

# Textbook of Medicinal Chemistry

Volume 1

Fourth Edition

is a widely appreciated text on the subject. Primarily meant for BPharm students, this textbook is also useful for MPharm, BSc and MSc students studying organic chemistry and pharmaceutical chemistry. It aims at eliminating the inadequacies in teaching and learning of medicinal chemistry by providing valuable information on the most relevant topics. The text adequately covers the latest syllabi of Pharmacy Council of India (PCI) and all major Indian Universities.

The fourth edition features new layout and design in an attractive two-color presentation.

#### Salient Features

- ❖ Serves as a unique and valuable textbook containing completely updated information on medicinal chemistry, adapting to the latest/revised syllabus prescribed by Pharmacy Council of India (PCI).
- ❖ Presents clear classification, synthetic schemes, mode of action, metabolism, assay, pharmacological uses with the dose and structure-activity relationship (SAR) of the drugs for the various body systems.
- ❖ Carries a complete section on drug design, describing the new drug development.
- ❖ Discusses briefly physiological and pathophysiological conditions of diseases and their treatment.
- ❖ Provides well-illustrated synthetic schemes and alternative synthetic routes for majority of drugs that help in quick and enhanced understanding of the subject.
- ❖ Explains physicochemical parameters with related information; includes two new chapters •Protein binding • Biotransformation or metabolism of drugs added in this edition.
- ❖ Features new chapters like •Pharmacophore modeling •Docking and antisense technology given under the section of drug design
- ❖ Embraces PCI syllabus-based classification of drugs for easy to study and write in examination.
- ❖ Incorporates updated information on several newer drugs in different chapters in consonance with the revised PCI syllabus.
- ❖ Serves as an excellent companion for the GPAT aspirants.

#### V Alagarsamy MPharm, PhD, FIC, DOMH

is Professor and Principal, MNR College of Pharmacy, and Director, MNR Foundation for Research and Innovation, Gr. Hyderabad, Telangana. He received his DPharm from Coimbatore Medical College, BPharm from Madurai Medical College, MPharm from LM College of Pharmacy, Ahmedabad, and PhD from The MS University, Baroda. He has been teaching medicinal chemistry and conducting research work in synthetic medicinal chemistry on novel heterocyclic bioactive compounds for more than two decades. For his research work he has been collaborated with various research laboratories/organizations like National Cancer Institute, USA; Rega Institute for Medical Research, Belgium; Southern Research Institute, USA; and Sudbury Regional Hospital, Ontario, Canada. He is a recipient of young scientist project from Department of Science and Technology, New Delhi. He is the author/co-author of over 200 papers, which include the original research articles and presentations in various conferences and symposiums, having one patent for his credit on bioactive heterocyclic molecule. He is the co-editor of the international journal *Antiinfective Agents*, published by Bentham Science Publishers. His books *Textbook of Medicinal Chemistry*, *Pharmaceutical Chemistry of Natural Products*, *Pharmaceutical Inorganic Chemistry*, *Organic Chemistry: A Comprehensive Approach*, *Pharmaceutical Organic Chemistry* and *Practical Pharmaceutical Inorganic Chemistry* are well appreciated in the academic community nationally and received international recognition too. His research activities are supported by the funding agencies like CSIR, DST and DSIR.

Prof Alagarsamy is a member of All India Board of Pharmaceutical Education (AIB-PE), AICTE, New Delhi, and a member of board of studies (pharmacy) in Osmania University, Hyderabad, and is a doctoral committee member and a recognized research guide for PhD scholars in various universities. Recently, he has been named among top 2% scientists in the world in the field of pharmacy by Stanford University, USA.



**CBS Publishers & Distributors Pvt Ltd**

4819/XI, Prahlad Street, 24 Ansari Road, Daryaganj, New Delhi 110 002, India

E-mail: delhi@cbspd.com, cbspubs@airtelmail.in; Website: www.cbspd.com

New Delhi | Bengaluru | Chennai | Kochi | Kolkata | Lucknow | Mumbai

Hyderabad | Jharkhand | Nagpur | Patna | Pune | Uttarakhand



QR code to access online CBS Catalogue

ISBN: 978-93-90709-68-7



Volume 1

# Textbook of Medicinal Chemistry

Fourth Edition

V Alagarsamy



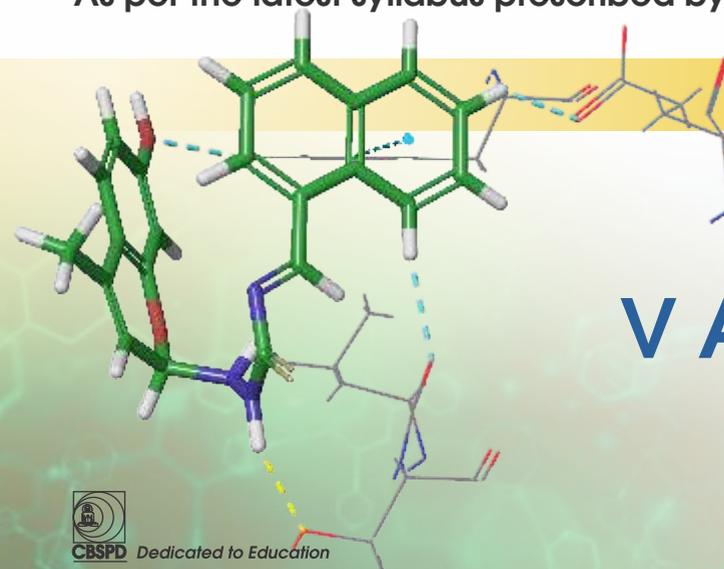
Volume 1

# Textbook of Medicinal Chemistry

As per the latest syllabus prescribed by Pharmacy Council of India

Fourth Edition

V Alagarsamy



Dedicated to Education

CBS Publishers & Distributors Pvt Ltd

Volume 1

Textbook of  
**Medicinal  
Chemistry**

As per the latest syllabus prescribed by Pharmacy Council of India

Fourth Edition



Volume 1

# Textbook of Medicinal Chemistry

As per the latest syllabus prescribed by Pharmacy Council of India

Fourth Edition

**V Alagarsamy** MPharm PhD FIC DOMH

Professor and Principal  
MNR College of Pharmacy, Sangareddy  
Greater Hyderabad, Telangana

Director  
MNR Foundation for Research and Innovation  
Sangareddy, Greater Hyderabad, Telangana

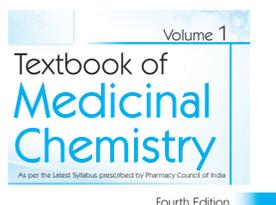


**CBS Publishers & Distributors** Pvt Ltd

New Delhi • Bengaluru • Chennai • Kochi • Kolkata • Lucknow • Mumbai  
Hyderabad • Jharkhand • Nagpur • Patna • Pune • Uttarakhand

#### Disclaimer

Science and technology are constantly changing fields. New research and experience broaden the scope of information and knowledge. The author has tried his best in giving information available to him while preparing the material for this book. Although all efforts have been made to ensure optimum accuracy of the material, yet it is quite possible some errors might have been left uncorrected. The publisher, the printer and the author will not be held responsible for any inadvertent errors or inaccuracies.



**ISBN:** 978-93-90709-68-7

Copyright © Author and Publisher

#### Fourth Edition: 2022

Third Edition: 2016

Reprint: 2017, 2019, 2020, 2021

Second Edition: 2014

First Edition: 2009

All rights reserved. No part of this book may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system without permission, in written from the author and the publisher.

Published by Satish Kumar Jain and produced by Varun Jain for

**CBS Publishers & Distributors** Pvt Ltd

4819/XI Prahlad Street, 24 Ansari Road, Daryaganj, New Delhi 110 002, India

Ph: 011-23289259, 23266861, 23266867

Fax: 011-23243014

Website: www.cbspd.com

e-mail: delhi@cbspd.com; cbspubs@airtelmail.in

Corporate Office: 204 FIE, Industrial Area, Patparganj, Delhi 110 092, India

Ph: 011-49344934

Fax: 011-49344935

e-mail: publishing@cbspd.com; publicity@cbspd.com

#### Branches

- **Bengaluru:** Seema House 2975, 17th Cross, K.R. Road, Banasankari 2nd Stage, Bengaluru 560 070, Karnataka, India  
Ph: +91-80-26771678/79 Fax: +91-80-26771680 e-mail: bangalore@cbspd.com
- **Chennai:** 7, Subbaraya Street, Shenoy Nagar, Chennai 600 030, Tamil Nadu, India  
Ph: +91-44-26680620, 26681266 Fax: +91-44-42032115 e-mail: chennai@cbspd.com
- **Kochi:** 42/1325, 1326, Power House Road, Opposite KSEB, Power House, Ernakulum 682 018, Kochi, Kerala, India  
Ph: +91-484-4059061-67 Fax: +91-484-4059065 e-mail: kochi@cbspd.com
- **Kolkata:** 147, Hind Ceramics Compound, 1st Floor, Nilgunj Road, Belghoria, Kolkata 700 056, West Bengal, India  
Ph: +91-33-25330055/56 e-mail: kolkata@cbspd.com
- **Lucknow:** Basement, Khushuma Complex, 7 Meerabai Marg (behind Jawahar Bhawan), Lucknow 226 001, UP, India  
Ph: +91-522-40000032 e-mail: tiwari.lucknow@cbspd.com
- **Mumbai:** PWD Shed, Gala No. 25/26, Ramchandra Bhatt Marg, Next JJ Hospital Gate No. 2, Opp. Union Bank of India, Noorbaug, Mumbai 400 009, Maharashtra, India  
Ph: +91-22-66661880/89 e-mail: mumbai@cbspd.com

#### Representatives

- |                    |              |                    |              |                      |              |
|--------------------|--------------|--------------------|--------------|----------------------|--------------|
| • <b>Hyderabad</b> | 0-9885175004 | • <b>Jharkhand</b> | 0-9811541605 | • <b>Nagpur</b>      | 0-9421945513 |
| • <b>Patna</b>     | 0-9334159340 | • <b>Pune</b>      | 0-9623451994 | • <b>Uttarakhand</b> | 0-9716462459 |

Printed at: India Binding House, Noida, UP, India.

# Preface to the Fourth Edition

The subject of medicinal chemistry has grown so fast and we find developments in many areas of this subject. Even though, it is a difficult task for the author to match the pace of developments of the subject, it is a great pleasure for the author and the publisher to present this revised and updated fourth edition of the *Textbook of Medicinal Chemistry*.

The enthusiastic comments received from faculty members and student community across India, as mentioned below, have inspired me to present this fourth and updated edition of the *Textbook of Medicinal Chemistry*.

- ✦ A unique book containing updated information about medicinal chemistry by complying the revised syllabus of Pharmacy Council of India (PCI).
- ✦ This book is comprehensive with all the aspects of medicinal chemistry discussed at one place.
- ✦ It is a good companion for GPAT aspirants.
- ✦ It is a favourite book for students willing to learn medicinal chemistry.
- ✦ It is presented in an attractive and easy-to-read manner.
- ✦ It is presented in student-friendly style and approach.
- ✦ It is presented in a down-to-earth fashion avoiding unnecessary complicated details.
- ✦ This is a perfect textbook.
- ✦ It helps faculty members a lot while teaching students.
- ✦ Elegant presentation of chemical structures helping students to remember and reproduce well in examinations.

Since its first edition, in 2009, *Textbook of Medicinal Chemistry*, serves as an authentic and reliable source for the medicinal chemistry aspects of the drugs. The overwhelming response to the first edition was immediate throughout the country due to its comprehensive content (especially, the classification, synthesis and drug profile and SAR). As the number of drugs available for therapeutic use is increasing day-by-day, all the chapters have been updated with newer drugs.

## New to this Edition

---

The major goal of the author is to provide the students of pharmacy and allied health professions with a book that not only describes the chemical aspects of drugs but also reflects pharmacological aspects that are important in the field of medicine. Following are some features of the fourth edition:

- ✦ **Updated information provided** and complied with the revised PCI syllabus.
- ✦ **Attractive layout and design.**
- ✦ **Physicochemical parameters** have been explained with further information and two new chapters—Protein Binding of Drugs and Biotransformation or Metabolism of Drugs—are added under the section Physicochemical Factors in Relation to Biological Activity of Drugs.

- ✦ **New topics** like Pharmacophore Modelling, Docking and Antisense Technology are added under the section Drug Design.
- ✦ **Based on PCI syllabus, new topics** like Drugs Used in Congestive Cardiac Failure, Thyroid and Antithyroid Drugs, Antiscabies and Antipedicular Agents, Preservatives and Diagnostic Agents are introduced.
- ✦ **Several newer drugs** are incorporated in different chapters.
- ✦ **PCI syllabus-based classification of drugs** is provided for easy to study and write in examination.

I hope this new edition of the *Textbook of Medicinal Chemistry* will be welcomed by the teachers and students of pharmacy, pharmaceutical chemistry, chemistry and the related fields. You are most welcome with your valuable feedback to [authoralagarsamy@gmail.com](mailto:authoralagarsamy@gmail.com).

V Alagarsamy

# Preface to the First Edition

Medicinal chemistry emerged as a specialized area due to the development in chemistry and biology, hence it is considered as a highly interdisciplinary science combining a wide variety of subjects such as organic chemistry, pharmacology, biochemistry, toxicology, pharmacognosy, molecular biology, genomics, proteomics, computational chemistry, physical chemistry and statistics. Now, the growth of medicinal chemistry has reached a stage where the activity-guided synthesis of compounds is possible rather than screening of synthesized compounds for different biological activities. This field also penetrates into the areas of gene therapy and biochemistry-based virtual drug receptors with the help of computer-aided molecular modelling techniques.

This book is an upshot of my vision to discover the best book on medicinal chemistry, which deals about the concise description of diseases, clear classification of drugs with their chemical structures, synthesis of each drug with different routes, mode of action, metabolism, physical and pharmacological properties along with their therapeutic uses, assay technique, dose, official dosage forms and summary of structure–activity relationship (SAR) studies. Swathing the entire features of medicinal chemistry, first of its kind, is the unique feature of this book. It facilitates the students to understand the subject more easily and interestingly.

While writing this book, I felt that the book will bring about a re-orientation in the teaching and learning process of medicinal chemistry. Academic community in India is faced with scarcity of books to cater to their needs. Numerous foreign writers' books deal well about basics and pharmacological aspects related to medicinal chemistry, but lack two major requirements, i.e. synthesis and clear classification of drugs used. Some Indian authors filled this lacuna to a certain extent by including the synthesis, but failed to give a clear classification of drugs with their chemical structure. For this, the content of this book has been carefully tailored to cater to the needs of the academicians belonging to all Indian universities, pharmacologists, clinical and industrial pharmacists by incorporating the missing links between general synthetic organic chemistry and medicinal chemistry.

This *Textbook of Medicinal Chemistry* is presented in two volumes. Volume I consists of six sections. The first section is devoted to the physicochemical properties and their relation to biological activities and the second section provides the framework of drug design, which together form the basic aspects of medicinal chemistry. The remaining sections, III to VI, deal with chemical, pharmacological, biochemical and toxicological aspects of organic medicinal compounds used in various diseases associated with different systems of the human body such as CNS, ANS, CVS and urinary system.

We hope that this special volume will be a good source of information and reference for not only graduate and postgraduate students but also basic and applied researchers in this field. Moreover, it will also be of interest to a wide range of scientists, including organic chemists, biochemists, pharmacologists and clinicians, who are interested in drug research. I welcome suggestions and constructive criticism from all corners of scientific community.

V Alagarsamy

# Acknowledgements

I wish to place on record my heartfelt thanks to everyone who have made this book possible, especially my beloved teachers from first standard to doctoral programme, guides, Dr Rajani Giridhar and Dr MR Yadav.

I am immensely grateful to Dr B Suresh and Dr RK Goyal for inspiring and initiating me to write the book. I am grateful to Shri MN Raju, Chairman, and Mr Ravi Varma, Vice-chairman, MNR Educational Trust, Hyderabad, for providing constant encouragement and moral support to achieve this goal.

I express my sincere appreciation to my students, Dr V Raja Solomon (postdoctoral researcher, Canada), Dr JC Hanish Singh, Dr P Parthiban, Mr S Thiru Senthil Murugan and Ms J Rajeshwari, for helping me author this book. I also thank my colleagues, especially, Dr S Satheesh Kumar, Dr B Subba Rao, Dr K Dhanabal, Mr M Murugan, Dr MT Sulthana, Dr B Narendhar and Dr K Lahari, for their untiring support in making this book.

The friendly interaction I had experienced with the Elsevier team—Mr Subodh K Chauhan, Mr Nitin Valecha and Mr Ankush—and Televijay Technologies, Project Manager Ms Usha K Nair, offered a plenty of energy to eliminate the fatigue during the preparation of this book. If the author gets such a cooperative and energetic publication team, publishing any number of books will not be a difficult task. I thank them wholeheartedly for helping me reach this target and am requesting them to continue their service to the author community in the same intensity.

I also acknowledge the support extended by the CBS Publishing team Mr YN Arjuna (Senior Vice-President, Publishing, Editorial and Publicity) and his entire team comprising Ms Ritu Chawla (AGM Production), Ms Baljeet (graphic artist), Ms Hemlata (DTP operator), and Mr Neeraj Kumar Sharma (editor) in this revised edition.

I am also grateful to the faculty members of Faculty of Technology, Osmania University, Hyderabad, for their academic support and encouragement.

The stimulation I got from my father, mother, sister, brothers and wife to reach this target is more than analeptics, and the patience and cooperation extended by my children, Aishwarya (B Pharm) and Abhinaya, made me think of the goal without any diversion. To express my thankfulness, I pray The Almighty to bless my children with teachers like those I got in my life so that they too are inspired by their teachers and dedicate to the field of medicinal chemistry and, in turn, serve for the suffering humanity.

V Alagarsamy

# Contents

<i>Preface to the Fourth Edition</i>	v
<i>Preface to the First Edition</i>	vii
Introduction to Medicinal Chemistry	1

## SECTION I

### Physicochemical Factors in Relation to Biological Activity of Drugs

1. Physicochemical Properties	11
2. Ferguson Principle	13
3. Hydrogen Bonding	16
4. Ionization and $pK_a$ Value	20
5. Redox Potential	24
6. Surface Tension	27
7. Complexation	29
8. Solubility	32
9. Partition Coefficient	39
10. Steric Features of Drugs	43
11. Bioisosterism	51
12. Protein Binding of Drugs	55
13. Biotransformation or Metabolism of Drugs	60

## SECTION II

### Drug Design

14. Concepts of Drug Design	105
15. Receptors	111

16. Computer-aided Drug Design	116
17. Structure–Activity Relationship and Quantitative Structure–Activity Relationship	128
18. Combinatorial Chemistry	144
19. High-throughput Screening	152
20. Prodrugs	157
21. Antisense Technology	165

### SECTION III

#### Drugs Acting on Central Nervous System

22. Central Nervous System	173
23. Sedatives and Hypnotics	175
24. General Anaesthetics	217
25. Local Anaesthetics	237
26. Tranquillizers	265
27. Antidepressants	295
28. CNS Stimulants	320
29. Narcotic Analgesics	337
30. Anticonvulsants	376
31. Antiparkinsonism Agents	411
32. Skeletal Muscle Relaxants	423
33. Alzheimer's Disease	437

### SECTION IV

#### Drugs Acting on Autonomic Nervous System

34. Autonomic Nervous System	445
35. Adrenergic Drugs	450
36. Cholinergic Drugs	477
37. Adrenergic Blockers	499
38. Anticholinergic Drugs	524

**SECTION V****Drugs Acting on Cardiovascular System**

39. Cardiovascular System	553
40. Antihypertensive Drugs	555
41. Antiarrhythmic Drugs	588
42. Antihyperlipidaemic Agents	613
43. Antianginals	636
44. Drugs Used in Congestive Cardiac Failure (CCF) or Congestive Heart Failure (CHF)	663

**SECTION VI****Drugs Acting on Urinary System**

45. Urinary System	673
46. Diuretics	675
<i>Index</i>	715

