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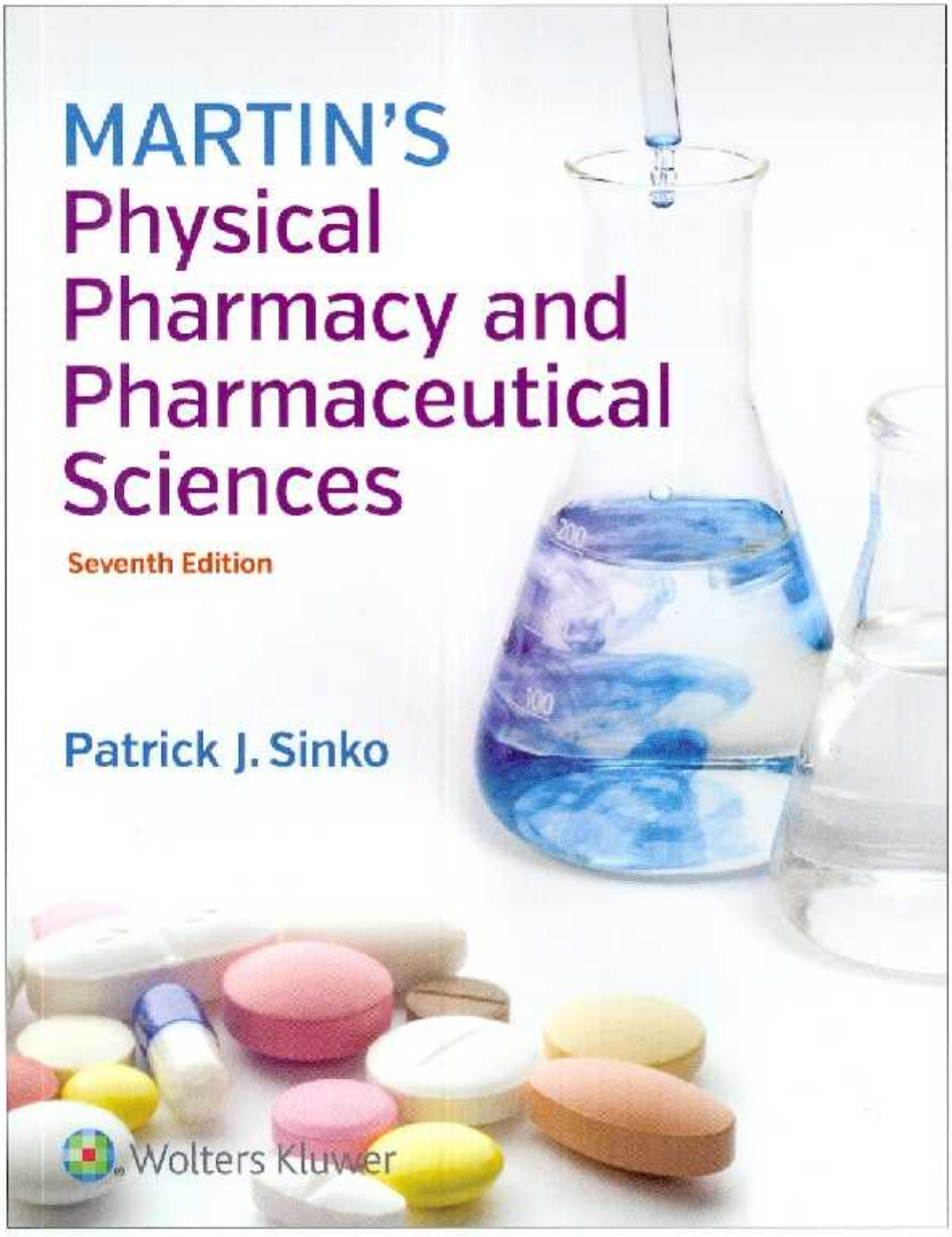

MARTIN'S Physical Pharmacy and Pharmaceutical Sciences

Seventh Edition

Patrick J. Sinko

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MARTIN'S

PHYSICAL PHARMACY AND PHARMACEUTICAL SCIENCES

Physical Chemical and Biopharmaceutical Principles in the Pharmaceutical Sciences

SEVENTH EDITION

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Preface

Pharmacy, like many other applied sciences, passed through a descriptive and empiric era. However, over the past several decades a firm scientific foundation has been developed, allowing the "art" of pharmacy to be transformed into a quantitative and mechanistic field of study. Physical pharmacy is associated with the quantitative and theoretical principles of physical chemistry as they apply to the practice of pharmacy. Physical pharmacy attempts to integrate the factual knowledge and broad principles of pharmacy in order to understand the solubility, stability, compatibility, and biologic action of drug products. With the expansion and transformation of physical pharmacy, the discipline of Pharmaceutics (sometimes known as Pharmaceutical Science) emerged. Initially Pharmaceutics focused on pharmaceutical technology—the design, formulation, manufacture and testing of dosage forms such as tablets, capsules, creams, ointments, and solutions. In recent years, Pharmaceutics has expanded since there is a need to understand how drug delivery systems perform in and respond to the normal and pathophysiologic states of the patient as well as use this knowledge to develop better drug delivery systems to improve therapy and patient outcomes.

There are two primarily target audiences for this book, students training to be pharmacists and students training to be pharmaceutical scientists. Pharmacists work with existing drug products, patients, and other healthcare practitioners to optimize patient care. Practicing pharmacists should have a thorough understanding of modern drug delivery systems as he or she advises patients on the best use of prescribed medicines. Pharmaceutical scientists develop new drugs and delivery systems and improve upon the various modes of administration to patients. While some pharmacists are also trained as pharmaceutical scientists, there are increasing numbers of biomedical, chemical, and material science engineers entering the field that are becoming pharmaceutical scientists as well.

"The book *Physical Pharmacy* was written in an effort to unite the theory and practice of the pharmaceutical sciences..." Dr. Alfred N. Martin wrote in the Preface of the First Edition of *Physical Pharmacy* in 1960.[1] The purpose of the Seventh Edition remains the same—to update information regarding the pharmaceutical sciences and to integrate new concepts with established ones. Dr. Martin continued "The book *Physical Pharmacy* must make its way among teachers, students and pharmaceutical practitioners, some of whom no doubt will not agree with the author's treatment of the subject. It is hoped, however, that as a result of their criticisms and suggestions a better book may evolve through the years which will serve the theoretical needs of the pharmacy student". Indeed, the book has continuously evolved in the over 50 years and now 7 editions since it was first published. The seventh edition of *Martin's Physical Pharmacy and Pharmaceutical Sciences* remains oriented toward pharmacists and pharmaceutical scientists all over the world. Versions of the text have been published in English, complex and simplified Chinese, Indonesian, Korean, and Portuguese.

More than ever before, the pharmacist and the pharmaceutical scientist are called upon to utilize a sound knowledge of biopharmaceutics, biochemistry, chemistry, pharmacology, physiology, and toxicology and an intimate understanding of the physical, chemical, and biopharmaceutical properties of drug products. Whether engaged in research and development, teaching, manufacturing, the practice of clinical or retail pharmacy, or any of the allied branches of the profession, you must recognize the need to rely heavily upon and apply the basic sciences. This stems from the fact that pharmacy is an applied science, composed of principles and methods that have been culled from other disciplines. More than any other medical profession, you will work at the boundaries between the various sciences of the physical, chemical, and biological fields in order to understand and contribute to increasingly rapid developments. You are also expected to provide concise and practical interpretations of highly technical drug information to your patients and colleagues. With the abundance of information and misinformation that is freely and publicly available (e.g., on the Internet), having the tools and ability to provide meaningful interpretations of data or understanding when there is insufficient data is critical.

The study of the material in this book should mark somewhat of a turning point in the study pattern of the student. In the latter part of the pharmacy curriculum, emphasis is placed upon the application of scientific principles to practical professional problems. Although facts must be the foundation upon which any body of knowledge is built, the rote memorization of disjointed "particles" of knowledge does not lead to logical systematic thought and problem solving.

[1] A. N. Martin, in *Physical Pharmacy*, 1st Ed., Lea & Febiger, Philadelphia, 1960, Preface.

"I HEAR AND I FORGET.
I SEE AND I REMEMBER.
I DO AND I UNDERSTAND."

The ancient Chinese proverb emphasizes the value of active participation in the learning process. Through the illustrative examples and practice problems in this book and on the online companion website, the student is encouraged to actively participate.

The comprehension of course material is primarily the responsibility of the student. A teacher can guide and direct, explain, and clarify, but competence in solving problems in the classroom and the laboratory depends largely on the student's understanding of theory, recall of facts, ability to integrate knowledge, and willingness to devote sufficient time and effort to the task. Each assignment should be read and outlined, and assigned problems should be solved outside the classroom. Active problem solving and practice effectively builds the mental "muscle memory" and skills to ultimately utilize the techniques in the real world. Just as it would be difficult to build physical muscle by simply reading about exercises, the skills and techniques presented here will be best mastered with active practice. Teacher comments will then serve to clarify questionable points and aid the student to improve judgment and reasoning abilities.

The scientific principles of pharmacy are not as complex as some would believe, and certainly they are not beyond the understanding of the well-educated pharmacist and pharmaceutical scientist of today. The continued integration of the biological, chemical, and physical sciences remains critical to the evolution of the pharmaceutical sciences. The theoretical links between the diverse scientific disciplines that serve as the foundation for pharmacy are reflected in this book. In the Seventh Edition, the reader will be directed through fundamental theory and experimental findings to practical conclusions that serve as the foundation for the pharmaceutical sciences. New chapters have been added (Excipients, Compounding) and others have been significantly expanded and/or updated (Interpretive Tools, Ionic Equilibria, Biopharmaceutics, Diffusion, Drug Release and Dissolution, and Drug Delivery Systems and Drug Product Design) to reflect the expanding scope and diversity of the pharmaceutical sciences.

Contents

INTERPRETIVE TOOLS

1

CHAPTER OBJECTIVES

At the conclusion of this chapter the student should be able to:

1. Understand the basic tools required to analyze and interpret data sets from the laboratory, clinic, or literature.
2. Use dimensional analysis.
3. Understand the difference between precision and accuracy.
4. Understand and apply the concept of significant figures.
5. Define determinant and indeterminant errors.
6. Calculate the mean, median, and mode of a data set.
7. Understand the concept of variability.
8. Calculate standard deviation and coefficient of variation and understand when it is appropriate to use these parameters.
9. Use graphical methods to determine the slope of lines and their statistical significance.
10. Interpret slopes of lines and how they relate to absorption and elimination from the body.

INTRODUCTION

Science begins with the observation and precise description of things and events. For the pharmaceutical scientist, many observations involve quantitative numerical data. And the description of things and events requires calculation and use of such data. The goal of this chapter is to provide a foundation for the *quantitative reasoning* skills that are fundamental to the pharmacy practitioner and pharmaceutical scientist. Mathematics and statistics are fundamental tools of the pharmaceutical sciences. You need to understand how and when to use these tools, and how to interpret the results of their use. You must also be careful not to overinterpret results. On the one hand, you may ask "do we really need to know how these equations and formulas were derived in order to use them effectively?" Logically, the answer would seem to be no. By analogy, you do not need to know how to build a computer in order to use one to send an e-mail message. On the other hand, graphically represented data convey a sense of dynamics that greatly benefit from understanding a bit more about the fundamental equations behind the behavior. These equations are merely part of a set of tools (that you should not memorize!) that allow for the transformation of a bunch of numbers into a behavior that one can interpret.

The mathematics and statistics covered in this chapter and this book are presented in a format to promote understanding and practical use. Many of the basic mathematical "tutorial" elements have been removed from previous editions, and in particular for this chapter, because of the migration of numerous college-level topics to secondary school courses. Statistical formulas and graphical method explanations have also been presented in a reduced format. Depending on your personal goals and the philosophy of your program of study, you may well need an in-depth treatment of the subject matter. Additional detailed treatments can be found on the website and in the recommended readings at the end of the chapter.

Data Analysis Tools

Readily available tools such as programmable calculators, computer spreadsheet programs (e.g., Microsoft Excel, Apple Numbers, or OpenOffice.org Calc), and statistical software packages (e.g., Minitab, SAS or SPSS) make the processing of data relatively easy. Spreadsheet programs have two distinct advantages: (1) data collection/entry is simple and can often be automated, reducing the possibility of errors in transcription, and (2) simple data manipulations and elementary statistical calculations are also easy to perform. In addition, many spreadsheet programs seamlessly interface with statistical packages when more robust statistical analysis is required. With very little effort, you can add data sets and generate pages of analysis. The processing of data is, in fact almost too easy, and it is not the same as understanding data. The student should appreciate that while it may be possible to automate data entry and have the computer perform calculations, knowing what is appropriate to calculate and the final interpretation of the results and statistical analysis is your responsibility! As you set out to analyze data keep in mind the simple acronym *GIGO—Garbage In, Garbage Out*. In other words, solid scientific results and sound methods of analysis will yield meaningful interpretations and conclusions. However, if the scientific foundation is weak or data are poor, statistical tools can not give bad data meaningful value.

Dimensional Analysis

Dimensional analysis (also called the factor-label method or the unit factor method) is a problem-solving method that uses the fact that any number or expression can be multiplied