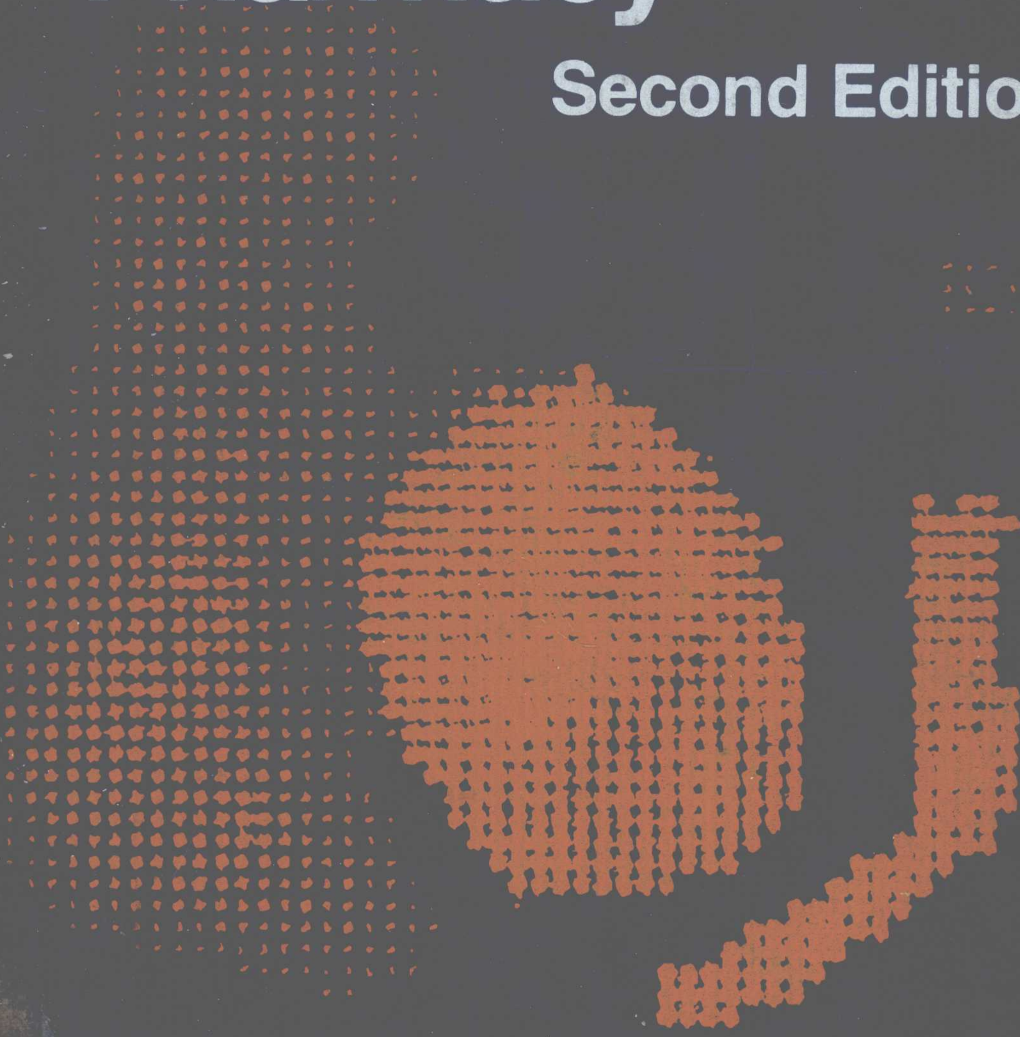
Gopal B. Saha

Fundamentals of Nuclear Pharmacy

Second Edition



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With 91 Illustrations

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To my wife, Sipra
and
my children, Prantik and Trina

Foreword

Nuclear medicine is an ever changing subject, and the emphasis and utility of one type of study is often abruptly supplanted by another. In this unstable environment, there is a set of circumstances that offers a basic unifying structure to the activities encountered in nuclear medicine. The pivotal importance of radiopharmaceuticals in these activities makes a thorough understanding of them paramount for all who would prescribe, dispense, or in any way utilize such materials.

In this volume, the author has distilled an awesome body of literature on nuclear pharmacy into a concise and readily understandable textbook. It is written from the viewpoint of one who not only has broad experience and knowledge in nuclear pharmacy, who daily guides and instructs a variety of students in the discipline, but who also directs a clinical nuclear medicine radiopharmacy program. In this second edition, he has avoided the esoteric and maintained an emphasis on the practical. The approach is not encyclopedic in nature, as adequate references refer the more interested reader to appropriate sources of detailed information, but one which ensures that the students will be able to absorb the essentials of nuclear pharmacy and practice it effectively with a broad understanding of the subject. At the end of each chapter a set of questions provokes the reader to assess the sufficiency of the knowledge gained.

Since nuclear pharmacy has become an essential central element of the nuclear medicine laboratory and involves a wide variety of participants, use of this book will undoubtedly benefit the practice of nuclear medicine generally and the patient specifically.

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Preface to the Second Edition

Many new radiopharmaceuticals and imaging techniques in nuclear medicine have been developed during the four and one-half years since the first edition of this book was published. Consequently, there have been many new developments in nuclear pharmacy which, along with the success of the first edition and the enthusiasm for it in the nuclear medicine and pharmacy communities, have prompted us to prepare this second edition.

Numerous additions and deletions, including the introduction of the System Internationale (SI) units, have been made and the text reorganized throughout the book. Chapter 3 now includes a section on short-lived radionuclides. In Chapter 5, a section on gamma-ray detecting instruments has been added. Several new methods of labeling have been described and up-to-date information on the structure of ^{99m}Tc-complexes has been included in Chapter 6. Radiation regulations have been updated in Chapter 10. In Chapter 12, topics such as lymphoscintigraphy, gastric emptying, gastrointestinal bleeding, Meckel's diverticulum, inflammatory diseases, adverse reactions, and iatrogenic alterations in the biodistribution of radiopharmaceuticals have been added to the text. Finally, additional review questions have been added at the end of several chapters.

I am grateful to Dr. M.K. Dewanjee of the Mayo Clinic and Mayo Foundation, Rochester, Minnesota, for his suggestions, and to my colleagues in College of Pharmacy, Radiopharmacy, University of New Mexico, for their comments and support in the preparation of this edition. Thanks are due to Ms. Elva Giron for her excellent typing of the manuscript. The sincere cooperation of the publisher, Springer-Verlag, is greatly appreciated.

Gopal B. Saha

Preface to the First Edition

The discipline of nuclear pharmacy has grown significantly along with the vast expansion of nuclear medicine so that it is now considered a separate unit in many nuclear medicine facilities. In many places, centralized nuclear pharmacies have been established to supply radiopharmaceuticals to more than one hospital. In view of such great appreciation of nuclear pharmacy, training programs are being instituted and courses on nuclear pharmacy are being offered in many schools of pharmacy and nuclear medicine technology. Obviously there is a definite need for a book to meet these demands.

This book is a ramification of my nuclear pharmacy courses offered to pharmacy students specializing in nuclear pharmacy, nuclear medicine residents, and nuclear medicine technology students at the University of Arkansas for Medical Sciences. The book is written in an integrated form from the basic concept of atomic structure to the practical clinical uses of radiopharmaceuticals. It should serve both as a texbook on nuclear pharmacy for pharmacy students and as a useful reference book for many professionals related to nuclear medicine, such as nuclear medicine physicians, residents, and technologists.

The book contains 12 chapters. Each chapter is written as comprehensively as possible based on my personal experience and understanding. At the end of each chapter, a section of pertinent questions and problems and some suggested reading materials are included.

Chapter 1 is a brief review of atomic structure, electronic configuration of atoms, chemical bonds, and nuclear structure. The chapter is primarily meant for the understanding of chemical bonds in compounds and nuclear structure along with different nomenclatures associated with nuclei and varying composition.

Chapter 2 deals with different decay modes of radionuclides and various mathematical equations related to them. A section is devoted to statistics of counting.

Chapter 3 describes the general methods of production of radionuclides in cyclotrons and reactors.

In Chapter 4, the principles of a radionuclide generator are elaborated. The detailed description of a ^{99}Mo–^{99m}Tc generator is presented along with quality control measures that are essential for this generator.

Chapter 5 defines the term "radiopharmaceutical," ideal characteristics of a radiopharmaceutical, and various dosage forms in which a radiopharmaceutical may be dispensed. This chapter also provides information about how to design a new radiopharmaceutical.

Chapter 6 reviews general principles of labeling of compounds with special reference to various factors that affect labeling. The methods of iodination and ^{99m}Tc-labeling are described in detail. A brief review of different additives used in radiopharmaceuticals is included.

Chapter 7 presents the general outlines of the preparations and various characteristics of specific radiopharmaceuticals that are routinely used in nuclear medicine. Various physicochemical factors affecting the yield and stability of the labeled compounds are presented for ready reference in the case of problems associated with any radiopharmaceutical.

In Chapter 8, the reader is introduced to various quality control tests of radiopharmaceuticals which must be carried out before administration to humans.

Chapter 9 provides a description of a nuclear pharmacy set-up with regard to its design and daily operation of preparation, quality control tests, and dispensing of radiopharmaceuticals.

In Chapter 10, the reader is acquainted with general aspects of radiation dosimetry, safety, and federal and state regulations governing the use of radiopharmaceuticals.

Chapter 11 deals with general principles of radioimmunoassay and brief methods of some pertinent in vitro tests.

Chapter 12 is concerned with the subject of radiopharmacology in nuclear medicine. In this chapter, there are several subsections under the heading of each organ to be imaged. At the beginning of each subsection, a brief description of the anatomy and physiology of the organ in question is presented, and then the use of various radiopharmaceuticals and the imaging technique of the organ are discussed. The mechanism of localization and the biological handling of each radiopharmaceutical are elucidated, wherever possible. A brief section is devoted to radionuclide therapy in this chapter.

Several appendices provide some useful data such as universal constants, decay factors of ^{99m}Tc and ^{131}I, and answers to the mathematical problems given in various chapters.

I do not pretend to be infallible in writing such a book of diversified scientific information. Many errors of both commission and omission are possible, and I would appreciate having them brought to my attention by interested readers.

It would have been impossible to complete this book without the help and suggestions of so many friendly people. First and foremost, I am ever grateful and thankful to Dr. Claude E. Epperson of the College of Pharmacy at the University of Arkansas for Medical Sciences, Little Rock, whose perusal of the entire manuscript, helpful criticism, invaluable suggestions, and friendly encouragement made this book possible.

Special gratitude is extended to Dr. Charles M. Boyd of the University of Arkansas for Medical Sciences, to whom I owe a great deal for his continued support and understanding.

I extend my sincere thanks and appreciation to Dr. M.K. Dewanjee of the Mayo Clinic and Mayo Foundation at Rochester, Minnesota, Mr. J.F. Vandergrift of the University of Arkansas for Medical Sciences, Little Rock, Dr. P.A. Farrer of the University of California at Davis, and Dr. F. Vieras of the Armed Forces Radiobiology Research Institute at Bethesda, Maryland, for suggestions and comments on various chapters of the book.

Thanks are due to Alice Guy Anne Ransom for her help in sorting out the suitable scans and scintiphotos, and to Susan Hudgens, Michael A. Morris, and others of Biomedical Communications at the University of Arkansas for Medical Sciences for their sincere assistance with the illustrations and photographic works. Cooperation and help in numerous ways from the members of the Division of Nuclear Medicine at the University of Arkansas for Medical Sciences at Little Rock is greatly appreciated.

I would like to sincerely express by heartfelt gratitude and thanks to Mrs. Vercie Vandergrift who typed the manuscript over and over so graciously, conscientiously, and efficiently, and whose tireless and painstaking effort played an instrumental role in bringing this book to fruition.

Finally, my wife, Sipra's inspiration, encouragement, and forbearance throughout this endeavor made work a pleasure.

Gopal B. Saha

Contents

Chapter 1
The Atom

According to Bohr's atomic theory, an atom is composed of a nucleus at the center and one or more electrons rotating around the nucleus along different energy orbits. The nucleus is primarily composed of protons and neutrons, collectively called nucleons. For an atom of a given element, the number of electrons moving around the nucleus equals the number of protons, balancing the electrical charge of the nucleus. The size of an atom is of the order of 10^{-8} cm (1 angstrom, Å) and that of a nucleus is of the order of 10^{-13} cm (equal to a unit termed the fermi, F, in honor of the famous physicist, E. Fermi). The electron configuration of the atom determines the chemical properties of an element, whereas the nuclear structure characterizes the stability and radioactive decay of the nucleus of an atom.

Electronic Structure of the Atom

The Bohr atomic theory states that electrons in an atom rotate around the nucleus in discrete *energy orbits or shells*. These energy shells, referred to as the *K* shell, *L* shell, *M* shell, *N* shell, etc., are stationary and arranged in order of increasing energy. When there is a transition of an electron from an upper orbit to a lower orbit, the energy difference between the two orbits is released as the photon radiation. If the electron is raised from a lower orbit to an upper orbit, the energy difference between the two orbits is absorbed and must be supplied for the transition to occur. Each orbit has a limited capacity to hold only a definite number of electrons; thus the innermost shell, designated as *K*, contains only 2 electrons, the next, the *L* shell, 8 electrons, the *M* shell 18 electrons, the *N* shell 32 electrons, and the *O* shell 50 electrons (Table 1-1).

The lightest element is hydrogen, whose atomic number is 1; the hydrogen atom contains one proton in the nucleus and one electron rotating about the nucleus. This electron is positioned in the *K* shell in the hydrogen atom in the normal state. The next element is helium with atomic number 2. The two electrons in the normal state of helium are positioned in the *K* shell. In subsequent heavier elements, additional electrons are positioned in the higher energy shells in a definite order according to quantum mechanical rules.

According to the quantum theory, each shell is designated by a quantum number *n*, called the *principal quantum number*, and denoted by integers, e.g.,