 480 \text{ mg}$$

(3) If the amount of dextromethorphan hydrobromide in 240 mL of cough syrup is 480 mg, what would be the volume required for a child's dose of 10 mg?

$$\frac{x \text{ mL}}{240 \text{ mL}} = \frac{10 \text{ mg}}{480 \text{ mg}}$$

$$x = \frac{10 \times 240}{480} = 5\text{mL}$$

(4) How many milligrams of dextromethorphan base (molecular weight = 271.4) are equivalent to 10 mg of dextromethorphan hydrobromide (molecular weight = 352.3)?

$$\frac{x \text{ mg}}{10 \text{ mg}} = \frac{271.4}{352.3}$$

$$x = 10 \times \frac{271.4}{352.3} = 7.7 \text{ mg}$$

b. Mixed ratios. Some pharmacists use mixed ratios (in which dissimilar units are used in the numerator and denominator of each ratio) in their proportion calculations. Such computations generally give correct answers, providing the conditions in which mixed ratios cannot be used are known. A later example shows mixed ratios leading to failure in the case of dilution, when inverse proportions are required. For **inverse proportions**, similar units must be used in the numerator and denominator of each ratio. Following is an example of a mixed ratio calculation using the previous problem.

$$\frac{480 \text{ mg}}{10 \text{ mL}} = \frac{240 \text{ mg}}{x \text{ mL}}$$

$$x = 240 \times \frac{10}{480} = 5 \text{ mL}$$

The **same answer** is obtained in this example whether we use proper ratios, with similar units in numerator and denominator, or mixed ratios. This is not the case when dealing with inverse proportions.

3. **Inverse proportion**. The most common example of the need for inverse proportion for the pharmacist is the case of **dilution**. Whereas in the previous examples of proportion the relationships involved direct proportion, the case of dilution calls for an inverse proportion (i.e., as volume increases, concentration decreases). The necessity of using inverse proportions for dilution problems is shown in this example.

If 120 mL of a 10% stock solution is diluted to 240 mL, what is the final concentration? Using inverse proportion,

$$\frac{120 \text{ mL}}{240 \text{ mL}} = \frac{x\%}{10\%}$$

$$120 \times \frac{10}{240} = 5\%$$

As expected, the final concentration is one-half of the original concentration because the volume is doubled. However, if the pharmacist attempts to use direct proportion and neglects to estimate an appropriate answer, the resulting calculation would provide an answer of 20%, which is twice the actual concentration.

$$\frac{120 \text{ mL}}{240 \text{ mL}} = \frac{10\%}{x\%}$$

$$240 \times \frac{10}{120} = 20\% \text{ (incorrect answer)}$$

Likewise, the pharmacist using mixed ratios fails in this case

$$\frac{120\text{ mL}}{10\%} = \frac{240\text{ mL}}{x\%}$$

and

$$10 \times \frac{240}{120} = 20\%\text{ (again, incorrect answer)}$$

B. Aliquot. A pharmacist requires the aliquot method of measurement when the **sensitivity** (the smallest quantity that can be measured with the required accuracy and precision) of the measuring device is not great enough for the required measurement. Aliquot calculations can be used for measurement of solids or liquids, allowing the pharmacist to realize the required precision through a process of measuring a multiple of the desired amount, followed by dilution, and finally selection and measurement of an aliquot part that contains the desired amount of material. This example problem involves weighing by the aliquot method, using a prescription balance.

A prescription balance has a sensitivity requirement of 6 mg. How would you weigh 10 mg of drug with an accuracy of ± 5% using a suitable diluent?

1. First, calculate the least weighable quantity for the balance with a sensitivity requirement of 6 mg, assuming ± 5% accuracy is required.

$$\frac{6\text{ mg}}{x\text{ mg}} = \frac{5\%}{100\%};\ x = 120\text{ mg (least weighable quantity for our balance)}$$

2. Now it is obvious that an aliquot calculation is required because 10 mg of drug is required, whereas the least weighable quantity is 120 mg to achieve the required percentage of error. Using the least weighable quantity method of aliquot measurement, use the smallest quantity weighable on the balance at each step to preserve materials.
   - **a.** Weigh 12 × 10 mg = 120 mg of drug.
   - **b.** Dilute the 120 mg of drug (from step **a**) with a suitable diluent by geometrical dilution to achieve a mixture that will provide 10 mg of drug in each 120-mg aliquot. The amount of diluent to be used can be determined through **proportion**.

$$\frac{120\text{ mg drug}}{10\text{ mg drug}} = \frac{x\text{ mg total mixture}}{120\text{ mg aliquot mixture}}$$

$$x = 1440\text{ mg total mixture}$$

$$1440\text{ mg total} - 120\text{ mg drug} = 1320\text{ mg diluent}$$

   - **c.** Weigh 120 mg (1/12) of the total mixture of 1440 mg that will contain the required 10 mg of drug, which is 1/12 of the 120 mg.

II. SYSTEMS OF MEASURE.

The pharmacist must be familiar with **three systems** of measure: the **metric system** and two common systems of measure (the **avoirdupois** and **apothecaries'** systems). The primary system of measure in pharmacy and medicine is the metric system. Most students find it easiest to convert measurements in the common systems to metric units. A table of conversion equivalents is provided and should be memorized by the pharmacist (see Appendix B). The metric system, because of its universal acceptance and broad use, will not be reviewed here.

A. Apothecaries' system of fluid measure. The apothecaries' system of fluid measure is summarized in Appendix B.

B. Apothecaries' system for measuring weight. The apothecaries' system for measuring weight includes units of grains, scruples, drams, ounces, and pounds (see Appendix B).

C. Avoirdupois system of measuring weight. The avoirdupois (AV) system of measuring weight includes the grain, ounce, and pound. The grain is a unit common with the apothecaries' system and allows for easy conversion between the systems. The avoirdupois pound, however, is 16 AV ounces in contrast to the apothecaries' pound that is 12 apothecaries' ounces (see Appendix B).

D. Conversion equivalents. See Appendix B.

III. REDUCING AND ENLARGING FORMULAS.

The pharmacist is often required to reduce or enlarge a recipe. Problems of this type are solved through proportion or by multiplication or division by the appropriate factor to obtain the required amount of each ingredient that will give the desired total mass or volume of the formula. Formulas can be provided in amounts or in parts.

A. Formulas that indicate parts. When dealing with formulas that specify parts, parts by weight will require the determination of weights of ingredients, whereas parts by volume warrant the calculation of volumes of ingredients. Always find the total number of parts indicated in the formula and equate that total with the total mass or volume of the desired formula in order to set up a proportion. Such a proportion will allow calculation of the mass or volume of each ingredient in units common to the total mass or volume.

What quantities should be used to prepare 100 g of "Diaper paste" from the following formula?

R_x	mineral oil	6 parts
	nystatin powder	1 part
	hydrocortisone powder	2 parts
	zinc oxide ointment	200 parts

Label: diaper paste, maximum 1 year expiration

Total number of parts = 200 + 2 + 1 + 6 = 209 parts

For each of the ingredients, the ratio is then set up, such as

$$\frac{6 \text{ parts}}{209 \text{ parts}} = \frac{x \text{ g}}{100 \text{ g}}, \text{ with } x = 2.87 \text{ g for mineral oil or}$$

$$\frac{1 \text{ part}}{209 \text{ parts}} = \frac{y \text{ g}}{100 \text{ g}}, \text{ with } y = 0.48 \text{ g for nystatin powder}$$

B. Formulas that indicate quantities. The following prescription for cold cream provides a 100-g quantity.

What mass of each ingredient is required to provide 1 lb (AV) of cream?

R_x	white wax	12.5 g
	mineral oil	60.0 g
	lanolin	2.5 g
	sodium borate	1.0 g
	rose water	24.0 g

1 lb = 454 g

$\frac{454}{100}$ = 4.54 (multiplication factor to use in calculating the quantities of each ingredient)

$$12.5 \text{ g} \times 4.54 = 56.8 \text{ g of white wax}$$
$$60.0 \text{ g} \times 4.54 = 272 \text{ g of mineral oil}$$
$$2.5 \text{ g} \times 4.54 = 11.4 \text{ g of lanolin}$$
$$1.0 \text{ g} \times 4.54 = 4.54 \text{ g of sodium borate}$$
$$24.0 \text{ g} \times 4.54 = 109 \text{ g of rose water}$$

IV. CALCULATING DOSES.

Calculation of doses generally can be performed with dimensional analysis. **Problems** encountered in the pharmacy include calculation of the number of doses, quantities in a dose or total mass/volume, amount of active or inactive ingredients, and size of dose. Calculation of **children's doses** is commonly performed by the pharmacist. Dosage is optimally calculated by using the child's body weight or mass and the appropriate dose in milligrams per kilogram (mg/kg). Without these data, the following formulas based on an adult dose can be used.

A. Fried's rule for infants

$$\frac{\text{age (in months)} \times \text{adult dose}}{150} = \text{dose for infant}$$

B. Clark's rule

$$\frac{\text{weight (lb)} \times \text{adult dose}}{\text{150 lb (avg wt of adult)}} = \text{dose for child}$$

C. Child's dosage based on body surface area (BSA)

$$\frac{\text{BSA of child (m}^2\text{)} \times \text{adult dose}}{1.73\ \text{m}^2\ \text{(avg adult BSA)}} = \text{approximate dose for child}$$

D. Young's rule for children 2 years old or older

$$\frac{\text{age (in years)}}{\text{age (in years)} + 12} \times \text{adult dose} = \text{dose for child}$$

E. Constant rate intravenous infusions. Some drugs are administered intravenously at a constant (zero-order) rate by using a continuous-drip infusion set or a constant-rate infusion pump. The flow rate (volume per unit time) required can be calculated from the volume to be administered and the duration of the infusion. The rate of drug administration can be calculated from the concentration of drug in the infused solution and the flow rate of the infusion set or pump. Conversion factors may be required to obtain the final answer in the correct units (drops per minute or milliliters per hour).

A vancomycin solution containing 1000 mg of vancomycin hydrochloride diluted to 250 mL with D_5W is to be infused at a constant rate with a continuous-drip intravenous infusion set that delivers 25 drops/mL. **What flow rate (drops per minute) should be used to infuse all 250 mL of the vancomycin hydrochloride solution in 2 hrs?**

$$\frac{250\ \text{mL}}{2\ \text{hrs}} \times \frac{1\ \text{hr}}{60\ \text{mins}} \times \frac{25\ \text{drops}}{1\ \text{mL}} = 52\ \text{drops/min}$$

V. PERCENTAGE, RATIO STRENGTH, AND OTHER CONCENTRATION EXPRESSIONS

A. Percentage weight in volume (w/v)

1. **Definition.** Percentage, indicating parts per hundred, is an important means of expressing concentration in pharmacy practice. Percentage w/v indicates the number of grams of a constituent per 100 mL of solution or liquid formulation. The pharmacist may be required to perform **three types** of calculations: determine the **weight** of active ingredient in a certain volume when given the percentage strength, determine the **percentage w/v** when the weight of substance and volume of liquid formulation are known, and determine the **volume** of liquid mixture when the percentage strength and amount of substance are known.
2. **Tolu balsam syrup (from the National Formulary).** Tolu balsam tincture contains 20% w/v tolu balsam.

   What is the percentage concentration of tolu balsam in the syrup from the formula shown in the following?

tolu balsam tincture	50 mL
magnesium carbonate	10 g
sucrose	820 g
purified water, q.s. a.d.	1000 mL

   a. First, determine what the amount of tolu balsam is contained in the 50 mL quantity of tincture used for the syrup. Then, by proportion, calculate the concentration of tolu balsam in the syrup.

$$\text{tolu balsam tincture} = 50\ \text{mL} \times \frac{20\ \text{g}}{100\ \text{mL}} = 10\ \text{g tolu balsam}$$

$$\frac{10\ \text{g}}{1000\ \text{mL}} = \frac{x\ \text{g}}{100\ \text{mL}}\ ;\ x = \frac{1\ \text{g}}{100\ \text{mL}} = 1\%\ \text{tolu balsam in the syrup}$$

In answering this one question, the first two types of problems listed beforehand have been solved, while exhibiting two methods of solving percentage problems—namely, by **dimensional analysis** and **proportion**.

b. For an example of the **third type** of percentage w/v problem, determine what volume of syrup could be prepared if we had only 8 g of magnesium carbonate. Use proportion to find the total volume of syrup that can be made using only 8 g of magnesium carbonate. If we have 10 g of magnesium carbonate in 1000 mL of solution, then, according to the recipe, 800 mL of solution can be prepared using all 8 g of the drug.

$$\frac{10\text{ g}}{1000\text{ mL}} = \frac{8\text{ g}}{x\text{ mL}};\ x = 800\text{ mL}$$

B. Percentage volume in volume (v/v). Percentage v/v indicates the number of milliliters of a constituent in 100 mL of liquid formulation. The percentage strength of mixtures of liquids in liquids is indicated by percentage v/v, which indicates the parts by volume of a substance in 100 parts of the liquid preparation. The **three types** of problems that are encountered involve calculating **percentage strength**, calculating **volume of ingredient**, and calculating **volume of the liquid preparation**. Using the same tolu balsam syrup formula from earlier, we'll now work a percentage v/v problem.

What is the percentage strength v/v of the tolu balsam tincture in the syrup preparation? By proportion, we can solve the problem in one step.

$$\frac{50\text{ mL tolu balsam tincture}}{x\text{ mL tolu balsam tincture}} = \frac{1000\text{ mL syrup}}{100\text{ mL syrup}};\ x = 5\%$$

C. Percentage weight in weight (w/w). Percentage w/w indicates the number of grams of a constituent per 100 g of formulation (solid or liquid). Solution of problems involving percentage w/w is straightforward when the total mass of the mixture is available or when the total mass can be determined from the available data. In calculations similar to those for percentage w/v and v/v, the pharmacist might need to solve several types of problems, including determination of the weight of a constituent, the total weight of a mixture, or the percentage w/w.

1. How many grams of drug substance should be used to prepare 240 g of a 5% w/w solution in water?

a. The first step in any percentage w/w problem is to attempt identification of the total mass of the mixture. In this problem, the total mass is, obviously, provided (240 g).

b. The problem can be easily solved through **dimensional analysis**.

$$240\text{ g mixture} \times \frac{5.0\text{ g drug}}{100\text{ g drug}} = 12\text{ g}$$

2. When the total mass of the mixture is unavailable or cannot be determined, an **extra step** is required in the calculations. Because it is usually impossible to know how much volume is displaced by a solid material, the pharmacist is unable to prepare a specified volume of a solution given the percentage w/w.

How much drug should be added to 30 mL of water to make a 10% w/w solution? The volume of water that is displaced by the drug is unknown, so the final volume is unknown. Likewise, even though the mass of solvent is known (30 mL × 1 g/mL = 30 g), it is not known how much drug is needed, so the total mass is unknown. The water represents 100% − 10% = 90% of the total mixture. Then, by proportion, the mass of drug to be used can be identified.

$$\frac{30\text{ g of mixture (water)}}{x\text{ g of mixture (drug)}} = \frac{90\%}{10\%};\ x = 3.33\text{ g of drug required to make a solution}$$

The **common error** that many students make in solving problems of this type is to assume that 30 g is the total mass of the mixture. Solving the problem with that assumption gives the following incorrect answer.

$$\frac{x\text{ g drug}}{10\text{ g drug}} = \frac{30\text{ g mixture}}{100\text{ g mixture}};\ x = 3\text{ g of drug (incorrect answer)}$$

D. Ratio strength. Solid or liquid formulations that contain low concentrations of active ingredients will often have concentration expressed in **ratio strength**. Ratio strength, as the name implies, is the expression of concentration by means of a ratio. The numerator and denominator of the ratio indicate grams (g) or milliliters (mL) of a solid or liquid constituent in the total mass (g) or volume (mL) of a solid or liquid preparation. Because **percentage strength** is essentially a ratio of parts per hundred, conversion between ratio strength and percentage strength is easily accomplished by proportion.

1. **Express 0.1% w/v as a ratio strength.**
   a. Ratio strengths are by convention expressed in reduced form, so in setting up our proportion to solve for ratio strength, use the numeral 1 in the numerator of the right-hand ratio as shown:

$$\frac{0.1\text{ g}}{100\text{ mL}} = \frac{1\text{ part}}{x\text{ parts}};\ = 1000\text{ parts, for ratio strength of 1:1000}$$

   b. Likewise, conversion from ratio strength to percentage strength by proportion is easy, as seen in the following example. Keep in mind the definition of percentage strength (parts per hundred) when setting up the proportion.
2. **Express 1:2500 as a percentage strength.**

$$\frac{1\text{ part}}{2500\text{ parts}} = \frac{x\text{ parts}}{100\text{ parts}};\ x = 0.04\text{, indicating } 0.04\%$$

E. Other concentration expressions

1. **Molarity** (M) is the expression of the number of moles of solute dissolved per liter of solution. It is calculated by dividing the moles of solute by the volume of solution in liters.

$$M_A = \frac{n_A}{\text{solution (L)}}$$

2. **Normality.** A convenient way of dealing with acids, bases, and electrolytes involves the use of equivalents. One equivalent of an acid is the quantity of that acid that supplies or donates 1 mole of H^+ ions. One equivalent of a base is the quantity that furnishes 1 mole of OH^- ions. One equivalent of acid reacts with one equivalent of base. Equivalent weight can be calculated for atoms or molecules.

$$\text{Equivalent weight} = \frac{\text{atomic weight or molecular weight}}{\text{valence}}$$

   The **normality** (N) of a solution is the number of gram-equivalent weights (equivalents) of solute per liter of solution. Normality is analogous to molarity; however, it is defined in terms of equivalents rather than moles.

$$\text{Normality} = \frac{\#\text{ equivalents of solute}}{\#\text{ liters of solution}}$$

3. **Molality** (m) is the moles of solute dissolved per kilogram of solvent. Molality is calculated by dividing the number of moles of solute by the number of kilograms of solvent. Molality offers an advantage over molarity because it is based on solvent weight and avoids problems associated with volume expansion or contraction owing to the addition of solutes or from a change in temperature.

$$m_A = \frac{n_A}{\text{mass}_{\text{solvent (kg)}}}$$

4. **Mole fraction** (X) is the ratio of the number of moles of one component to the total moles of a mixture or solution.

$$X_A = \frac{n_A}{n_A, n_B, n_C \ldots},\ \text{where } X_A + X_B + X_C + \ldots = 1$$

VI. DILUTION AND CONCENTRATION.

If the amount of drug remains constant in a dilution or concentration, then any change in the mass or volume of a mixture is inversely proportional to the concentration.

A. Dilution and concentration problems can be solved by the following:

1. Inverse proportion (as mentioned earlier)
2. The equation $\text{quantity}_1 \times \text{concentration}_1 = \text{quantity}_2 \times \text{concentration}_2$

3. Determining the amount of active ingredient present in the initial mixture and, with the assumption that the initial quantity does not change, calculating the final concentration of the new total mass or volume
4. **Alligation medial.** A method for calculating the average concentration of a mixture of two or more substances
5. **Alligation alternate.** A method for calculating the number of parts of two or more components of known concentration to be mixed when the final desired concentration is known

B. Dilution of alcohols and acids

1. **Dilution of alcohols.** When alcohol and water are mixed, a contraction of volume occurs. As a result, the final volume of solution cannot be determined accurately, nor can the volume of water needed to dilute to a certain percentage v/v be identified. Accordingly, percentage w/w is often used for solutions of alcohol.
2. The **percentage strength** of concentrated acids is expressed as percentage w/w. The concentration of diluted acids is expressed as percentage w/v. Determining the volume of concentrated acid to be used in preparing a diluted acid requires the specific gravity of the concentrated acid.

C. Dilution and concentration of liquids and solids. Dilution and concentration problems are solved by identifying the amount of drug involved followed by use of an appropriate proportion.

1. **How many milliliters of a 1:50 stock solution of ephedrine sulfate should be used in compounding the following prescription?**

Rx	ephedrine sulfate	0.25%
	rose water, a.d.	30 mL

$$\frac{0.25\text{ g}}{100\text{ mL}} \times 30\text{ mL} = 0.075\text{ g drug required}$$

$$\frac{50\text{ mL}}{1\text{ g}} = \frac{x\text{ mL}}{0.075\text{ g}};$$

$$x = 3.75\text{ mL of stock solution required for prescription}$$

2. **How many milliliters of a 15% w/v concentrate of benzalkonium chloride should be used in preparing 300 mL of a stock solution such that 15 mL diluted to 1 L will yield a 1:5000 solution?**

   a. First, determine the amount of drug in 1 L of a 1:5000 solution.

$$\frac{5000\text{ mL}}{1000\text{ mL}} = \frac{1\text{ g}}{x\text{ g}}; = 0.2\text{ g of benzalkonium chloride in the final solution}$$

   b. Now, because 15 mL of the stock solution is being diluted to 1 L, a stock solution is needed in which 15 mL contain 0.2 g of drug. The amount of drug required to make 300 mL of the stock solution is found by proportion.

$$\frac{0.2\text{ g}}{x\text{ g}} = \frac{15\text{ mL}}{300\text{ mL}}; x = 4\text{ g of drug required to make 300 mL of solution}$$

   c. Finally, to determine the amount of 15% concentrate required.

$$\frac{15\text{ g}}{4\text{ g}} \times \frac{100\text{ mL}}{x\text{ mL}}; x = 26.7\text{ mL of 15\% solution required to obtain necessary drug}$$

3. When the relative amount of components must be determined for preparation of a mixture of a desired concentration, the problem can be solved using alligation alternate.

   How many grams of 2.5% hydrocortisone cream should be mixed with 360 g of 0.25% cream to make a 1% hydrocortisone cream?

2.5%		0.75 parts of 2.5% cream	= 1 part	0.75/2.25 = 1/3
	1%			
0.25%		1.5 parts of 0.25% cream	= 2 parts	1.5/2.25 = 2/3
		2.25 parts total	= 3 parts	

   The relative amounts of the 2.5% and 1% creams are 1 to 2, respectively. By proportion, the mass of 2.5% cream to use can be determined. **If 2 parts of 0.25% cream is represented by 360 g, then the total mass (3 parts) is represented by what mass?**

$$\frac{2 \text{ parts}}{3 \text{ parts}} = \frac{360 \text{ g}}{x \text{ g}}; x = 540 \text{ g total}$$

With the total mass known, the amount of 2.5% cream can be identified. If 3 parts represent the total mass of 540 g, then 1 part represents the mass of 2.5% cream (x g = 180 g).

$$\frac{1 \text{ part}}{3 \text{ parts}} = \frac{x \text{ g}}{540 \text{ g}}; x = 180 \text{ g of 2.5\% cream}$$

VII. ELECTROLYTE SOLUTIONS.

Electrolyte solutions contain species (electrolytes) that dissociate into ions. The **milliequivalent** (mEq) is the unit most frequently used to express the concentration of electrolytes in solution. *Table 1-1* exhibits some physiologically important ions and their properties.

A. Milliequivalents. The milliequivalent is the amount, in milligrams, of a solute equal to 1/1000 of its gram-equivalent weight. Conversion of concentrations in the form of milliequivalent to concentrations in percentage strength, milligrams per milliliter (mg/mL) or any other terms, begins with calculation of the number of milliequivalents of drug. The following examples demonstrate the computation of milliequivalents and manipulation of data from *Table 1-1* to perform the required calculations for preparing electrolyte solutions.

What is the concentration, in percent w/v, of a solution containing 2 mEq of potassium chloride per milliliter?

Calculations involving milliequivalents are easily solved if the practitioner follows a predefined procedure to determine the milliequivalent weight. This involves three steps.

1. Find the molecular weight (mol wt).

$$\text{Atomic wt K} = 39$$
$$\text{Atomic wt Cl} = 35.5$$
$$39 + 35.5 = 74.5 \text{ g} = \text{mol wt of KCl}$$

Table 1-1 VALENCES, ATOMIC WEIGHTS, AND MILLIEQUIVALENT WEIGHTS OF SELECTED IONS

Ion	Formula	Valence	Atomic/Formula Weight	Milliequivalent Weight (mg)
Aluminum	A^{+++}	3	27	9
Ammonium	NH_4^+	1	18	18
Calcium	Ca^{++}	2	40	20
Ferric	Fe^{+++}	3	56	18.7
Ferrous	Fe^{++}	2	56	28
Lithium	Li^+	1	7	7
Magnesium	Mg^{++}	2	24	12
Bicarbonate	HCO_3^-	1	61	61
Carbonate	CO_3^-	1	60	30
Chloride	Cl^-	1	35.5	35.5
Citrate	$C_6H_5O_7^{---}$	3	189	63
Gluconate	$C_6H_{11}O_7^-$	1	195	195
Lactate	$C_3H_5O_3^-$	1	89	89
Phosphate	$H_2PO_4^-$	1	97	97
Sulfate	SO_4^{--}	2	96	48
Potassium	K^+	1	29	39
Sodium	Na^+	1	23	23
Acetate	$C_2H_3O_2^-$	1	59	59

2. Calculate the equivalent weight (Eq wt) of KCl.

$$\text{Eq wt} = \frac{\text{mol wt}}{\text{valence}} = \frac{74.5}{1} = 74.5\text{ g}$$

3. Determine the milliequivalent weight, which is 1/1000 of the equivalent weight.

$$\text{mEq wt} = 74.5\text{ g}/1000 = 0.745\text{ g or }74.5\text{ mg}$$

Now that we know the milliequivalent weight, we can calculate by dimensional analysis and proportion the concentration in percentage in a fourth step.

4. 0.0745 g/mEq × 2 mEq = 0.149 g of drug

$$\frac{0.149\text{ g drug}}{1\text{ mL}} = \frac{x\text{ g drug}}{100\text{ mL}}; x = 14.9\text{ g}/100\text{ mL} = 14.9\%$$

How many milliequivalents of Na^+ would be contained in a 15-mL volume of the following buffer?

$Na_2HPO_4{\cdot}7H_2O$		180 g
$NaH_2PO_4{\cdot}H_2O$		480 g
Purified water	a.d.	1000 mL

For each salt, the mass (and milliequivalents) must be found in a 15-mL dose.

$$\text{mol wt } Na_2HPO_4{\cdot}7H_2O\text{ (disodium hydrogen phosphate)} = 268\text{ g}$$
$$\text{Eq wt} = 268/2 = 134\text{ g}$$
$$1\text{ mEq} = 0.134\text{ g or }134\text{ mg}$$

$$\frac{180\text{ g}}{x\text{ g}} = \frac{1000\text{ mL}}{15\text{ mL}}; x = 2.7\text{ g of disodium hydrogen phosphate in each 15 mL}$$

$$2.7\text{ g} \times \frac{1\text{ mEq}}{0.134\text{ g}} = 20.1\text{ mEq of disodium hydrogen phosphate}$$

$$\text{mol wt } NaH_2PO_4{\cdot}H_2O\text{ (sodium biphosphate)} = 138\text{ g}$$
$$\text{Eq wt} = 138\text{ g}$$
$$1\text{ mEq} = 0.138\text{ g}$$

$$\frac{480\text{ g}}{x\text{ g}} = \frac{1000\text{ mL}}{15\text{ mL}}; x = 7.2\text{ g of sodium biphosphate in each 15 mL}$$

$$7.2\text{ g} \times \frac{1\text{ mEq}}{0.138\text{ g}} = 52.2\text{ mEq of sodium biphosphate}$$

$$20.1\text{ mEq} + 52.2\text{ mEq} = 72.3\text{ mEq of sodium in each 15 mL of solution}$$

B. Milliosmoles (mOsmol). Osmotic pressure is directly proportional to the total number of particles in solution. The milliosmole is the unit of measure for osmotic concentration. For nonelectrolytes, 1 millimole represents 1 mOsmol. However, for electrolytes, the total number of particles in a solution is determined by the number of particles produced in a solution and influenced by the degree of dissociation. Assuming complete dissociation, 1 millimole of KCl represents 2 mOsmol of total particles, 1 millimole of $CaCl_2$ represents 3 mOsmol of total particles, etc. The ideal osmolar concentration can be calculated with the following equation.

$$\text{mOsmol/L} = \frac{\text{wt of substance in g/L}}{\text{mol wt in g}} \times \text{number of species} \times 1000$$

The pharmacist should recognize the difference between **ideal** osmolar concentration and **actual** osmolarity. As the concentration of solute increases, interaction between dissolved particles increases, resulting in a reduction of the actual osmolar values.

C. Isotonic solutions. An **isotonic** solution is one that has the same osmotic pressure as body fluids. **Isosmotic** fluids are fluids with the same osmotic pressure. Solutions to be administered to patients should be isosmotic with body fluids. A **hypotonic** solution is one with a lower osmotic pressure than body fluids, whereas a **hypertonic** solution has an osmotic pressure that is greater than body fluids.

1. **Preparation of isotonic solutions.** Colligative properties, including freezing point depression, are representative of the number of particles in a solution and are considered in preparation of isotonic solutions.
   a. When 1 g mol wt of any nonelectrolyte is dissolved in 1000 g of water, the freezing point of the solution is depressed by 1.86°C. By proportion, the weight of any nonelectrolyte needed to make the solution isotonic with body fluid can be calculated.
   b. Boric acid (H_3BO_3) has a mol wt of 61.8 g. Thus, 61.8 g of H_3BO_3 in 1000 g of water should produce a freezing point of 1.86°C. Therefore, knowing that the freezing point depression of body fluids is −0.52°C,

$$\frac{-1.86°\text{C}}{-0.52°\text{C}} = \frac{61.8\text{ g}}{x\text{ g}};\ x = 17.3\text{ g}$$

   and 17.3 g of H_3BO_3 in 1000 g of water provides a solution that is **isotonic**.
   c. The degree of dissociation of electrolytes must be taken into account in such calculations. For example, NaCl is approximately 80% dissociated in weak solutions, yielding 180 particles in a solution for each 100 molecules of NaCl. Therefore,

$$\frac{-1.86°\text{C} \times 1.8}{-0.52°\text{C}} = \frac{58\text{ g}}{x\text{ g}};\ x = 9.09\text{ g}$$

   indicating that 9.09 g of NaCl in 1000 g of water (0.9% w/v) should make a solution isotonic. Lacking any information on the degree of dissociation of an electrolyte, the following **dissociation values** (i) may be used:
   (1) Substances that dissociate into two ions: 1.8
   (2) Substances that dissociate into three ions: 2.6
   (3) Substances that dissociate into four ions: 3.4
   (4) Substances that dissociate into five ions: 4.2

2. **Sodium chloride equivalents.** The pharmacist will often be required to prepare an isotonic solution by adding an appropriate amount of another substance (drug or inert electrolyte or nonelectrolyte). Considering that isotonic fluids contain the equivalent of 0.9% NaCl, the question arises, how much of the added ingredient is required to make the solution isotonic? A **common method** for computing the amount of added ingredient to use for reaching isotonicity involves the use of **sodium chloride equivalents**.
   a. **Definition.** The sodium chloride equivalent represents the amount of NaCl that is equivalent to the amount of particular drug in question. For every substance, there is one quantity that should have a constant tonic effect when dissolved in 1000 g of water. This is 1 g mol wt of the substance divided by its dissociation value (i).
   b. **Examples**
   (1) Considering H_3BO_3, from the last section, 17.3 g of H_3BO_3 is equivalent to 0.52 g of NaCl in tonicity. Therefore, the relative quantity of NaCl that is equivalent to H_3BO_3 in tonicity effects is determined as follows:

$$\frac{\text{mol wt of NaCl}/i\text{ value}}{\text{mol wt of }H_3BO_3/i\text{ value}} = \frac{58.5/1.8}{61.8/1.0}$$

   Applying this method to atropine sulfate, recall that the molecular weight of NaCl and the molecular weight of atropine sulfate are 58.5 and 695 g, respectively, and their i values are 1.8 and 2.6, respectively. Calculate the mass of NaCl represented by 1 g of atropine sulfate (*Table 1-2*).

$$\frac{695 \times 1.8}{58.5 \times 2.6} = \frac{1\text{ g}}{x\text{ g}};\ x = 0.12\text{ g NaCl represented by 1 g of atropine sulfate}$$

Table 1-2 SODIUM CHLORIDE (NaCl) EQUIVALENTS

Substance	NaCl Equivalent
Atropine sulfate (H_2O)	0.12
Boric acid	0.52
Chlorobutanol	0.24
Dextrose (anhydrous)	0.18
Ephedrine hydrochloride	0.29
Phenacaine hydrochloride	0.20
Potassium chloride	0.78

(2) An example of the practical use of sodium chloride equivalents is seen in the following problem:

How many grams of boric acid should be used in compounding the following prescription?

Rx	phenacaine hydrochloride	1%
	chlorobutanol	0.5%
	boric acid	q.s.
	purified water, a.d.	60.0 mL
	make isotonic solution	

The prescription calls for 0.3 g of chlorobutanol and 0.6 g of phenacaine. How much boric acid is required to prepare this prescription? The question is best answered in four steps:

(a) Find the mass of sodium chloride represented by all ingredients.

$0.20 \times 0.6 = 0.120$ g of sodium choloride represented by phenacaine hydrochloride

$0.24 \times 0.3 = \underline{0.072 \text{ g}}$ of sodium chloride represented by chlorobutanol

0.192 g of sodium chloride represented by the two active ingredients

(b) Find the mass of sodium chloride required to prepare an equal volume of isotonic solution.

$$\frac{0.9 \text{ g NaCl}}{100 \text{ mL}} = \frac{x \text{ g NaCL}}{60 \text{ mL}}; x = 0.540 \text{ g of sodium chloride}$$

in 60 mL of an isotonic sodium chloride solution

(c) Calculate, by subtraction, the amount of NaCl required to make the solution isotonic.

0.540 g NaCl required for isotonicity
$\underline{0.192 \text{ g}}$ NaCl represented by ingredients
0.348 g NaCl required to make isotonic solution

(d) Because the prescription calls for boric acid to be used, one last step is required

$$\frac{0.348 \text{ g}}{0.52} \text{ (sodium chloride equivalent for boric acid)} = 0.669 \text{ g of boric acid to be used}$$

Study Questions

Directions for questions 1–30: Each question, statement, or incomplete statement in this section can be correctly answered or completed by **one** of the suggested answers or phrases. Choose the **best** answer.

1. If a vitamin solution contains 0.5 mg of fluoride ion in each milliliter, then how many milligrams of fluoride ion would be provided by a dropper that delivers 0.6 mL?

(A) 0.30 mg
(B) 0.10 mg
(C) 1.00 mg
(D) 0.83 mg

2. How many chloramphenicol capsules, each containing 250 mg, are needed to provide 25 mg/kg/d for 7 days for a person weighing 200 lb?

(A) 90 capsules
(B) 64 capsules
(C) 13 capsules
(D) 25 capsules

3. If 3.17 kg of a drug is used to make 50000 tablets, how many milligrams will 30 tablets contain?

(A) 1.9 mg
(B) 1900 mg
(C) 0.0019 mg
(D) 3.2 mg

4. A capsule contains ⅛ gr of ephedrine sulfate, ¼ gr of theophylline, and 1/16 gr of phenobarbital. What is the total mass of the active ingredients in milligrams?

(A) 20 mg
(B) 8 mg
(C) 28 mg
(D) 4 mg

5. If 1 fluid ounce of a cough syrup contains 10 gr of sodium citrate, how many milligrams are contained in 10 mL?

(A) 650 mg
(B) 65 mg
(C) 217 mg
(D) 20 mg

6. How many capsules, each containing ¼ gr of phenobarbital, can be manufactured if a bottle containing 2 avoirdupois ounces of phenobarbital is available?

(A) 771 capsules
(B) 350 capsules
(C) 3500 capsules
(D) 1250 capsules

7. Using the formula for calamine lotion, determine the amount of calamine (in grams) necessary to prepare 240 mL of lotion.

calamine	80 g
zinc oxide	80 g
glycerin	20 mL
bentonite magma	250 mL
calcium hydroxide topical solution	sufficient quantity to make 1000 mL

(A) 19.2 g
(B) 140.0 g
(C) 100.0 g
(D) 24.0 g

8. From the following formula, calculate the amount of white wax required to make 1 lb of cold cream. Determine the mass in grams.

cetyl esters wax	12.5 parts
white wax	12.0 parts
mineral oil	56.0 parts
sodium borate	0.5 parts
purified water	19.0 parts

(A) 56.75 g
(B) 254.24 g
(C) 54.48 g
(D) 86.26 g

9. How many grams of aspirin should be used to prepare 1.255 kg of the powder?

Aspirin	6 parts
phenacetin	3 parts
caffeine	1 part

(A) 125 g
(B) 750 g
(C) 175 g
(D) 360 g

10. A solution contains 1.25 mg of a drug per milliliter. At what rate should the solution be infused (drops per minute) if the drug is to be administered at a rate of 80 mg/hr? (1 mL = 30 drops)

(A) 64.00 drops/min
(B) 1.06 drops/min
(C) 32.00 drops/min
(D) 20.00 drops/min

11. The recommended maintenance dose of aminophylline for children is 1.0 mg/kg/hr by injection. If 10 mL of a 25-mg/mL solution of aminophylline is added to a 100-mL bottle of 5% dextrose, what should be the rate of delivery in mL/hr for a 40-lb child?

(A) 2.30 mL/hr
(B) 8.00 mL/hr
(C) 18.90 mL/hr
(D) 18.20 mL/hr

12. For children, streptomycin is to be administered at a dose of 30 mg/kg of body weight daily in divided doses every 6 to 12 hrs. The dry powder is dissolved by adding water for injection, in an amount to yield the desired concentration as indicated in the following table (for a 1-g vial).

Approximate Concentration (mg/mL)	Volume (mL)
200	4.2
250	3.2
400	1.8

Reconstituting at the lowest possible concentration, what volume (in mL) would be withdrawn to obtain a day's dose for a 50-lb child?

(A) 3.40 mL
(B) 22.73 mL
(C) 2.50 mL
(D) 2.27 mL

13. The atropine sulfate is available only in the form of 1/150 gr tablets. How many atropine sulfate tablets would you use to compound the following prescription?

atropine sulfate	1/200 gr
codeine phosphate	¼ gr
aspirin	5 gr
d.t.d.	#24 capsules
Sig:	1 capsule p.r.n.

(A) 3 tablets
(B) 6 tablets
(C) 12 tablets
(D) 18 tablets

14. In 25.0 mL of a solution for injection, there are 4.00 mg of the drug. If the dose to be administered to a patient is 200 μg, what quantity (in mL) of this solution should be used?

(A) 1.25 mL
(B) 125.00 mL
(C) 12.00 mL
(D) None of the above

15. How many milligrams of papaverine will the patient receive each day?

R_x	papaverine hcl	1.0 g
	aqua	30.0 mL
	syrup tolu, q.s. a.d.	90.0 mL
	Sig:	1 teaspoon t.i.d.

(A) 56.0 mg
(B) 5.6 mg
(C) 166.0 mg
(D) 2.5 mg

16. Considering the following formula, how many grams of sodium bromide should be used in filling this prescription?

R_x	sodium bromide	1.2 g
	syrup tolu	2.0 mL
	syrup wild cherry, q.s. a.d.	5.0 mL
	d.t.d.	#24

(A) 1.2 g
(B) 1200.0 g
(C) 28.8 g
(D) 220.0 g

17. How many milliliters of a 7.5% stock solution of $KMnO_4$ should be used to obtain the KMnO needed?

$KMnO_4$, q.s.
Distilled water, a.d. 1000 mL
Sig: 2 teaspoons diluted to 500 mL yield a 1:5000 solution

(A) 267.0 mL
(B) 133.0 mL
(C) 26.7 mL
(D) 13.3 mL

18. The formula for Ringer's solution follows. How much sodium chloride is needed to make 120 mL?

R_x	sodium chloride	8.60 g
	potassium chloride	0.30 g
	calcium chloride	0.33 g
	water for injection, q.s. a.d.	1000 mL

(A) 120.00 g
(B) 1.03 g
(C) 0.12 g
(D) 103.00 g

19. How many grams of talc should be added to 1 lb of a powder containing 20 g of zinc undecylenate per 100 g to reduce the concentration of zinc undecylenate to 3%?

(A) 3026.7 g
(B) 2572.7 g
(C) 17.0 g
(D) 257.0 g

20. How many milliliters of a 0.9% aqueous solution can be made from 20.0 g of sodium chloride?

(A) 2222 mL
(B) 100 mL
(C) 222 mL
(D) 122 mL

21. The blood of a reckless driver contains 0.1% alcohol. Express the concentration of alcohol in parts per million.

(A) 100 ppm
(B) 1000 ppm
(C) 1 ppm
(D) 250 ppm

22. Syrup is an 85% w/v solution of sucrose in water. It has a density of 1.313 g/mL. How many milliliters of water should be used to make 125 mL of syrup?

(A) 106.25 mL
(B) 164.10 mL
(C) 57.90 mL
(D) 25.00 mL

23. How many grams of benzethonium chloride should be used in preparing 5 gal of a 0.025% w/v solution?

(A) 189.25 g
(B) 18.90 g
(C) 4.73 g
(D) 35.00 g

24. How many grams of menthol should be used to prepare this prescription?

R_x	menthol	0.8%
	alcohol, q.s. a.d.	60.0 mL

(A) 0.48 g
(B) 0.80 g
(C) 4.80 g
(D) 1.48 g

25. How many milliliters of a 1:1500 solution can be made by dissolving 4.8 g of cetylpyridinium chloride in water?

(A) 7200.0 mL
(B) 7.2 mL
(C) 48.0 mL
(D) 4.8 mL

26. The manufacturer specifies that one Domeboro tablet dissolved in 1 pint of water makes a modified Burow's solution approximately equivalent to a 1:40 dilution. How many tablets should be used in preparing ½ gal of a 1:10 dilution?

(A) 16 tablets
(B) 189 tablets
(C) 12 tablets
(D) 45 tablets

27. How many milliosmoles of calcium chloride ($CaCl_2 \cdot 2H_2O$ − mol wt = 147) are represented in 147 mL of a 10% w/v calcium chloride solution?

(A) 100 mOsmol
(B) 200 mOsmol
(C) 300 mOsmol
(D) 3 mOsmol

28. How many grams of boric acid should be used in compounding the following prescription?

Phenacaine HCl 1.0% (NaCl eq = 0.17)
Chlorobutanol 0.5% (NaCl eq = 0.18)
Boric acid, q.s. (NaCl eq = 0.52)
Purified H_2O, a.d. 30 mL
Make isotonic solution
Sig: 1 drop in each eye

(A) 0.37 g
(B) 0.74 g
(C) 0.27 g
(D) 0.47 g

29. A pharmacist prepares 1 gal of KCl solution by mixing 565 g of KCl (valence = 1) in an appropriate vehicle. How many milliequivalents of K^+ are in 15 mL of this solution? (atomic weights: K = 39; Cl = 35.5)

(A) 7.5 mEq
(B) 10.0 mEq
(C) 20.0 mEq
(D) 30.0 mEq
(E) 40.0 mEq

30. A vancomycin solution containing 1000 mg of vancomycin hydrochloride diluted to 250 mL with D_5W is to be infused at a constant rate with an infusion pump in 2 hrs. What is the rate of drug administration?

(A) 2.08 mg/min
(B) 8.33 mg/min
(C) 4.17 mg/min
(D) 16.70 mg/min
(E) 5.21 mg/min

Answers and Explanations

1. **The answer is A** *[see I.A.2]*.
2. **The answer is B** *[see II]*.
3. **The answer is B** *[see II]*.
4. **The answer is C** *[see II]*.
5. **The answer is C** *[see I.A.2]*.
6. **The answer is C** *[see II]*.
7. **The answer is A** *[see III]*.
8. **The answer is C** *[see II; III.A]*.
The formula tells the pharmacist that white wax (W.W.) represents 12 parts out of the total 100 parts in the prescription. What we wish to determine is the mass of white wax required to prepare 454 g (1 lb) of the recipe. This can be easily solved by proportion:

$$\frac{12 \text{ parts W.W.}}{100 \text{ parts total}} = \frac{x}{454 \text{ parts (grams)}};\ x = 54.48 \text{ g}$$

9. **The answer is B** *[see III.A]*.
10. **The answer is C** *[see IV.E]*.
11. **The answer is B** *[see II; IV]*.
12. **The answer is A** *[see IV]*.
13. **The answer is D** *[see II; III.B]*.
14. **The answer is A** *[see I.A.2; II]*.
Dimensional analysis is often useful for calculating doses. Considering that 4 mg of the drug is present in each 25 mL of solution, we can easily calculate the number of milliliters to be used to give a dose of 0.200 mg (200 μg). Always include units in your calculations.

$$\frac{25 \text{ mL}}{4 \text{ mg}} \times 0.200 \text{ mg} = 1.25 \text{ mL}$$

15. **The answer is C** *[see III.B]*.
16. **The answer is C** *[see III.B]*.
17. **The answer is B** *[see V.A; VI]*.
First, determine the mass of drug in the final diluted solution.

$$\frac{1 \text{ part}}{5000 \text{ parts}} = \frac{x \text{ g}}{500 \text{ g}};\ x = 0.1 \text{ g}$$

Now, if 0.1 g of drug is present in 500 mL of 1:5000 solution, 2 teaspoons (10 mL) of the prescription contains the same amount of drug (0.1 g) before dilution. From this, the amount of drug in 1000 mL (the total volume) of the prescription can be determined:

$$\frac{0.1 \text{ g}}{10 \text{ mL}} = \frac{x \text{ g}}{1000 \text{ mL}};\ x = 10 \text{ g}$$

Finally, to obtain the correct amount of drug to formulate the prescription (10 g), we are to use a 7.5% stock solution. Recalling the definition of percentage strength w/v

$$\frac{100 \text{ mL}}{7.5 \text{ g}} \times 10 \text{ g} = 133.3 \text{ mL or } 133 \text{ mL}$$

18. **The answer is B** *[see III.B]*.
19. **The answer is B** *[see V.C; VI.C]*.
20. **The answer is A** *[see I.A.2; V.A]*.
Using dimensional analysis

$$\frac{20 \text{ g} \times 100 \text{ mL}}{0.9 \text{ g}} = 2222 \text{ mL}$$

21. **The answer is B** *[see V.D.1]*.
22. **The answer is C** *[see I.A; V.A.1]*.
Using the density, the weight of 125 mL of syrup can be calculated:

$$125 \text{ mL} \times 1.313 \text{ g/mL} = 164.125 \text{ g}$$

Using proportion and the sucrose concentration in w/v, the weight of sucrose in 125 mL of syrup can be calculated:

$$\frac{100 \text{ mL}}{125 \text{ mL}} = \frac{85 \text{ g}}{x \text{ g}};\ x = 106.25 \text{ g}$$

Finally, the weight of water in 125 mL of syrup can be calculated:

$$164.125 \text{ g} - 106.25 \text{ g} = 57.875 \text{ g}$$

which has a volume of 57.90 mL.

23. **The answer is C** *[see I; II; V]*.
24. **The answer is A** *[see I; V]*.
25. **The answer is A** *[see I; V]*.
The problem is easily solved by proportion. The question to be answered is if 1 g of drug is present in 1500 mL of a solution, what volume can be made with 4.8 g of drug?

$$\frac{1 \text{ g}}{4.8 \text{ g}} = \frac{1500 \text{ mL}}{x \text{ mL}};\ x = 7200.0 \text{ mL}$$

(the volume of 1 to 1500 solution that can be prepared from 4.8 g of drug)

26. **The answer is A** *[see I; V]*.

27. The answer is C *[see VII.B]*.
Recalling the expression for ideal osmolar concentration:

$$\text{mOsmol/L} = \frac{100 \text{ g/L}}{147 \text{ g/mol}} \times 3 \times 1000$$
$$= \text{mOsmol/L} \times 0.147 \text{ L}$$
$$= 300 \text{ mOsmol}$$

28. The answer is A *[see VII.C]*.

29. The answer is D *[see VII.A]*.

30. The answer is B *[see IV.E]*.
Using dimensional analysis:

$$\frac{1000 \text{ mg}}{250 \text{ mL}} \times \frac{250 \text{ mL}}{2 \text{ hr}} \times \frac{1 \text{ hr}}{60 \text{ min}} = 8.33 \text{ mg/min}$$