COMPUTER-AIDED DRUG DESIGN

PRINCIPLES, TECHNIQUES, AND APPLICATIONS | PART 2

Editors:
Ajmer Singh Grewal
Viney Lather
Geeta Deswal
Kumar Guarve

Bentham Books

Computer-Aided Drug Design: Principles, Techniques, and Applications

(Part 2)

Edited by

Ajmer Singh Grewal
Guru Gobind Singh College of Pharmacy
Yamuna Nagar, Haryana, India

Viney Lather
Amity Institute of Pharmacy
Amity University, Noida
Uttar Pradesh, India

Geeta Deswal
Guru Gobind Singh College of Pharmacy
Yamuna Nagar, Haryana, India

&

Kumar Guarve
Guru Gobind Singh College of Pharmacy
Yamuna Nagar, Haryana, India

Computer-Aided Drug Design: Principles, Techniques, and Applications
(Part 2)

Editors: Ajmer Singh Grewal, Viney Lather, Geeta Deswal & Kumar Guarve

ISBN (Online): 979-8-89881-825-8

ISBN (Print): 979-8-89881-826-5

ISBN (Paperback): 979-8-89881-827-2

© 2026, Bentham Books imprint.

Published by Bentham Science Publishers Pte. Ltd. Singapore, in collaboration with Eureka Conferences, USA. All Rights Reserved.

First published in 2026.

BENTHAM SCIENCE PUBLISHERS LTD.

End User License Agreement (for non-institutional, personal use)

This is an agreement between you and Bentham Science Publishers Ltd. Please read this License Agreement carefully before using the ebook/echapter/ejournal (**"Work"**). Your use of the Work constitutes your agreement to the terms and conditions set forth in this License Agreement. If you do not agree to these terms and conditions then you should not use the Work.

Bentham Science Publishers agrees to grant you a non-exclusive, non-transferable limited license to use the Work subject to and in accordance with the following terms and conditions. This License Agreement is for non-library, personal use only. For a library / institutional / multi user license in respect of the Work, please contact: permission@benthamscience.org.

Usage Rules:

1. All rights reserved: The Work is the subject of copyright and Bentham Science Publishers either owns the Work (and the copyright in it) or is licensed to distribute the Work. You shall not copy, reproduce, modify, remove, delete, augment, add to, publish, transmit, sell, resell, create derivative works from, or in any way exploit the Work or make the Work available for others to do any of the same, in any form or by any means, in whole or in part, in each case without the prior written permission of Bentham Science Publishers, unless stated otherwise in this License Agreement.
2. You may download a copy of the Work on one occasion to one personal computer (including tablet, laptop, desktop, or other such devices). You may make one back-up copy of the Work to avoid losing it.
3. The unauthorised use or distribution of copyrighted or other proprietary content is illegal and could subject you to liability for substantial money damages. You will be liable for any damage resulting from your misuse of the Work or any violation of this License Agreement, including any infringement by you of copyrights or proprietary rights.

Disclaimer:

Bentham Science Publishers does not guarantee that the information in the Work is error-free, or warrant that it will meet your requirements or that access to the Work will be uninterrupted or error-free. The Work is provided "as is" without warranty of any kind, either express or implied or statutory, including, without limitation, implied warranties of merchantability and fitness for a particular purpose. The entire risk as to the results and performance of the Work is assumed by you. No responsibility is assumed by Bentham Science Publishers, its staff, editors and/or authors for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products instruction, advertisements or ideas contained in the Work.

Limitation of Liability:

In no event will Bentham Science Publishers, its staff, editors and/or authors, be liable for any damages, including, without limitation, special, incidental and/or consequential damages and/or damages for lost data and/or profits arising out of (whether directly or indirectly) the use or inability to use the Work. The entire liability of Bentham Science Publishers shall be limited to the amount actually paid by you for the Work.

General:

1. Any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims) will be governed by and construed in accordance with the laws of Singapore. Each party agrees that the courts of the state of Singapore shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims).
2. Your rights under this License Agreement will automatically terminate without notice and without the

need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.

3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

Bentham Science Publishers Pte. Ltd.
No. 9 Raffles Place
Office No. 26-01
Singapore 048619
Singapore
Email: subscriptions@benthamscience.net

CONTENTS

FOREWORD i

PREFACE ii

LIST OF CONTRIBUTORS iv

CHAPTER 1 DESIGNING DRUGS FROM SCRATCH: THE COMPUTATIONAL AND AI REVOLUTION IN *DE NOVO* DRUG DISCOVERY 1

Shaikh Mohmed Adnan Mohmed Javid, Sonam M. Gandhi, Nemat Ali and *Devesh U. Kapoor*

INTRODUCTION 2

PRINCIPLES OF *DE NOVO* DRUG DESIGN 2

De Novo Software and Its Methodology 2

Determining the Protein Structure 3

Modeling the Binding Site 3

Defining the Concept of *De Novo* Drug Design 4

The Role of Computational Tools in Generating Novel Molecules 4

Key Advantages and Challenges in *De Novo* Drug Design 5

RECEPTOR/ENZYME INTERACTION ANALYSIS 6

Fundamentals of Drug-Receptor and Drug-Enzyme Interactions 6

Identifying Key Binding Interactions: Hydrogen Bonds, Hydrophobic Effects, and Ionic Interactions 6

Computational Tools for Analyzing Interactions 7

Molecular Docking in De Novo Design 7

Molecular Dynamics Simulations for Interaction Validation 7

RECEPTOR/ENZYME CAVITY ANALYSIS 7

Importance of Cavity Analysis in Drug Design 7

Methods for Predicting Cavity Size and Shape 8

Grid-Based Approaches for Cavity Detection 8

Molecular Surface Mapping 8

Algorithms for Predicting Cavity Volume 9

Tools for Receptor/Enzyme Cavity Analysis 9

CASTp (Computed Atlas of Surface Topography of Proteins) 9

SiteMap 9

Cavity-Specific Design Strategies 9

Shape-Based Drug Design 10

Hydrophobicity Matching 10

Allosteric Modulation 10

Structure-Based Optimization 10

Fragment-Based Approaches 10

PREDICTING FUNCTIONAL COMPONENTS OF BINDING CAVITIES 11

Identifying Key Binding Residues in Receptors and Enzymes 11

Predicting Active and Allosteric Sites 11

Role of Electrostatic and Hydrophobic Properties in Functional Site Prediction 11

Case Studies: Functional Component Identification in Key Targets 11

FRAGMENT-BASED DRUG DESIGN (FBDD) 11

Fundamentals of Fragment-Based Drug Design 12

Steps in FBDD: Screening, Optimization, and Development 12

Fragment Libraries: Composition and Selection Criteria 12

Methods for Identifying Fragments Binding to Targets 13

Biophysical Techniques: X-ray Crystallography and NMR 13

Computational Approaches in Fragment Identification 13
Fragment Linking, Growing, and Merging Strategies 13
Advantages and Challenges of FBDD 13
Case Studies: Successful Drugs Developed Through FBDD 14
COMPUTATIONAL STRATEGIES FOR *DE NOVO* DRUG DESIGN 14
Ligand-Based Approaches for Novel Compound Generation 14
Structure-Based Approaches for Target-Specific Design 15
Role of Artificial Intelligence and Machine Learning in *De Novo* Drug Design 15
Integration of Quantum Mechanics for Enhancing Molecular Generation 16
APPLICATIONS OF *DE NOVO* DRUG DESIGN 16
Generating Novel Scaffolds for Drug Discovery 16
Tailoring Molecules for Specific Disease Targets 17
Addressing Challenges in Multi-Target Drug Design 18
CHALLENGES AND FUTURE DIRECTIONS 18
CONCLUSION 19
AI DISCLOSURE STATEMENT 20
ACKNOWLEDGEMENTS 20
REFERENCES 20

CHAPTER 2 PHARMACOPHORE MAPPING: PRINCIPLES, TECHNIQUES, AND APPLICATIONS 33
Jyoti Monga, Riya Singla, Deepika Choudhary, Minky Mukhija and *Rajender Kumar*
INTRODUCTION 34
PHARMACOPHORE FEATURES AND THEIR IDENTIFICATION 35
Kinds of Pharmacophore Attributes 35
Hydrogen Bond Acceptors and Hydrogen Bond Donors 35
Hydrophobic Areas 36
Aromatic Groups 36
Positively and Negatively Ionizable Groups 37
Metal Coordinating Areas 37
Methods for Identifying Pharmacophore Features 37
PHARMACOPHORE MODELING 38
Overview of Pharmacophore Modelling 38
Steps in Pharmacophore Modelling: 39
Data Collection 39
Selection of Active Constituents 40
Feature Identification 40
Pharmacophore Hypothesis Generation 40
Pharmacophore Alignment 40
Validation of the Pharmacophore Model 40
Virtual screening and lead 41
Software and Tools for Pharmacophore Modeling 41
CONFORMATIONAL SEARCHES IN PHARMACOPHORE MODELING 41
Methodologies of Conformational Searches 42
Systematic Searches 43
Random Searches 43
Molecular Dynamics (MD) Simulations 43
Monte Carlo (MC) Simulations 44
Genetic Algorithms (GA) 44
Distance Geometry Methods 44

Conformational Analysis and Its Role in Refining Pharmacophores 44
APPLICATIONS OF PHARMACOPHORE MAPPING 45
Lead Compound Identification 45
Drug-Receptor Interaction Optimization 45
Virtual Screening and In Silico Screening 45
CASE STUDIES AND PRACTICAL EXAMPLES 46
Case Study 1: Identification of a Natural AKT1 Inhibitor *via* Pharmacophore Modeling and Virtual Screening 46
Case Study 2: Discovery Designing of Protein Arginine Deiminase Inhibitors based on Pharmacophore Mapping 47
Case Study 3: Designing Novel Inhibitors of SARS-CoV-2 3-Chymotrypsin- Like Protease 48
CHALLENGES AND FUTURE DIRECTIONS 48
Challenges in Pharmacophore Mapping 48
Future Perspectives in Pharmacophore Mapping 49
CONCLUSION 49
AI DISCLOSURE STATEMENT 50
REFERENCES 50

CHAPTER 3 FROM MOLECULES TO MEDICINES: VIRTUAL SCREENING AND IN SILICO DESIGN IN MODERN DRUG DISCOVERY 58
Dishank Purandare, Prajakta Adsule, Satyawan Jadhav and *Anuruddha Chabukswar*
INTRODUCTION 58
SIMILARITY-BASED METHODS FOR VIRTUAL SCREENING 60
Principle of Similarity-Based Screening 60
Types of Molecular Similarity 61
2D and 3D Similarity 61
Topological Similarity 61
Tools and Software for Similarity-Based Screening 62
Chemoinformatics Tools and Software 62
PHARMACOPHORE-BASED VIRTUAL SCREENING 63
Overview of Pharmacophore-Based Virtual Screening (PBVS) 63
Steps in Pharmacophore-Based Virtual Screening 63
Pharmacophore Model Generation 63
Screening of Compound Libraries and Hit Identification and Validation 64
Pharmacophore Screening Tools and Platforms 65
Applications of Pharmacophore-Based Screening 65
Targeting Specific Biological Pathways and Screening for Drug-Protein Interactions 65
STRUCTURE-BASED IN SILICO VIRTUAL SCREENING PROTOCOLS 66
Introduction to Structure-Based Virtual Screening 66
Receptor-Based Virtual Screening (RBVS) 66
Target Selection and Preparation and Docking Protocols 67
Ligand-Based Virtual Screening 67
Ligand-Protein Interaction Analysis 67
Molecular Dynamics Simulations 68
Hybrid Approaches Combining Structure and Ligand-Based Screening 68
Software and Tools for Structure-Based Screening 68
HIGH-THROUGHPUT VIRTUAL SCREENING (HTVS) 69
Introduction to HTVS and Its Benefits 69
Integrating HTVS with Virtual Screening Techniques 70
Applications in Drug Discovery 70

Challenges and Limitations of HTVS 71
EVALUATING HITS AND IDENTIFYING LEAD CANDIDATES 72
Hit Identification Criteria 72
Hit Validation and Further Screening 73
Lead Optimization Techniques 73
Structure-Activity Relationship (SAR) Analysis 73
In Vitro and In Vivo Validation 73
The Role of Molecular Docking in Lead Selection 74
APPLICATIONS OF VIRTUAL SCREENING IN DRUG DISCOVERY 74
Drug Target Identification and Validation 75
Discovery of Small-Molecule Inhibitors 75
Drug Repurposing and New Indications 76
Antiviral, Anticancer, and Antibiotic Drug Discovery 76
Antiviral Drug Discovery 76
Anticancer Drug Discovery 76
Antibiotic Drug Discovery 77
Hit/Lead Compounds Identified Through Virtual Screening 77
CONCLUSION 78
AI DISCLOSURE STATEMENT 79
REFERENCES 79

CHAPTER 4 INTEGRATING ARTIFICIAL INTELLIGENCE (AI) AND MACHINE LEARNING (ML): REVOLUTIONIZING COMPUTER-AIDED DRUG DESIGN 84
Joy Das, Gouri Shankar Chakraborty, Utpal Bhui, Joy Chakra Bortty and *Neha Sharma*
INTRODUCTION 85
CORE AI AND ML TECHNIQUES IN DRUG DESIGN 86
Supervised Learning 86
Regression Models 87
Classification Algorithms 88
Unsupervised Learning 88
Clustering and Dimensionality Reduction 89
Anomaly Detection 90
Reinforcement Learning 90
Exploration and Exploitation in Drug Optimization 91
Applications in Drug Design 91
Deep Learning 92
Neural Networks and Deep Neural Networks 92
Convolutional Neural Networks (CNNs) and Recurrent Neural Networks (RNNs) 93
AI AND ML FOR MOLECULAR PROPERTY PREDICTION 93
Molecular Descriptors and Feature Extraction 93
Prediction of ADMET 94
QSAR Modelling 95
Enhancements in Molecular Property Prediction through Deep Learning 96
Case Studies in Molecular Property Prediction 97
TARGET IDENTIFICATION AND VALIDATION USING AI AND ML 98
Overview of Target Identification Process 98
AI-Based Algorithms for Identifying Biological Targets 98
Network-Based Approaches and Drug-Target Interactions 99
ML for Predicting Off-Target Effects 99
Case Studies in Target Identification 100

AI-DRIVEN DRUG OPTIMIZATION AND DESIGN 101
Drug Lead Optimization Using Machine Learning 101
Generative Models for *De Novo* Drug Design 102
Variational Autoencoders (VAEs) 102
Generative Adversarial Networks (GANs) 103
Structure-Based Drug Design with AI Enhancements 103
AI for Ligand and Receptor Binding Prediction 104
Real-World Examples of AI in Drug Optimization 104
AI IN VIRTUAL SCREENING AND COMPOUND LIBRARY ANALYSIS 105
AI and ML Approaches to Virtual Screening 105
Enhancements in High-Throughput Screening *via* Machine Learning 105
Ligand-Based and Structure-Based Virtual Screening Using AI 106
Predictive Models for Screening Large Compound Libraries 106
Case Studies in Virtual Screening 107
AI AND ML FOR PREDICTIVE ADMET ANALYSIS 107
Introduction to ADMET in Drug Development 107
Machine Learning Models for ADMET Prediction 108
AI in Toxicity Prediction and Risk Assessment 109
Integrating AI and ML for Comprehensive ADMET Profiling 109
Case Studies in ADMET Prediction 110
CASE STUDIES IN AI AND ML-DRIVEN DRUG DISCOVERY 111
Case Study 1: AI in the Development of COVID-19 Therapeutics 111
Case Study 2: Application of Machine Learning in Cancer Drug Discovery 111
Case Study 3: AI for Antiviral Drug Design 112
Case Study 4: Machine Learning for Antibiotic Discovery 112
CHALLENGES AND FUTURE DIRECTIONS 112
CONCLUSION 113
ACKNOWLEDGEMENT 114
REFERENCES 114

CHAPTER 5 DRUG REPURPOSING: COMPUTATIONAL APPROACHES AND SUCCESS STORIES 123
Haema Ganapathi, Karthikeyan Ramadoss, Shanmuganathan Seetharaman, Saravanan Ravindiran and *Palanirajan Vijayarajkumar*
INTRODUCTION 124
COMPUTATIONAL APPROACHES FOR DRUG REPURPOSING 125
Data-Driven Approaches 126
Machine Learning and AI for Drug Repurposing 128
Role of Big Data and Bioinformatics in Identifying Drug Candidates 130
Molecular Docking and Simulation Techniques 131
Applications in Target Identification 132
Success Stories Using Molecular Docking 133
Network-Based Approaches 133
Network Pharmacology in Drug Repurposing 133
Drug-Target Interaction Prediction Using Network Models 135
Omics-Based Approaches 136
Transcriptomics, Proteomics, and Metabolomics in Repurposing 136
Integrating Multi-Omics Data for Target Recognition 137
SUCCESS STORIES OF REPURPOSED DRUGS 138
Repurposed Drugs for Infectious Diseases 139
Oncology Applications 140

Neurological Disorders 141
INTEGRATING A.I. AND M.L. 141
AI-Driven Prediction of Drug-Target Interactions 141
Use of Natural Language Processing (NLP) for Literature Mining 142
Examples of AI-Based Platforms for Drug Repurposing 142
TOOLS AND DATABASES FOR DRUG REPURPOSING 143
Overview of Key Tools 143
CANDO (Computational Analysis of Novel Drug Opportunities) 143
DrugBank 144
LINCS (Library of Integrated Network-Based Cellular Signatures) 144
Case Studies Using Popular Tools 144
CHALLENGES AND FUTURE DIRECTIONS 145
CONCLUSION 145
AI DISCLOSURE STATEMENT 146
REFERENCES 146

CHAPTER 6 MOLECULAR DYNAMICS: INSIGHTS AND APPLICATIONS IN COMPUTER-AIDED DRUG DESIGN 151
Ritu Raj Kumar, Arun Mittal, Rohit Pandey, Satish Sardana, Nandini Sharma and *Pragati Gupta*
INTRODUCTION 152
THEORETICAL FOUNDATIONS OF MOLECULAR DYNAMICS 152
Principles of Classical Mechanics in MD 152
Force Fields and Potential Energy Functions 153
Commonly Used Force Fields in Drug Design 153
Comparison of Force Field Accuracy 156
Simulation Algorithms in MD 156
Integration Algorithms 157
Boundary Conditions 157
Thermodynamic Ensembles 159
WORKFLOW OF MOLECULAR DYNAMICS SIMULATIONS 160
System Preparation and Parameterisation 161
Ligand and Receptor Preparation 161
Solvation and Ionisation 162
Energy Minimisation and Equilibration 163
Production Runs and Sampling 164
File Uploading, Trajectory Handling, and Data Extraction in Major MD Software 164
APPLICATIONS OF MOLECULAR DYNAMICS IN DRUG DESIGN 165
Conformational Sampling and Protein Flexibility 165
Ligand-Receptor Interactions 166
Binding Free Energy Calculations 166
Hotspot Identification in Binding Sites 167
Virtual Screening and Lead Optimisation 168
Predicting the Effects of Mutations on Drug Binding 168
ADVANCED MD TECHNIQUES FOR DRUG DESIGN 169
Accelerated MD (aMD) and Enhanced Sampling Methods 169
Replica Exchange Molecular Dynamics (REMD) 170
Free Energy Perturbation (FEP) and Alchemical Transformations 171
Hybrid Quantum Mechanics/Molecular Mechanics Simulations 171
CASE STUDIES 173
MD Simulations in Designing Kinase Inhibitors 173

Application of MD in Antiviral Drug Development 174
MD for Understanding Resistance Mechanisms in Antibiotics 175
CHALLENGES AND FUTURE DIRECTIONS 176
CONCLUSION 177
CONSENT FOR PUBLICATIONS 177
AI DISCLOSURE STATEMENT 178
REFERENCES 178

CHAPTER 7 HANDS-ON CADD LEARNING: DATASETS, TOOLS, AND SOFTWARE TUTORIALS 186
Anwesha Pal, Dimple Pandey, Pradeep Kumar, Poulomi Ghosh, Afreen Bano, Shubhanshi Kulshrestha and *Salim Albukhaty*
INTRODUCTION 186
DATASETS FOR PRACTICAL EXERCISES 187
Curating Reliable Datasets for CADD 187
Types of Datasets and Their Applications 188
QSAR Modeling Datasets 188
Molecular Docking Datasets 189
Pharmacophore Mapping Datasets 190
ADMET Prediction Datasets 191
Sources of Publicly Available CADD Datasets 191
PubChem 191
Source of information 192
ChEMBL 192
DrugBank 192
SOFTWARE TUTORIALS FOR CADD 193
Overview of CADD Software Tools 193
Open-Source Tools 193
Commercial Softwares 193
Step-by-Step Guides for Popular Tools 193
Molecular Docking with AutoDock and AutoDock Vina 193
Preparation of protein 194
vina --config config.txt --log log.txt 194
Virtual Screening 195
Pharmacophore Mapping with MOE 196
ADMET Prediction Using SwissADME 199
QSAR Modeling with Schrodinger's QSAR Module 203
PRACTICAL CASE STUDIES 207
Case Study 1: Designing HIV Protease Inhibitors Using Molecular Docking 207
Problem Definition and Workflow 207
Tools and Datasets Used 208
Analysis of Results and Insights 208
Case Study 2: QSAR Modeling for Anticancer Agents 209
Building Predictive Models for Cytotoxic Activity 209
Validation and Application in Drug Design 210
Case Study 3: Using Pharmacophores to get the Most Out of Leads for Kinase Inhibitors ... 211
Uncovering Salient Pharmacophoric Properties 212
Increasing Binding Affinity by Lead Optimization 212
EXERCISES AND CHALLENGES 213
QSAR Modeling Challenge: Predicting Antibacterial Activity 213
Task 1: Availability and Quality of Data 213

Task 2: Selection of Molecular Descriptors 213
Task 3: Dataset Unbalance 213
Task 4: Choosing a Model and Overfitting 213
Task 5: Generalizability and External Validation 214
Task 6: Mechanistic Interpretation and Models Without a Box 214
Task 7: Limitations in the Applicability Domain (AD) 214
Docking Exercise Drug-Receptor Interactions for Cholinesterase Inhibitors 214
Assignment: 214
Challenges: 215
Challenges: 215
Pharmacophore Mapping Task: Designing Novel Compounds for Anti-Inflammatory Targets 215
Task 1: Gaining Knowledge on Pharmacophore Mapping 215
Task 2: Development of Novel Ligands using Pharmacophore Mapping 215
Task 3: Online Screening 216
ADMET Anticipation Challenge: Looking at the Pharmaceutical Properties of New Compounds 216
Task 1: Apply SwissADME to make a good estimate of the ADMET values 216
Task 2: Assessing the Drug-Like Properties of New and Existing Compounds 216
Task 3: Making the Best Oral Therapeutic Formulation 216
Task 4: Drugs, Rankings Based on ADMET 217
RESOURCES AND REFERENCES FOR FURTHER LEARNING 217
Recommended Readings and Tutorials 217
Books 217
Research Papers for Academic Research 217
Online Tutorials and Courses 217
Online Platforms for CADD Training 218
Online Tools for CADD 218
Key References for Further Study 218
CONCLUSION 218
AI DISCLOSURE STATEMENT 219
REFERENCES 219

SUBJECT INDEX 226

FOREWORD

The rapid advancement of computational technologies continues to redefine the landscape of modern drug discovery. The convergence of computational science with pharmaceutical research has created unprecedented opportunities for innovation, enabling researchers to address increasingly complex biological questions through data-driven and predictive approaches. Within this evolving environment, computer-aided drug design (CADD) has become an essential component of contemporary therapeutic development.

This volume, Computer-Aided Drug Design: Advanced Techniques and Emerging Applications, arrives at a pivotal moment in the global pharmaceutical arena, where digital transformation is influencing every stage of the drug discovery pipeline. The chapters presented in this book highlight how advanced computational methodologies are expanding the boundaries of what is possible in pharmaceutical research and development. The contents of this volume reflect the modern evolution of CADD, encompassing innovative approaches such as *de novo* drug design, pharmacophore mapping, virtual screening, artificial intelligence, and machine learning. The inclusion of drug repurposing strategies and molecular dynamics simulations further emphasizes the interdisciplinary scope of computational drug design and its growing importance in understanding complex biological systems. Collectively, these topics illustrate how emerging technologies are accelerating discovery, improving predictive accuracy, and facilitating the identification of novel therapeutic opportunities.

Particularly noteworthy is the practical orientation. The incorporation of tutorials, software-based exercises, and real-world examples enhances its educational value by encouraging readers to apply computational concepts within their own academic and research environments. This combination of advanced theory and experiential learning transforms the book into both a reference text and a valuable guide for developing expertise in the field.

The contributors to this volume represent a diverse scientists and academicians whose collective experience spans multiple domains of pharmaceutical and computational sciences. Their efforts have culminated in a work that captures the dynamic and rapidly evolving nature of CADD, while maintaining scientific rigor and practical relevance.

I commend the editors, Dr. Ajmer Singh Grewal, Dr. Viney Lather, Dr. Geeta Deswal, and Dr. Kumar Guarve, for their outstanding work and dedication in bringing this comprehensive and insightful edited book to fruition. It is a must-read for researchers, healthcare professionals, and students eager to stay abreast of the latest developments in the pharmaceutical and biomedical sciences.

Monika Gupta
Department of Pharmaceutical Chemistry
Amar Shaheed Baba Ajit Singh Jujhar Singh Memorial College of Pharmacy
Bela, Ropar, Punjab, India

PREFACE

The rapid advancement of computational technologies has expanded the scope of computer-aided drug design (CADD) far beyond its traditional applications. Increasing computational power, sophisticated algorithms, extensive molecular databases, and the emergence of artificial intelligence have collectively transformed the strategies employed in modern drug discovery. These developments have enabled researchers not only to predict molecular properties and investigate drug-target interactions but also to design novel therapeutic candidates with greater efficiency and precision.

This volume, Computer-Aided Drug Design: Advanced Techniques and Emerging Applications, focuses on the modern methodologies that are shaping the future of pharmaceutical research. Building upon foundational concepts, the chapters presented herein explore innovative computational approaches that address current challenges in drug discovery and development. Emphasis is placed on the integration of advanced modeling techniques with practical applications that accelerate therapeutic innovation.

Among the major themes of this volume are de novo drug design and virtual screening, both of which exemplify the capacity of computational tools to identify and optimize promising candidates from vast chemical spaces. Pharmacophore mapping is presented as an important strategy for defining essential molecular features associated with biological activity, thereby facilitating lead identification and refinement. The application of computational methods in drug repurposing further illustrates how existing therapeutic agents can be systematically evaluated for novel clinical indications. The transformative role of artificial intelligence and machine learning in CADD constitutes another important focus of this volume. The discussions highlight the incorporation of deep learning methodologies, reinforcement learning strategies, and advanced analytical approaches into drug discovery workflows. These developments demonstrate the potential of emerging technologies to enhance predictive performance and support the design of innovative molecular entities.

Dedicated chapters also address molecular dynamics simulations as powerful tools for investigating biomolecular flexibility, conformational changes, and the thermodynamic factors governing drug–target interactions. Through these approaches, readers gain insight into the dynamic nature of biological systems and the mechanisms that influence therapeutic efficacy. To strengthen practical understanding, the volume incorporates tutorials and software-oriented exercises that encourage the direct application of theoretical concepts within academic and research environments.

This volume reflects the collaborative contributions of experts representing diverse areas of pharmaceutical sciences, computational chemistry, and bioinformatics. Their collective knowledge has resulted in a text that combines advanced methodologies with real-world perspectives on their implementation in drug discovery. It is intended to support the needs of researchers, educators, and graduate students seeking to understand the expanding applications of computational approaches in the pharmaceutical sciences.

As computer-aided methodologies continue to evolve, their influence on the discovery and development of medicines will undoubtedly increase. It is our sincere hope that this volume will not only provide readers with an overview of current advances but also inspire further innovation in the pursuit of safer, more targeted, and more effective therapeutic interventions.

Ajmer Singh Grewal
Guru Gobind Singh College of Pharmacy
Yamuna Nagar, Haryana, India

Viney Lather
Amity Institute of Pharmacy
Amity University, Noida
Uttar Pradesh, India

Geeta Deswal
Guru Gobind Singh College of Pharmacy
Yamuna Nagar, Haryana, India

&

Kumar Guarve
Guru Gobind Singh College of Pharmacy
Yamuna Nagar, Haryana, India

List of Contributors

Anuruddha Chabukswar	School of Health Sciences and Technology, Dr. Vishwanath Karad MIT World Peace University, Pune, Maharashtra, India
Arun Mittal	Hindu College of Pharmacy, Sonipat, Haryana, India
Anwesha Pal	Department of Bioinformatics, MMV, Banaras Hindu University, Varanasi, Uttar Pradesh, India
Afreen Bano	Department of Bioinformatics, MMV, Banaras Hindu University, Varanasi, Uttar Pradesh, India
Devesh U. Kapoor	Dr. Dayaram Patel Pharmacy College, Bardoli-394601, Gujarat, India
Deepika Choudhary	Department of Pharmaceutical Sciences and Natural Products, Central University of Punjab, Bathinda, Punjab, India
Dishank Purandare	School of Health Sciences and Technology, Dr. Vishwanath Karad MIT World Peace University, Pune, Maharashtra, India
Dimple Pandey	Department of Bioinformatics, MMV, Banaras Hindu University, Varanasi, Uttar Pradesh, India
Gouri Shankar Chakraborty	Department of Computer Science and Engineering, Lovely Professional University, Phagwara, Punjab, India
Haema Ganapathi	School of Pharmacy, Sri Balaji Vidyapeeth (Deemed to be University), SBV Campus, Pillaiyarkuppam, Bahour, Puducherry 607402, India
Jyoti Monga	Ch. Devi Lal College of Pharmacy, Jagadhri, Haryana, India
Joy Das	School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, Punjab, India
Joy Chakra Bortty	Department of Computer Science, Westcliff University, Irvine, California, USA
Karthikeyan Ramadoss	School of Pharmacy, Sri Balaji Vidyapeeth (Deemed to be University), SBV Campus, Pillaiyarkuppam, Bahour, Puducherry 607402, India
Minky Mukhija	Ch. Devi Lal College of Pharmacy, Jagadhri, Haryana, India
Nemat Ali	College of Pharmacy, King Saud University, Riyadh, Saudi Arabia
Neha Sharma	School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, Punjab, India
Nandini Sharma	Faculty of Pharmacy, Swami Vivekananda Subharti University, Meerut, Uttar Pradesh, India
Prajakta Adsule	School of Health Sciences and Technology, Dr. Vishwanath Karad MIT World Peace University, Pune, Maharashtra, India
Palanirajan Vijayarajkumar	Faculty of Pharmaceutical Sciences, UCSI University, Kuala Lumpur (South Wing) No.1, Jalan Menara Gading, UCSI Heights 56000, Kuala Lumpur, Malaysia
Pragati Gupta	University of Leipzig, Saxony, Germany
Pradeep Kumar	Department of Botany, MMV, Banaras Hindu University, Varanasi, Uttar Pradesh, India

Poulomi Ghosh	Department of Bioinformatics, MMV, Banaras Hindu University, Varanasi, Uttar Pradesh, India
Riya Singla	Ch. Devi Lal College of Pharmacy, Jagadhri, Haryana, India
Rajender Kumar	Department of Biomedical and Clinical Sciences, Division of Infection and Inflammation, Linköping University, Linköping, Sweden Department of Chemistry, School of Engineering Sciences in Chemistry, Biotechnology and Health, KTH Royal Institute of Technology, AlbaNova University Center, Stockholm 106 91, Sweden
Ritu Raj Kumar	I T S College of Pharmacy, Muradnagar, Ghaziabad, Uttar Pradesh 201206, India
Rohit Pandey	Dr. KN Modi Institute of Pharmaceutical Education and Research, Modinagar, Ghaziabad, Uttar Pradesh, India
Shaikh Mohmed Adnan Mohmed Javid	Shree Dhanvantary Pharmacy College, Kim-394110, Gujarat, India
Sonam M. Gandhi	Shree Dhanvantary Pharmacy College, Kim-394110, Gujarat, India
Satyawan Jadhav	Alnylam Pharmaceuticals Ltd, Boston, USA
Shanmuganathan Seetharaman	School of Pharmacy, Sri Balaji Vidyapeeth (Deemed to be University), SBV Campus, Pillaiyarkuppam, Bahour, Puducherry 607402, India
Saravanan Ravindiran	Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India
Satish Sardana	Amity Institute of Pharmacy, Amity University, Gurugram, Haryana, India
Shubhanshi Kulshrestha	Department of Bioinformatics, MMV, Banaras Hindu University, Varanasi, Uttar Pradesh, India
Salim Albukhaty	Department of Chemistry, College of Science, University of Misan, Amarah, Mayasan 62001, Iraq
Utpal Bhui	School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, Punjab, India Department of Pharmaceutical Sciences, NSHM Institute of Pharmaceutical Technology, NSHM Knowledge Campus, Durgapur, West Bengal 713212, India

CHAPTER 1

Designing Drugs from Scratch: The Computational and AI Revolution in *De Novo* Drug Discovery

Shaikh Mohmed Adnan Mohmed Javid[1], Sonam M. Gandhi[1], Nemat Ali[2] and **Devesh U. Kapoor[3,*]**

[1] *Shree Dhanvantary Pharmacy College, Kim-394110, Gujarat, India*

[2] *College of Pharmacy, King Saud University, Riyadh, Saudi Arabia*

[3] *Dr. Dayaram Patel Pharmacy College, Bardoli-394601, Gujarat, India*

Abstract: The computational design of new drugs (also known as *de novo* drug design) enables researchers to create a completely new therapeutic molecule without requiring any previous knowledge of an existing drug or compound for inspiration, through the use of Advanced Algorithms and Structural Information. The methodologies and techniques for this type of molecular discovery are thoroughly covered in this chapter and introduce readers to the foundational Principles and Importance of Drug Discovery. The methodology section details the various approaches (both structure-based and ligand-based) that can be taken when performing *de novo* drug design, as well as the atom- and fragment-based methods for constructing molecules. This chapter details the importance of Sampling Methods in the exploration of Chemical Space and the need for various sampling methods (*i.e.*, Monte Carlo, Genetic Algorithms, *etc.*) in order to produce a diverse library of potential compounds. As such, this chapter will serve as a useful reference for both New and Experienced Researchers and/ or Professionals interested in learning about cutting-edge methodologies of drug discovery *via de novo* design and their application to the Research and Development of Therapeutic Agents (*i.e.*, Drugs). The latter section discusses the use of Evolutionary Algorithms and related concepts based on Evolutionary Principles (*i.e.*, adaptation based on natural selection) that are beneficial for optimising Molecular Design. In addition, this chapter will provide an overview of the emergent technologies of Deep Reinforcement Learning (DRL) and will discuss the potential of these technologies to transform the Automation and Optimization of Drug Discovery Processes. Finally, in the Future Perspectives section, we will discuss Emerging Trends, Challenges, and Opportunities related to the use of DRL for Drug Design.

[*] **Corresponding author Devesh U. Kapoor:** Dr. Dayaram Patel Pharmacy College, Bardoli-394601, Gujarat, India; E-mail: dev7200@gmail.com

Ajmer Singh Grewal, Viney Lather, Geeta Deswal & Kumar Guarve (Eds.)
All rights reserved-© 2026 Bentham Science Publishers

Keywords: Atom-centric design, AutoGrow, Computational approaches to drug discovery, Evolutionary computation, Exploration of chemical diversity and optimization in drug design, Fragment-oriented design, Innovative drug creation, Lamarckian evolutionary method, Molecular exploration.

INTRODUCTION

De novo drug design is a sophisticated and intricate process that involves the generation of entirely new lead compounds characterized by desirable pharmacological effects and optimal physicochemical properties conducive to therapeutic applications [1, 2]. These advanced computational models possess the remarkable ability to synthesize and generate a wide array of molecular structures that exhibit particular and predetermined physical or biological characteristics, achieved through the sophisticated integration of both predictive and generative neural network architectures that work in tandem to optimize the molecular design process [3, 4].

PRINCIPLES OF *DE NOVO* DRUG DESIGN

The fundamental concept of *de novo* drug design pertains to the synthesis of innovative drug-like entities from a foundational level, employing sophisticated computational methodologies and artificial intelligence. This methodology aspires to enhance the drug discovery paradigm by producing compounds endowed with targeted pharmacological characteristics, consequently diminishing the temporal and material investments customarily necessitated by conventional approaches. The subsequent sections delineate critical components of *de novo* drug design [5, 6]. The approach to designing drugs based on the structure begins with an in-depth grasp of the spatial arrangement of a protein of interest. This particular protein acts as the cornerstone for the identification of potential drug-binding sites [7].

De Novo Software and Its Methodology

De novo software tools are essential in various scientific disciplines for creating novel molecules, genetic assemblies, and peptide sequences without relying on existing templates. These tools employ various methodologies, from rule-based systems to modern artificial-intelligence systems. In drug discovery, AutoGrow4 employs a genetic algorithm to evolve small molecules through mutation and crossover, optimizing based on docking scores [8]. REINVENT integrates reinforcement learning with SMILES-based generative models to produce molecules with desired pharmacological profiles [9]. Another approach, the deep graph molecular generator, utilizes graph neural networks to simultaneously generate compounds and predict their properties [10]. The drug AI platform

merges transformer-based deep learning with the Monte Carlo Tree Search to efficiently explore the chemical space [11]. In genomics, SOAPdenovo-Trans assembles transcriptomes from RNA-Seq data without a reference genome using a de Bruijn graph model to handle alternative splicing and gene variation [12]. HipMer scales this task for large genomes by using parallel processing to assemble the sequences on supercomputers [13]. For metagenomics, DIME applies a divide-and-conquer strategy by clustering reads and merging partial assemblies to improve accuracy and performance. In proteomics, Point Novo leverages deep neural networks to predict peptide sequences directly from mass spectra, thereby enhancing performance across different resolutions [14]. Contra Novo applies contrastive learning to improve the identification of peptide-spectrum matches [15], whereas Vonode uses mass accuracy scoring to improve *de novo* peptide identification [16]. These tools highlight the growing integration of AI and high-performance computing in biological design and analysis, thereby driving innovation in drug development and genomics and proteomics research.

Determining the Protein Structure

The preliminary phase of the drug discovery continuum entails the acquisition of structural information on the target protein. Using techniques such as X-ray crystallography, Nuclear Magnetic Resonance (NMR), or cryo-electron microscopy [17], researchers can uncover the shape and surface details of a protein, helping them understand how it functions and interacts with other molecules. The identification of pivotal pockets and grooves within proteins is essential for the formulation of molecules capable of effective interactions [18].

Modeling the Binding Site

When the protein structure is available, computational models are used to delineate and scrutinize the binding sites [7]. The procedure includes thorough mapping of the chemical and physical features of the site, incorporating hydrophobic segments, hydrogen bond donors and acceptors, and electrostatic interactions [19]. By constructing a model of this pocket, investigators can forecast which categories of molecules may fit and engage optimally [7].

Designing a Molecule: That Fits. Grounded in the binding site model, chemists and computational biologists collaborate to engineer prospective drug candidates. These compounds are meticulously designed to align with the shape and chemical characteristics of the pocket, thereby ensuring a robust and specific interaction [7]. Utilizing computational docking and molecular dynamics simulations, the stability and binding efficacy of these compounds are assessed prior to progressing to laboratory experimentation [19].

CHAPTER 2

Pharmacophore Mapping: Principles, Techniques, and Applications

Jyoti Monga[1], Riya Singla[1], Deepika Choudhary[2], Minky Mukhija[1] and Rajender Kumar[3,4,*]

[1] *Ch. Devi Lal College of Pharmacy, Jagadhri, Haryana, India*

[2] *Department of Pharmaceutical Sciences and Natural Products, Central University of Punjab, Bathinda, Punjab, India*

[3] *Department of Biomedical and Clinical Sciences, Division of Infection and Inflammation, Linköping University, Linköping, Sweden*

[4] *Department of Chemistry, School of Engineering Sciences in Chemistry, Biotechnology and Health, KTH Royal Institute of Technology, AlbaNova University Center, Stockholm 106 91, Sweden*

Abstract: Pharmacophore modeling is a highly advantageous approach in drug discovery, as it examines the chemical features of a structure to identify its biological properties. Ligand refinement and virtual screening correlate the biological activity of a compound with its chemical structure, thereby accelerating the drug discovery process. There are two major types of pharmacophore modeling, namely ligand-based pharmacophore modeling, where the pharmacophore model is derived from the information inferred from the active ligands, and structure-based pharmacophore modeling, where the pharmacophore model is derived from the three-dimensional structure of the target protein. However, this step is normally followed by molecular docking simulation and molecular dynamics simulation to calculate the binding affinity energy between the target protein and ligands. Conformational search plays a very significant role in pharmacophore modeling, where there is an accurate representation of the biological active conformations. Various computational methods are used extensively for the effective sampling of the conformations. Validation of the model becomes very essential for the predictive accuracy of the model, where the models can be validated using parameters such as ROC curves, Enrichment factors, or Goodness-of-Hit scores. Once validated, the pharmacophore models can be used in high-throughput virtual screenings and allow researchers the opportunity to efficiently identify drug candidates. Ongoing advancements in computational methodologies, combined with preclinical investigations, have significantly enhanced the ability of pharmacophore modelling to support lead molecule identification.

* **Corresponding author Rajender Kumar:** Department of Chemistry, School of Engineering Sciences in Chemistry, Biotechnology and Health, KTH Royal Institute of Technology, AlbaNova University Center, Stockholm 106 91, Sweden; E-mail: rajbioinformaticshau@gmail.com

Ajmer Singh Grewal, Viney Lather, Geeta Deswal & Kumar Guarve (Eds.)
All rights reserved-© 2026 Bentham Science Publishers

Keywords: Aromatic rings, Hydrogen bond donor, Hydrogen bond acceptor, Hydrophobic interactions, Ligand-based drug design, Pharmacophore modeling, Virtual screening, 3D pharmacophore.

INTRODUCTION

Pharmacophore modelling is a critical computational approach that identifies the biological properties based on the chemical features of lead compounds [1]. It relies on the structural diversity of ligands and their therapeutic potential and serves as an essential tool for determining the pharmacophoric features of novel compounds [2]. This technological framework aids in detecting and evaluating potential interactions between ligands and receptors, guided by electronic and steric attributes required for biological response activation [3]. The methodology incorporates a diverse set of lead compounds, which are screened based on toxicity profiling of all ligands [4]. Common applications of pharmacophore modelling include prediction of absorption, distribution, metabolism, excretion, and toxicity with the help of specialized databases, and prediction of off-target interactions, which may provide therapeutic advantages [5]. The effectiveness of pharmacophoric approaches is evaluated by several metrics. Many software platforms, such as LigandScout, Discovery Studio, Schrödinger's Phase, Molecular Operating Environment (MOE), PharmMapper, and ZINC Pharmer, support the pharmacophore modelling workflow [6]. These tools play an important role in developing and aligning virtual screening programs with pharmacophore modelling. However, some challenges still exist. These include those associated with the quality of the data generated, the representation of the molecular structure, and the computational cost. These affect the results of the computations performed [7]. Current research has centered around the combination of AI tools based on quantum mechanics principles. This increases the efficiency of the computations as well as decreases the computational cost [8]. An important component of the pharmacophore modeling process is the search for the structure's conformation. This is crucial for the identification and analysis of the pharmacophoric properties presented by their biologically active forms [9]. Because molecules are inherently flexible in nature, they can adopt various conformations that are explored using techniques such as systematic searches, Monte Carlo simulations, molecular dynamics, genetic algorithms, and distance geometry [10]. Effective conformational searches greatly enhance predictive accuracy. Pharmacophore model verification is also necessary because it allows discrimination between active and inactive compounds to guarantee efficient screening [11]. The use of goodness-of-fit score measures, receiver operating characteristic plots, and enrichment factors represents some of the criteria applied to assess pharmacophoric model success. The development of a pharmacophoric model is capable of facilitating efficient high-throughput virtual screening to

rapidly assess thousands of compounds with high predictive accuracy [12]. Therefore, pharmacophoric model generation has emerged as a core tool in contemporary drug development. The ability to accurately identify crucial molecular properties to facilitate virtual screening and characterization of compounds [13] makes pharmacophoric model generation a very efficient drug development technique [14]. Continued advancements in computational techniques and their integration with experimental work contribute to rational drug therapy and design, resulting in more effective therapies with enhanced bioavailability [15].

PHARMACOPHORE FEATURES AND THEIR IDENTIFICATION

The process of pharmacophoric modelling is fundamentally based on the principle that similar spatial arrangements and shared chemical functionalities are responsible for biological activity in compounds targeting similar receptors [16, 17]. In pharmacophoric models, the chemical characteristics of molecules that interact with a receptor are represented geometrically through elements such as spheres, planes, and vectors. The essential pharmacophoric features include Hydrogen Bond Acceptors (HBAs), Hydrogen Bond Donors (HBDs), hydrophobic regions (H), ionizable groups (both positively and negatively charged; PI/NI), aromatic groups (AR), and metal-coordination sites, as illustrated in Fig. (**1**). Additonally, constraints related to the spatial dimensions of these features may be incorporated through shape constraints or exclusion volumes (XVOL), which define sterically forbidden regions and effectively represent the size and contours of receptor binding pockets [18, 19].

Kinds of Pharmacophore Attributes

Hydrogen Bond Acceptors and Hydrogen Bond Donors

HBDs are the name given to the atoms or functional groups in a chemical entity that have the ability to donate a hydrogen atom in the formation of hydrogen bonds. Common examples include hydroxyl (-OH), amines (-NH), and sulfur (-SH) compounds. The process of identifying the HBDs in a chemical entity is the analysis of the hydrogen atoms bonded to the electronegative atoms oxygen, nitrogen, or sulfur. In contrast, HBAs are atoms or groups capable of accepting hydrogen bonds, commonly represented by carbonyl groups (C=O), ethers (R-O-R), and tertiary amines (R_3N). The identification of HBAs involves the location of highly electronegative atoms with lone pairs, which in most cases include oxygen, nitrogen, or fluorine. This is done with the use of molecular modeling software [20, 21].

CHAPTER 3

From Molecules to Medicines: Virtual Screening and *In Silico* Design in Modern Drug Discovery

Dishank Purandare[1], Prajakta Adsule[1], Satyawan Jadhav[2] and **Anuruddha Chabukswar[1,*]**

[1] *School of Health Sciences and Technology, Dr. Vishwanath Karad MIT World Peace University, Pune, Maharashtra, India*

[2] *Alnylam Pharmaceuticals Ltd, Boston, USA*

Abstract: *In silico* drug design has emerged as a vital component of pharmaceutical research, offering a faster and more economical way to discover and optimize new therapeutic agents. Through the use of molecular modelling and both structure-based and ligand-based strategies, researchers can predict how potential molecules behave long before laboratory testing begins. Structure-based design makes use of detailed protein structures to understand ligand binding by means of molecular docking and molecular dynamics, while ligand-based design depends on quantitative structure-activity relationships, molecular similarity, and *de novo* chemical design to explore new scaffolds. Virtual screening, which draws from both these approaches, allows large compound libraries to be examined efficiently to identify candidates with favorable binding profiles and pharmacokinetic features. The growing role of computational intelligence has refined the accuracy of such predictions, leading to better hit selection and faster optimization of lead molecules. Despite these advances, certain challenges remain, including high computational demand, limitations of force-field models, and occasional false-positive predictions. This chapter outlines the essential principles and techniques used in computational drug discovery, summarizes key tools and databases, and highlights recent developments through selected case studies. It also reflects on ethical and regulatory aspects of this evolving field, emphasizing how these digital methods are reshaping modern drug development and paving the way for more personalized therapeutic solutions.

Keywords: Drug discovery, *In-silico* drug design, MD Simulations, Molecular docking, QSAR, Virtual screening.

INTRODUCTION

In silico drug design has become a defining element of modern pharmaceutical research, transforming how new medicines are discovered and refined. It involves

[*] **Corresponding author Anuruddha Chabukswar:** School of Health Sciences and Technology, Dr. Vishwanath Karad MIT World Peace University, Pune, Maharashtra, India; E-mail: anuruddha.chabukswar@mitwpu.edu.in

Ajmer Singh Grewal, Viney Lather, Geeta Deswal & Kumar Guarve (Eds.)
All rights reserved-© 2026 Bentham Science Publishers

the use of computer-based models and algorithms to understand, predict, and modify potential drug molecules long before experimental testing begins [1]. These tools make it possible to screen enormous chemical libraries, anticipate molecular behaviour, and estimate pharmacokinetic and toxicological profiles, all within a fraction of the time required for conventional experimentation [2]. Traditional discovery methods often depend on high-throughput screening and structure-activity studies that demand extensive laboratory work, specialized assays, and animal testing [3]. Although such methods have produced many successful drugs, they are slow, expensive, and sometimes inefficient when scaled to modern research needs [4]. Failures in late-stage clinical trials, frequently caused by poor efficacy or unanticipated toxicity, further underline the need for more predictive, data-driven approaches [5]. Computational discovery methods use molecular docking, virtual screening, molecular dynamics, and QSAR modelling to simulate how molecules interact with biological targets [6]. This allows researchers to identify a smaller, more promising set of candidates for laboratory validation, sharply reducing the time and cost associated with wet-lab work. Among the major advantages of these techniques is the ability to forecast ADMET properties and to focus on molecules with suitable pharmacokinetic and safety characteristics [1, 7]. Both structure-based and ligand-based virtual screening contribute to this process. The former explores ligand–target binding using atomic-level data, while the latter searches for compounds with activity similar to known drugs through pharmacophore analysis and molecular fingerprints [8, 9]. Together, these approaches help identify potential leads more efficiently and eliminate weak or unsuitable candidates at an early stage. A further benefit of computational methods lies in their potential for cost control. Developing a new drug through conventional procedures can require more than ten years and immense financial investment. *In silico* screening, by narrowing down the list of viable compounds early, reduces unnecessary synthesis and testing, conserving both time and resources [10]. Another growing use of these methods is in drug repurposing, evaluating existing approved molecules for new therapeutic purposes, an approach that shortens development timelines and lowers regulatory risks [11]. This strategy has proved particularly valuable when rapid solutions are needed, such as during epidemic outbreaks. While computational drug design has made remarkable progress, it still faces certain limitations. The accuracy of results depends heavily on the quality of experimental and structural data available for model training. Incomplete or inconsistent datasets can yield misleading predictions, which must be cross-checked through laboratory validation. Moreover, docking methods often treat proteins as rigid structures, whereas their actual interactions are dynamic and complex; molecular dynamics simulations are therefore essential to capture realistic binding behaviour [12]. Continuous advances in modelling, combined with improvements in experimental

structural biology, are expected to make predictions more reliable and broadly applicable. Overall, *in silico* design represents a cost-effective and time-saving approach that complements traditional research. By uniting molecular docking, virtual screening, QSAR analysis, and predictive modelling, it has redefined the early stages of drug discovery, improving both accuracy and the likelihood of clinical success.

SIMILARITY-BASED METHODS FOR VIRTUAL SCREENING

Similarity-based virtual screening has become one of the most practical tools in modern computational drug discovery. It is mainly applied to locate new molecules that may display biological activity similar to that of known drugs or reference ligands [13]. Rather than relying on a detailed three-dimensional structure of the target protein, this approach is guided by the long-standing observation that compounds sharing close structural or physicochemical features often produce comparable biological responses. This concept, commonly termed the similarity activity relationship, has been demonstrated repeatedly in many discovery programs and continues to serve as a fundamental idea in cheminformatics. In practice, similarity-based screening measures how closely two molecules resemble each other through numerical descriptors and statistical comparison methods. Because of its flexibility and speed, it is frequently chosen for the early sorting of very large compound libraries, particularly in situations where accurate structural data for the biological target are missing or incomplete [14].

Principle of Similarity-Based Screening

The guiding idea behind similarity-based screening is that compounds sharing close structural or physicochemical traits are likely to interact with the same biological target or display comparable activity. This notion follows the neighbourhood behaviour concept, which holds that small structural alterations usually lead to gradual changes in biological effect. In practice, the process begins with a compound already known to be active, often called the reference or query molecule, and evaluates other molecules in a chemical database to determine how closely they resemble it. Molecules surpassing a predefined similarity threshold are retained as putative hits for further experimental or computational evaluation. The similarity can be quantified using molecular fingerprints, molecular graphs, or three-dimensional molecular fields, and scored using various coefficients such as Tanimoto, Dice, or Cosine similarity indices. Despite its empirical nature, this approach has been remarkably effective in identifying hits for orphan targets, scaffold hopping, and lead expansion in various therapeutic areas [15].

CHAPTER 4

Integrating Artificial Intelligence (AI) and Machine Learning (ML): Revolutionizing Computer-Aided Drug Design

Joy Das[1], **Gouri Shankar Chakraborty**[2], **Utpal Bhui**[1,4], **Joy Chakra Bortty**[3] and **Neha Sharma**[1,*]

[1] *School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, Punjab, India*

[2] *Department of Computer Science and Engineering, Lovely Professional University, Phagwara, India*

[3] *Department of Computer Science, Westcliff University, Irvine, California, USA*

[4] *Department of Pharmaceutical Sciences, NSHM Institute of Pharmaceutical Technology, NSHM Knowledge Campus, Durgapur, West Bengal 713212, India*

Abstract: The emergence of ML and AI systems has transformed how computers assist in drug design, helping us find drugs faster while saving money and making more accurate predictions. This book takes readers into the connection between AI, ML, and pharma research to show how these tools transform drug development. This book delves into basic AI and ML aspects as it shows how these systems work with established CADD procedures. Our book explains how AI methods make molecular docking and drug design tools faster and more specific. Through deep learning technology, the book studies how predictions work in drug-target interactions while exploring pharmacokinetics and toxicity, as well as NLP applications in biomedical research. The book shows how generative AI identifies new drug compounds, reinforcement learning improves design results, and AI analyses multiple types of biological data. It combines practical examples of AI-assisted discovery with modern advances in the field. We discuss both ethical issues and practical problems linked to AI use in drug research, as well as the rules governing this technology. Thus, this chapter provides detailed information for anyone who wants to use AI and ML to help find better drugs faster.

Keywords: Artificial Intelligence, Computer-aided drug design, Deep learning, Drug discovery, Machine learning, Molecular docking.

[*] **Corresponding Author Neha Sharma:** School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, Punjab, India; E-mails: c4nehagautam@gmail.com, neha.20527@lpu.co.in

Ajmer Singh Grewal, Viney Lather, Geeta Deswal & Kumar Guarve (Eds.)
All rights reserved-© 2026 Bentham Science Publishers

INTRODUCTION

Modern drug discovery and development processes experience transformation through Artificial Intelligence (AI) and Machine Learning (ML), which deliver innovative approaches to reduce operational expenses and shorten the developmental time [1]. Drug discovery, together with design, presents substantial complexity and requires substantial resources to identify targets, develop safe medications with therapeutic effects, and reduce harmful effects throughout the process [2]. Advanced drug design processes emerged when researchers incorporated computer-aided drug design (CADD) systems to perform biomedical data analysis for target identification, hit hunting, and lead discovery. Drug discovery progress has sped up because of the introduction of AI and ML into CADD [3]. The extensive growth of biological, chemical, and pharmaceutical datasets allows advanced algorithms to analyze massive databases and find hidden connections that lead to new drug discoveries. Predictions of drug efficacy and safety result from supervised learning methods, which include both regression models and classification algorithms [4]. The exploration of complex biological data through clustering and dimensionality reduction techniques occurs without predefined labels. Reinforcement learning demonstrates its value as an advanced tool for formulating drugs through feedback loops, while deep learning methods featuring neural networks and convolutional neural networks (CNNs) successfully analyze drug chemical makeup and anticipate how they function [5]. The development of ML technologies, together with AI systems, strengthens the process of predicting essential drug design properties. These technologies have predictive power in terms of accurate identification of features from Absorption Distribution Metabolism Excretion and Toxicity (ADMET) properties using molecular descriptors and feature extraction techniques [6]. The use of deep learning to integrate into Quantitative Structure-Activity Relationship (QSAR) modeling provides new results regarding how chemical structures are related to biological responses [7]. These technologies have been shown to be practical for forecasting critical properties of drug safety and efficacy. Algorithms driven by AI give support to the essential process of discovering and validating drug targets in drug discovery research. AI-based algorithms are used to identify and validate drug targets, which is an important process in drug discovery for achieving better results. Utilizing predictive methods along with off-target assessment mechanisms guarantees better drug-target interactions [8]. Complex biological visualization is augmented by network-based methodologies to aid in a better understanding of disease mechanisms and, hence, the development of better drugs. Generative models such as Generative Adversarial Networks (GANs) and Variational Autoencoders (VAEs) have emerged as the contemporary flavor of generative model development for the study of *de novo* drug design [9]. Advanced models are used to generate new molecules with favorable properties. Using AI in

structure-based drug discovery methods, together with receptor-ligand binding prediction techniques, results in a better identification of effective therapeutic compounds. The revolution that AI enabled in compound analysis is virtual screening, which uses enhanced high-throughput screening (HTS) to identify better drug candidates from large libraries. By combining vast amounts of data sources, AI, together with ML, makes predictive drug safety and efficacy testing techniques possible in a wide variety of ways. AI-enhanced drug discovery has demonstrated its value in the creation of COVID-19 treatments and other groundbreaking cancer medicines and has great potential to address the most important global healthcare problems [10]. Although recent achievements in the application of AI and ML for drug discovery have been made, we still face some roadblocks, such as data quality issues, the required interpretability of algorithms, and regulatory compliance requirements. The advancements of these technologies show potential to generate new capabilities for precise medical treatments and customized therapeutic methods [11]. In this book chapter, we will explore how AI and ML techniques support drug design practices while examining their molecular property prediction capabilities alongside target identification and validation methods. The chapter analyzes drug optimization methods enabled by AI, as well as virtual screening practices and predictive ADMET analysis methods. The chapter demonstrates drug discovery successes along with practical investigations of AI and ML in drug discovery through several case examples. Finally, the exploration concludes by examining modern obstacles and anticipated future directions in the realm of AI and ML in computer-aided drug design.

CORE AI AND ML TECHNIQUES IN DRUG DESIGN

Supervised Learning

Supervised learning (SL) is a cornerstone technique in the field of drug design within the broader curriculum of AI and ML methodologies [12]. The approach follows model training on labelled datasets and predicting the model outcome from input data, which is part of drug discovery pipelines. SL is primarily used in the case of Quantitative Structure Activity Relationship (QSAR) modelling, in which chemical structures are analysed by SL algorithms in order to predict their biological activity. Using known compound activity pairs to learn, these models can predict the efficacy of novel compounds, reducing the number of candidates for potential drug uses [13]. Supervised learning can also be used to predict toxicity by studying molecular features and environmental concerns related to the toxicity likelihood of drug candidates earlier in the development process to improve their safety profile. Supervised models used in virtual screening evaluate vast chemical libraries in order to identify compounds with desired biological activities, minimizing the time and cost usually expended in experimental

CHAPTER 5

Drug Repurposing: Computational Approaches and Success Stories

Haema Ganapathi[1], Karthikeyan Ramadoss[1,*], Shanmuganathan Seetharaman[1], Saravanan Ravindiran[2] and **Palanirajan Vijayarajkumar[3]**

[1] School of Pharmacy, Sri Balaji Vidyapeeth (Deemed to be University), SBV Campus, Pillaiyarkuppam, Bahour, Puducherry 607402, India

[2] Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India

[3] Faculty of Pharmaceutical Sciences, UCSI University, Kuala Lumpur (South Wing) No.1, Jalan Menara Gading, UCSI Heights 56000, Kuala Lumpur, Malaysia

Abstract: Drug repurposing or repositioning has blossomed into an effective avenue to uncover groundbreaking therapeutic scenarios for already-approved medications, substantially expediting development periods, along with pared monetary costs. With the objective to discern plausible drug candidates and foresee drug-target interactions, computational approaches, which leverage the use of contemporary techniques like machine learning, network pharmacology, and molecular docking, are imperative components of this process. Repurposed medication has been tackled radically by virtue of data-driven methods, notably through the integration of massive data and bioinformatics, which renders it feasible to discover new drug-disease liaisons promptly. Network-based models aid in gaining insight into subtle drug-target interactions, while molecular docking and simulation techniques are considered paramount in the identification of possible therapeutic targets. Target identification is further enhanced by omics-based techniques such as transcriptomics, proteomics, and metabolomics. A number of successful cases of repurposed medications in the treatment of neurological disorders, cancer, and infectious diseases are also highlighted in this review. Drug Repurposing could be augmented by expanding the utilization of AI and machine learning to retrieve literature and infer drug-target interactions. For this purpose, the databases and computational tools, especially CANDO, DrugBank, and LINCS, are used. Regulatory obstacles, data integration, and validation are some of the obstacles that drug repurposing must overcome despite its potential. It relies on the seamless fusion of innovative computational techniques with stern experimental validation to overcome these challenges.

[*] **Corresponding Author Karthikeyan Ramadoss:** School of Pharmacy, Sri Balaji Vidyapeeth (Deemed to be University), SBV Campus, Pillaiyarkuppam, Bahour, Puducherry 607402, India;
E-mail: professorrkn@gmail.com

Ajmer Singh Grewal, Viney Lather, Geeta Deswal & Kumar Guarve (Eds.)
All rights reserved-© 2026 Bentham Science Publishers

Keywords: Artificial intelligence, AI-driven prediction, Bioinformatics, CANDO, Drug repurposing, Drug-target interactions, Infectious diseases, LINCS, Machine learning, Molecular docking, Metabolomics, Network pharmacology, Natural language processing, Neurological disorders, Oncology, Proteomics, Transcriptomics.

INTRODUCTION

Drug discovery and development are highly complex, time-consuming, tedious, labour-intensive, and usually remain uncertain. It involves target identification, lead molecule discovery, scaffold development, optimizing the lead, preclinical testing, clinical trials, and regulatory body approval. Thus, for a drug to reach a market, it usually takes 10 to 14 years, making it a time-intensive endeavour [1]. Despite these efforts success rate is very low due to drug interactions and toxicity profiles. Nevertheless, the increasing investment in drug discovery is hampered by the growing need for innovative xenobiotics to treat deadly diseases like cancer, HIV/AIDS, coronary artery disease, respiratory infections, and COPD. Exploring alternate strategies, such as the use of computational tools, artificial intelligence, and innovative medication delivery methods, is essential given the rising costs and the comparatively low chance of success [2]. These developments may eventually cut down the time and expense required to create novel, efficient treatments by streamlining the discovery process and increasing forecast accuracy. Classical drug discovery is time consuming span and often leads to unsuccessful outcomes [3], whereas repurposing a drug is a low-risk strategy that could surpass the comprehending pharmacokinetic parameter evaluation, favouring preclinical and clinical stages. Despite being targeted to a particular protein molecule, maximal medications exhibit polypharmacology, that they act at multiple targets or pathways. Leveraging the fact, drug repurposing (also called drug repositioning, drug reprofiling, drug reformulating, or drug redirecting) is a phenomenon that involves utilizing or redeveloping the existing FDA-approved drug or unapproved drug that has previously gone through both preclinical and clinical stages but failed to enter the market [4]. This therapeutic switching involves only four steps: molecule recognition, compound procurement, advancement, and FDA post-market safety surveillance. which together facilitates for de novo drug design. During a pandemic situation like COVID, the researchers have turned to repurposing HIV protease inhibitors [5]. Even in contemporary medical practice, enormous medications are utilized for both primary and secondary conditions. For instance, aspirin was first made commercially as a Non-Steroidal Anti-Inflammatory Drug (NSAID), but it was revamped as an antithrombotic. In a similar vein, zidovudine was first introduced in 1964 as an anticancer drug before being repurposed in 1987 as an anti-HIV medication. However, it is necessary to ensure that the repurposed drug addresses

the mentioned indication through an effective literature survey and proper evidence [6]. The intellectual property landscape is an intriguing facet of the shielding approach pertaining to FDA-approved drugs. Drugs for which patent rights on substances and/or indications have expired frequently become the centrepiece of drug repurposing. The advent of commercial chemical libraries made up of medications that are no longer under patent has facilitated this process. Completely new therapeutic applications are sought for medications that are perpetually covered by active patents. It could be argued that in order to get market exclusivity, composition-of-matter patents are necessary [7]. However, Merz reused memantine for Alzheimer's illness, and Celgene successfully repurposed thalidomide for leprosy. Thus, repurposing drugs that remain sheltered by intellectual property is feasible under the right licensing. Another strategy is to substitute deuterium for hydrogen in certain regions; certain approved drugs currently have clinical trials with deuterated versions [8]. The target space that can be explored in drug development has risen with the dawn of new computational techniques [9]. Researchers can find new therapeutic uses for current medications more quickly than ever before by improving target profiling's recall and precision, combining various biological data, and applying sophisticated modeling tools. This expedites the drug development process and optimizes the use of already-approved drugs, which eventually leads to better treatment alternatives for patients. This chapter delves into the facilitation of Machine Learning (ML) and Artificial Intelligence (AI) for the drug repurposing method *via* data-driven approaches. It bears the spotlight on how molecular docking, bioinformatics, and big data are used in target identification. Together with omics-based techniques, including transcriptomics, proteomics, and metabolomics, network pharmacology and drug-target interaction prediction models are explored.

COMPUTATIONAL APPROACHES FOR DRUG REPURPOSING

Computational methods have revolutionized drug reprofiling, offering reliable methods for uncovering alternative therapeutic possibilities of already-approved drugs. Deploying molecules that had prior FDA approval, this technique merely lowers expense but also expedites the research process. Included among these are molecular docking, which determines how well a compound fits into target proteins by assessing its binding affinity; network pharmacology, which examines the interactions of drugs with biological networks as complex systems; machine learning, which can help predict new drug-disease relationships; and omics technologies, which analyze proteomics, metabolomics, and genomics data to identify new drug target interactions [10]. These approaches considerably reduce the time and cost that are inevitably part of the drug discovery process, and thus make repurposing a feasible way of responding to unmet medical needs and

CHAPTER 6

Molecular Dynamics: Insights and Applications in Computer-Aided Drug Design

Ritu Raj Kumar[1], Arun Mittal[2], Rohit Pandey[3], Satish Sardana[4,*], Nandini Sharma[5] and **Pragati Gupta[6]**

[1] *I T S College of Pharmacy, Muradnagar, Ghaziabad, Uttar Pradesh 201206, India*

[2] *Hindu College of Pharmacy, Sonipat, Haryana, India*

[3] *Dr. KN Modi Institute of Pharmaceutical Education and Research, Modinagar, Ghaziabad, Uttar Pradesh, India*

[4] *Amity Institute of Pharmacy, Amity University, Gurugram, Haryana, India*

[5] *Faculty of Pharmacy, Swami Vivekananda Subharti University, Meerut, Uttar Pradesh, India*

[6] *University of Leipzig, Saxony, Germany*

Abstract: Molecular Dynamics (MD) simulations have become an indispensable tool in computer-aided drug design, providing atomic-level insights into biomolecular interactions, ligand–receptor binding, and conformational dynamics. Unlike static molecular modelling methods, MD simulations offer a dynamic perspective that strengthens drug development by enabling the assessment of binding affinities, thermodynamic properties, and structural flexibility. The application of MD in pharmaceutical design extends to improving kinase inhibitors, developing antiviral agents, and elucidating mechanisms of antibiotic resistance. Advanced techniques such as metadynamics, Replica-Exchange Molecular Dynamics (REMD), and Free-Energy Perturbation (FEP) further enhance the predictive power of MD simulations, enabling more accurate modelling of complex biomolecular systems. Despite these advantages, significant challenges remain, including high computational costs, the need for precise force fields, and limitations in simulating long timescales. The integration of artificial Intelligence (AI) and machine learning into MD is expected to alleviate many of these limitations by improving sampling efficiency and predictive accuracy. Additionally, cloud-based platforms and hybrid quantum mechanics/molecular mechanics (QM/MM) approaches are being explored to overcome computational constraints. With continuous advancements in computational power and algorithmic methods, MD simulations are poised to play an increasingly critical role in rational drug design, accelerating the discovery of innovative therapeutics with enhanced efficacy and specificity.

[*] **Corresponding author Satish Sardana:** Amity Institute of Pharmacy, Amity University, Gurugram, Haryana, India; E-mail: ssardana@ggn.amity.edu

Ajmer Singh Grewal, Viney Lather, Geeta Deswal & Kumar Guarve (Eds.)
All rights reserved-© 2026 Bentham Science Publishers

Keywords: Binding free energy, Computer-aided drug design, Conformational sampling, Force fields, Ligand-receptor interactions, Lead optimisation, Molecular dynamics, Protein flexibility, Thermodynamic ensembles, Virtual screening.

INTRODUCTION

Molecular dynamics (MD) simulations have emerged as a cornerstone technique in Computer-Aided Drug Design (CADD). Their strength lies in explicitly modelling the dynamic behaviour of biomolecules, such as proteins and nucleic acids, and their interactions with potential drug candidates. Unlike static structural approaches, MD simulations capture the inherent flexibility and time-dependent conformational changes of these molecules [1]. These are essential because biomolecules are not rigid; they constantly fluctuate and adapt to their environment, including the presence of ligands. By simulating these molecular motions at various temperatures, MD can reveal hidden or transient binding sites that might be overlooked by static methods such as X-ray crystallography or uclear Magnetic Resonance (NMR) spectroscopy. It enables researchers to predict the most probable binding poses of a drug molecule, evaluate the stability of the drug–target complex, and estimate the thermodynamic and kinetic parameters associated with binding [2, 3]. Such insights are invaluable for optimising drug candidates to achieve higher affinity, selectivity, and efficacy. MD simulations provide these advantages by explicitly accounting for structural flexibility and entropic contributions. Traditional computational methods often neglect or approximate these factors, leading to inaccuracies in predicting drug-target interactions.

In contrast, MD considers the many degrees of freedom within the system, offering a more realistic and accurate representation of biological behaviour. The growing adoption of MD and other molecular modelling tools across the pharmaceutical industry highlights their value in drug discovery. As computational power continues to expand and simulation methodologies advance, MD is expected to play an increasingly significant role in drug development, potentially transforming how new therapeutics are designed and optimised. The ability to simulate atomic and molecular behaviour over time holds great promise for accelerating discovery, reducing development costs, and ultimately yielding more effective and safer medications [4, 5].

THEORETICAL FOUNDATIONS OF MOLECULAR DYNAMICS

Principles of Classical Mechanics in MD

At its core, MD relies on the principles of classical mechanics to simulate the

motion of atoms and molecules. Although quantum mechanics governs electron behaviours, the motion of the heavier atomic nuclei can be accurately described by classical laws such as Newton's equations of motion [6]. This approximation is justified because nuclei are much more massive than electrons, allowing the separation of electronic and nuclear motion as described by the Born-Oppenheimer approximation. In computational drug discovery, this means that the forces acting on each atom are calculated according to classical mechanics. These forces determine each atom's acceleration, which is then used to update its velocity and position over time [7, 8]. By repeatedly computing these forces and updating the atomic coordinates, MD simulations generate a continuous trajectory that reveals the system's dynamic evolution. The classical description is implemented using an empirical potential energy function, commonly referred to as a force field. This function expresses the system's potential energy as a function of the atomic coordinates and serves as the basis for calculating the forces acting on each atom [9, 10].

Force Fields and Potential Energy Functions

To obtain a classical-mechanics description of molecular interactions, an empirical potential energy function is introduced. This simplified representation, known as a force field (FF) or molecular mechanics (MM), is fundamental to MD simulations because it determines the accuracy and reliability of the results. The force field defines how atoms interact with one another, encompassing bonded interactions such as bond stretching, angle bending, and torsional rotation, as well as non-bonded interactions such as van der Waals forces and electrostatic interactions. The potential energy function, denoted as V(x), is a mathematical expression that calculates the total potential energy of the system based on the positions of all atoms (represented by x). A typical force field decomposes the total energy into several distinct terms, each accounting for a specific type of molecular interaction [11, 12].

Commonly Used Force Fields in Drug Design

A common representation of the potential energy function V(x) is as follows:

$$\mathbf{V(x)} = \sum_{\mathbf{bonds}} \mathbf{k_l\,(l\text{-}l_0)^2} + \sum_{\mathbf{angles}} \mathbf{k\alpha\,(\alpha\text{-}\alpha_0)^2} + \sum_{\mathbf{dihedrals}} \mathbf{k_\theta\,(\theta)} + \sum_{\mathbf{non\text{-}bonded}} \left[\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^{6}}\right]$$

Where:

Bond Stretching: The first term, $\sum_{bonds} k_l\,(l\text{-}l_0)^2$, describes the energy associated with stretching or compressing a bond between two atoms. Here, l is the actual

CHAPTER 7

Hands-On CADD Learning: Datasets, Tools, and Software Tutorials

Anwesha Pal[1], Dimple Pandey[1], Pradeep Kumar[2], Poulomi Ghosh[1], Afreen Bano[1], Shubhanshi Kulshrestha[1] and **Salim Albukhaty[3,*]**

[1] *Department of Bioinformatics, MMV, Banaras Hindu University, Varanasi, Uttar Pradesh, India*

[2] *Department of Botany, MMV, Banaras Hindu University, Varanasi, Uttar Pradesh, India*

[3] *Department of Chemistry, College of Science, University of Misan, Amarah, Mayasan 62001, Iraq*

Abstract: The endeavor of finding and creating a new medication is widely regarded as being extremely difficult and time-consuming. The efficacy of the drug development and development process is therefore increased by the widespread utilization of computer-aided drug design techniques worldwide. Depending on its needs, different CADD strategies are assessed as intriguing methods; among such things, structure-based and ligand-based drug design strategies are regarded as highly effective and potent methods in drug discovery and development. All of the above methods can be used in virtual screening for leading optimization and recognition using molecular docking techniques. Nowadays, the health sector utilizes computer-based drug screening for the treatment of various health complications. This chapter provides a new insight into the screening of the bioactive molecules (plant-based or animal-derived) as well as chemically synthesized compounds by implication of the CADD. CADD has the efficacy to identify the specific target of the disease as well as its binding affinity with screen compounds *via* molecular docking, virtual screening, structure-based drug design, ligand-based drug design, and computer-aided drug discovery, as well as network pharmacology.

Keywords: Bioinformatics, Computer-aided drug design, Drug development, *In silico* drug discovery, Lead optimization, Ligand-based drug design, Molecular docking, Network pharmacology, Structure-based drug design, Target identification, Virtual screening.

INTRODUCTION

Identifying and developing novel medicines is becoming more difficult for the pharmaceutical industry as a consequence of rising expenses, protracted develop-

* **Corresponding author Salim Albukhaty:** Department of Chemistry, College of Science, University of Misan, Amarah, Maysan 62001, Iraq, E-mail: albukhaty.salim@uomisan.edu.iq

Ajmer Singh Grewal, Viney Lather, Geeta Deswal & Kumar Guarve (Eds.)
All rights reserved-© 2026 Bentham Science Publishers

ment periods, and greater rates of rejection. Computer-Aided Drug Design (CADD) has become an essential tool to enhance success rates, reduce cost, and accelerate the drug development process. CADD helps in experimental methods by suggesting new insights on molecular interactions, possible targets, and eligible drug leads using computational methods and extensive biological datasets. With the objective to offer readers the building knowledge along with useful competence needed to execute an effective drug discovery process using computational methods, this chapter provides a hands-on introduction to CADD. By careful selection of datasets, revolutionary instruments, and software tutorials, this chapter bridges the theory-based ideas with the real-world applications. The aim is to provide learners with the opportunity to work on practical problems at their own pace, to encourage an increased awareness of the pros and cons of CADD. Various studies have documented recent advancements in computational drug design, such as [1] on the role of structure-based as well as ligand-based strategies in contemporary drug discovery and its capability to reduce the time for growth and expense, and [2] the integration of machine learning with CADD for enhancing drug effectiveness and toxicity predictions. As showcased by a study [3], evaluating the ChEMBL database, evolution in the discipline has been observed because of the growing accessibility of the database. In the case of the docking algorithms, developments have been seen, such as AutoDock Vina, having a simplified user interface for computational screening procedures, making high-throughput screening much easier [4]. Future scientists and experts in this field will be able to handle the various upcoming challenges regarding drug development in the upcoming era of computers if CADD is incorporated in the curriculum.

DATASETS FOR PRACTICAL EXERCISES

Curating Reliable Datasets for CADD

Because the integrity of information significantly impacts the effectiveness of forecasting algorithms, curating trustworthy datasets is essential to the advancement of CADD. ChEMBL, a professionally maintained chemical repository of biologically active substances with drug-like properties, is a well-known source for this field. In order to develop complex examination portfolios and make breakthrough development in the search for drugs easier, ChEMBL offers comprehensive biological activity information across pharmacological targets, encompassing metrics like Ki, Kd, IC_{50}, and EC_{50} [5]. The DrugOOD standard was created to tackle issues related to Out-Of-Distribution (OOD) information. This website presents a freely available Python software which streamlines curation of data and OOD assessment procedures, with an emphasis upon drug-target binding capacity forecasting. DrugOOD improves the durability

of prognostic models used in practical applications by allowing scientists to rigorously assess the effectiveness of models across a variety of subject changes and interference circumstances using automatic datasets curating and simple-to-use customisation procedures [6]. A further major issue with CADD involves an inequitable distribution of information. The following is addressed through the ImDrug benchmark, which provides a whole collection of instruction assignments, information sets, plus benchmark techniques designed for educational environments that are unbalanced. It includes estimates about interactions between drug targets as well as molecular simulation, among other phases of the pharmaceutical development workflow. ImDrug makes it easier to build and assess procedures that manage data disparities by offering an easily navigable and adaptable experimentation, which enhances the extension of models and impartiality [6]. When offering a single platform that covers a broad range of predictive modeling activities within the pharmaceuticals domain, the Therapeutics Data Commons (TDC) additionally helps with dataset curation. Multiple AI-ready samples covering different phases of pharmaceutical study and development are included within TDC. Additionally, it provides a network that includes volunteer assets and resources, including public ranking systems, assessment techniques, and information operations, all of which are incorporated within a publicly available Python library. This substantial asset facilitates the methodical evaluation and comparison of rehabilitative automated learning algorithms [6]. The forecasting capacity of CADD techniques models might be improved by including quantum mechanics features in databases. It is addressed *via* the QMugs information set, which offers fundamental mechanical information for more than 665,000 compounds with biological importance. This comprises atomically and molecular characteristics computed at deeper theoretical stages, along with optimum structural geometry and thermodynamic information acquired by partially empirical techniques. Improved understanding of the connections underlying the structure of molecules and biological function is made possible by the creation of algorithms that acquire molecular information at various theoretical layers, thanks to such extensive datasets [6].

Types of Datasets and Their Applications

QSAR Modeling Datasets

Utilizing provided structural descriptions, a computerized technique known as Quantitative Structure-Activity Relationship (QSAR) modeling allows it to be simpler to predict a compound's reaction by connecting its chemical structure to biological actions. Chemical analysis of environments, along with the creation of medications, both benefit greatly from the above approach [7].

SUBJECT INDEX

A

Absorption 34, 87, 191, 200, 201
Active 8, 9, 10, 11, 17, 37, 40, 42, 45, 47, 66, 67, 69, 71, 73, 74, 78, 194, 197, 198, 207, 214, 215
  compounds 37, 40, 42, 45, 47, 66, 67, 73, 78, 197, 198
  site 8, 9, 10, 11, 17, 66, 69, 71, 74, 194, 207, 214, 215
Adaptive sampling 173, 176
Absorption distribution metabolism excretion and toxicity (ADMET) 85, 87, 94, 107, 108, 200, 201, 217
ADMET 74, 75, 78, 91, 94, 102, 107, 108, 110, 111, 113, 199, 201, 216, 219
  predictions 74, 75, 78, 94, 108, 110, 111, 199
  profiles 91, 102, 107, 201
  properties 94, 108, 113, 201, 216, 219
Allosteric sites 8, 10, 11, 13, 17
AlphaFold 95, 96, 100
AMBER 67, 155, 160, 164
Accelerated molecular dynamics (aMD) 164, 169, 170, 172
Antibiotics 77, 112, 175
Aromatic rings 34, 36, 40, 63, 196, 199
Artificial neural networks (ANNs) 87, 128, 129
AutoDock 8, 37, 44, 134, 193, 194, 195, 219
AutoDock Vina 70, 73, 187, 193, 194, 195, 196, 214, 218, 219
Autoencoders 88, 110

B

Binding 3, 6, 7, 8, 9, 10, 11, 16, 67, 68, 69, 70, 75, 101, 104, 112, 131, 164, 166, 167, 168, 171, 173, 175, 177, 194, 195, 196, 199, 212
  affinities 16, 68, 69, 75, 101, 104, 112, 164, 171, 173, 177
  pockets 6, 75, 131, 175, 194, 195
  sites 3, 7, 8, 9, 10, 11, 67, 70, 166, 167, 168, 194, 196, 199, 212
Bioavailability 10, 15, 16, 73, 91, 102, 103
Biological 4, 6, 42, 59, 60, 63, 69, 72, 86, 87, 92, 93, 101, 102, 105, 106, 107, 108, 109, 190, 192, 193, 196, 203, 204, 205, 206, 207, 208
  activity 86, 87, 92, 93, 101, 102, 105, 106, 108, 109, 196, 203, 204, 205, 206
  targets 4, 6, 42, 59, 60, 63, 69, 72, 107, 190, 192, 193, 207, 208
Biomolecular interactions 151, 176, 177
Biomolecules 99, 132, 152, 155, 156, 163, 172
Blood-brain barrier (BBB) 141, 202, 216

C

Case studies 11, 46, 47, 48, 107, 110, 111, 112, 133, 173, 175, 176, 207, 209, 211
CHARMM 155, 160, 164
ChEMBL 108, 131, 187, 189, 191, 192, 196, 203, 208, 213, 216
Chemical 1, 3, 19, 42, 45, 59, 60, 63, 74, 85, 86, 87, 90, 92, 94, 95, 97, 101, 102, 103, 105, 106, 107, 108, 109, 110, 126, 131, 134, 137, 141, 143, 162, 191, 196, 200, 214, 216
  databases 60, 143, 162, 196, 200, 214, 216
  libraries 45, 59, 74, 86, 107, 110, 191
  properties 42, 94, 95, 97, 196, 200
  space 1, 3, 19, 63, 87, 90, 92, 102, 103, 105, 106
  structures 85, 86, 87, 101, 108, 109, 126, 131, 134, 137, 141, 143
Cheminformatics 6, 60, 76, 100, 192, 196

Ajmer Singh Grewal, Viney Lather, Geeta Deswal & Kumar Guarve (Eds.)
All rights reserved-© 2026 Bentham Science Publishers

Chimera 69, 193, 194, 195, 209
Clinical trials 76, 92, 100, 104, 108, 124, 125, 140, 142, 208
Clustering 3, 61, 85, 89, 127, 129, 164
Convolutional Neural Networks (CNNs) 85, 87, 88, 93, 101, 104, 108, 109, 142, 189
Comparative molecular field analysis (CoMFA) 37, 210, 211
Computational methodologies 4, 5, 9, 13, 14, 18, 19, 33, 174
Conformational sampling 152, 165, 172
Cross-validation (CV) 40, 108, 172, 189, 198, 205, 206, 210, 213
Cryo-electron microscopy (Cryo-EM) 3, 15, 50, 132

D

De novo drug design 1, 2, 4, 5, 6, 14, 15, 16, 17, 18, 19, 20, 88, 89, 102
Deep Learning (DL) 84, 85, 92, 96, 100, 102, 105, 106, 107, 128, 129
Deep Neural Networks (DNNs) 3, 88, 92, 100, 102
Deep Reinforcement Learning (DRL) 1, 5, 20
Descriptors 61, 204, 205, 206, 210, 213
Density Functional Theory (DFT) 16, 45, 132, 171
Discovery Studio 34, 37, 39, 42, 44, 46, 47, 50, 65, 195, 196
Docking simulations 10, 67, 91, 104, 106, 107, 193, 196, 197
Docking tools 193, 195, 196, 218
Drug 1, 2, 4, 7, 9, 12, 14, 15, 33, 38, 46, 62, 74, 75, 76, 84, 85, 86, 87, 88, 90, 91, 92, 93, 95, 97, 98, 99, 101, 102, 103, 104, 107, 108, 110, 112, 113, 124, 125, 129, 131, 133, 137, 138, 141, 165, 166, 167, 168, 169, 171, 173, 174, 176, 210, 211, 212, 217, 218
  candidates 4, 7, 12, 15, 74, 75, 91, 95, 102, 103, 104, 107, 110
  design 1, 2, 84, 86, 87, 91, 92, 102, 104, 165, 166, 167, 169, 210, 211
  discovery 1, 2, 85, 86, 90, 91, 93, 97, 98, 102, 103, 112, 113, 131, 133, 165, 171, 176, 217, 218
  discovery pipelines 62, 86, 87, 88, 90, 91, 99, 108, 129
  discovery processes 9, 14, 15, 33, 38, 92, 95, 101, 107, 125, 129
  repositioning 76, 124, 137, 138, 141
  resistance 46, 168, 173, 174, 212
Drug-target interactions (DTIs) 88, 89, 90, 92, 98, 99, 101, 123, 124, 128, 129, 130, 131, 135, 141
DrugBank 123, 134, 144, 145, 191, 192, 203, 215, 219

E

Extended-connectivity fingerprints (ECFP) 61, 63, 94, 108
Electrostatic interactions 3, 7, 72, 153, 154, 167, 208, 211
Energy minimization 43, 67, 160, 195, 207
Enhanced sampling techniques 164, 165, 170, 172
Enrichment factor (EF) 33, 34, 40, 50, 64, 68
Enzymes 4, 6, 11, 17, 18, 19, 38, 42, 173, 175, 202, 208
External validation 40, 198, 206, 210, 214

F

Fragment-based Drug Design (FBDD) 11, 12, 13, 14, 65, 71, 76, 78
Free Energy Perturbation (FEP) 15, 151, 164, 166, 168, 170, 171, 175, 176
Fingerprints 61, 62, 94, 97
Force fields 67, 151, 152, 153, 155, 156, 157, 160, 161, 162, 171, 172, 176, 177, 197
Free energies 74, 152, 156, 164, 166, 167, 170, 171, 175, 176

G

Generative Adversarial Networks (GANs) 15, 16, 85, 89, 90, 91, 100, 102, 103, 129
Graph Convolutional Networks (GCNs) 100, 135, 142, 145
Gene expression 89, 98, 99, 109, 132, 135, 136, 137, 141
Generative models 4, 5, 85, 89, 91, 92,
Genetic Algorithms (GA) 1, 2, 34, 44, 67, 68, 213

Genomics 3, 38, 75, 99, 100, 128, 131, 136, 137, 138
Glide 37, 45, 48, 69, 70, 73
Graph Neural Networks (GNNs) 2, 89, 92, 94, 96, 97, 99, 108
GROMACS 164, 193, 208

H

Hydrogen Bond Acceptors (HBAs) 3, 6, 12, 34, 35, 36, 40, 46, 47, 63, 72, 196, 197, 199, 202
Hydrogen Bond Donors (HBDs) 3, 6, 12, 34, 35, 40, 63, 72, 196, 197, 199, 202, 210, 212, 215
Hydrogen bonds 6, 7, 8, 9, 35, 47, 67, 133, 156, 164, 167, 169, 190, 195, 196, 202, 212, 215
Hydrophobic interactions 6, 8, 34, 47, 195, 196, 208, 215
High-throughput Screening (HTS) 59, 69, 86, 87, 90, 92, 105, 106, 107, 109, 187
High-throughput Virtual Screening (HTVS) 33, 34, 69, 70, 71, 72, 75, 77

I

Inhibitors 14, 17, 45, 46, 47, 65, 70, 71, 75, 76, 100, 107, 128, 140, 167, 168, 173, 174, 175, 207, 209, 211, 214, 215
Inhibitory activity 207, 209, 210, 211
Internal validation 40, 206, 210

K

Kinase inhibitors 11, 18, 19, 151, 173, 174, 211, 212
Kinases 11, 14, 17, 18, 19, 65, 71, 76, 77, 78, 100, 133, 173, 174, 211, 212

L

Lead optimization 101, 168, 212
Ligand-based Virtual Screening (LBVS) 59, 66, 67, 68, 75, 76, 106, 107, 199
Ligand 11, 37, 44, 47, 69, 70, 74, 75, 162, 165, 167, 168, 169, 170, 172, 176, 194, 207, 208
  binding 11, 37, 44, 47, 69, 74, 75, 162, 165, 167, 168, 169, 170, 172, 176
  preparation 69, 70, 162, 194, 207, 208
Ligand-protein interactions 15, 64, 67, 68, 100, 104, 105, 132, 167, 208
Ligand-receptor interactions 5, 7, 10, 15, 45, 104, 152, 166
Ligands 8, 10, 33, 34, 40, 42, 49, 64, 66, 67, 69, 74, 75, 104, 106, 131, 132, 134, 161, 162, 166, 171, 193, 196, 197, 199, 208, 214, 218
LigandScout 34, 37, 50, 64, 65, 193, 215
Lipinski's rule 40, 72, 201, 216
Lipophilicity (LogP) 12, 72, 108, 201

M

Machine Learning (ML) 14, 15, 67, 68, 70, 90, 94, 98, 100, 106, 108, 110, 112, 142, 144, 146, 156, 162, 176, 189, 190, 191, 205, 213, 214
Metabolomics 123, 124, 125, 128, 131, 135, 136, 137, 138
Metadynamics 151, 164, 165, 170, 172, 176, 177
Molecular Mechanics Generalized Born Surface Area (MM-GBSA) 45, 68, 74, 166, 168
Molecular Operating Environment (MOE) 9, 34, 37, 38, 39, 42, 65, 193, 196, 197, 199, 215, 218, 219
Molecular 4, 7, 10, 13, 15, 33, 42, 48, 58, 59, 60, 61, 62, 66, 67, 68, 69, 70, 72, 74, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 113, 123, 125, 131, 134, 151, 152, 160, 162, 164, 168, 186, 189, 191, 192, 193, 194, 196, 197, 199, 200, 201, 203, 204, 205, 207, 208, 210, 213, 214, 215, 216, 217
  descriptors 85, 87, 88, 89, 93, 94, 100, 108, 109, 110, 204, 205, 210, 213
  docking 4, 7, 10, 13, 15, 33, 42, 48, 58, 66, 67, 68, 69, 70, 74, 84, 88, 91, 101, 104, 105, 106, 107, 113, 123, 125, 131, 134, 186, 189, 192, 193, 194, 196, 197, 199, 207, 208, 214,

215, 216, 217
dynamics (MD) 3, 4, 5, 7, 13, 15, 43, 66, 68, 69, 103, 104, 105, 111, 113, 151, 152, 160, 162, 164, 168, 204, 217
fingerprints 59, 60, 61, 62, 88, 94, 97, 108, 189, 191
property prediction 86, 92, 93, 94, 96, 97
structures 42, 43, 44, 89, 90, 91, 92, 93, 94, 95, 96, 102, 103, 105, 108, 111, 203
Weight (MW) 12, 72, 108, 200, 201, 204
Molecules 1, 2, 4, 5, 7, 11, 12, 16, 17, 18, 38, 43, 44, 45, 58, 59, 60, 61, 64, 71, 75, 91, 92, 102, 103, 112, 125, 127, 129, 136, 142, 144, 155, 158, 161, 162, 163, 165, 167, 173, 174, 186, 189, 190, 192, 193, 195, 197, 200, 202, 204, 207, 211, 212, 214
Monte Carlo (MC) 1, 3, 34, 44, 50, 67, 91, 164
Multi-omics 69, 99, 100, 101, 137, 138
Mutations 2, 43, 44, 76, 132, 137, 160, 164, 165, 168, 169, 171, 173, 174, 175, 211, 212

N

Network pharmacology 18, 19, 123, 124, 125, 133, 134, 186
Neural Networks (NNs) 85, 87, 89, 92, 93, 94, 95, 96, 97, 102, 103, 108, 110, 128, 129, 133, 135
Nuclear magnetic resonance (NMR) 3, 12, 13, 14, 15, 50, 64, 66, 132, 152, 156, 161, 208

O

Off-target effects 5, 8, 15, 65, 75, 77, 88, 99, 100, 128, 167, 173
Open Babel 62, 162, 195, 196
Optimization 1, 2, 5, 6, 10, 12, 13, 18, 19, 41, 42, 49, 50, 58, 68, 69, 73, 87, 90, 91, 102, 103, 106, 111, 129, 186, 195, 197

P

Periodic Boundary Conditions (PBCs) 68, 158
Principal Component Analysis (PCA) 88, 89, 164, 205, 213
Protein Data Bank (PDB) 47, 48, 194, 195, 196, 207, 208, 214
Pharmacokinetics 5, 16, 59, 73, 84, 89, 91, 92, 94, 101, 107, 109, 140, 191, 200
Pharmacophore 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 63, 64, 65, 78, 196, 197, 198, 199, 212, 216, 219
features 35, 36, 37, 40, 47, 48, 64, 197
modeling 33, 34, 35, 37, 38, 39, 41, 43, 44, 45, 46, 48, 49, 64, 65, 78, 197, 219
models 33, 38, 42, 44, 45, 46, 47, 48, 49, 50, 63, 64, 196, 197, 198, 199, 212, 216
Pharmacophores 34, 38, 40, 45, 46, 49, 190, 191, 197, 198, 199, 211, 215
Pharmacophoric features 34, 35, 37, 38, 42, 43, 61, 63, 64, 75, 197
Physicochemical properties 2, 72, 100, 108, 168, 200
Potential energy functions 153, 156, 171
Precision medicine 77, 78, 90, 110
Predictive accuracy 33, 34, 35, 78, 91, 95, 97, 106, 151, 176, 205
Predictive models 18, 19, 87, 89, 93, 94, 106, 107, 108
Protein 3, 58, 66, 67, 78, 92, 93, 95, 96, 128, 131, 133, 142, 146, 152, 160, 162, 165, 173, 174, 175, 193, 194, 208
flexibility 66, 78, 152, 160, 165
Kinases (PKs) 133, 173, 175
structure prediction 93, 95, 96
structures 3, 58, 67, 92, 96, 128, 131, 142, 146, 160, 162, 165, 174, 193, 194, 208
Protein-Protein Interactions (PPIs) 13, 17, 66, 99, 134, 167
Proteins 3, 9, 17, 66, 67, 70, 71, 75, 76, 77, 92, 96, 100, 101, 107, 111, 112, 128, 131, 132, 135, 136, 137, 155, 162, 163, 165, 168, 169, 171, 174, 176, 194, 196, 209

Proteomics 3, 45, 123, 124, 125, 128, 130, 131, 135, 136, 137, 138, 141
PubChem 131, 134, 144, 189, 191, 192, 196, 203, 208, 213, 214, 216
PyMOL 69, 160, 194, 195, 196, 208, 209, 214
PyRx 134, 193, 195, 196, 218, 219

Q

Quantum mechanics (QM) 16, 34, 151, 153, 171, 172, 176, 188
Quantitative Structure-Activity Relationship (QSAR) 14, 42, 58, 59, 60, 62, 65, 73, 75, 85, 86, 87, 89, 92, 95, 134, 173, 188, 189, 191, 192, 193, 203, 204, 205, 206, 207, 209, 210, 211, 213, 214, 217, 219
QSAR models 89, 95, 173, 203, 205, 206, 207, 210, 211, 213, 214

R

Random Forest (RF) 87, 88, 100, 105, 106, 108, 110, 129, 213
Receptor-Based Virtual Screening (RBVS) 66, 67
Receptors 6, 7, 11, 17, 18, 19, 34, 35, 38, 40, 42, 44, 64, 66, 69, 70, 104, 140, 161, 168, 190, 193, 207, 212, 215, 218
Reinforcement Learning (RL) 1, 2, 5, 84, 85, 90, 91, 92, 100, 102, 105, 106, 111, 113
Replica-Exchange Molecular Dynamics (REMD) 151, 164, 165, 170, 171, 172, 176, 177
Repurposed drugs 76, 124, 128, 138, 139, 143
Root-Mean-Square Deviation (RMSD) 68, 156, 164, 165, 189, 209
Root Mean Squared Error (RMSE) 205, 206, 214
Root-Mean-Square Fluctuation (RMSF) 68, 164, 165, 209
Receiver Operating Characteristic (ROC) 33, 40, 50, 64, 198

S

Structure-Activity Relationship (SAR) 37, 42, 50, 59, 60, 62, 73, 74, 95, 106, 133, 198
Structure-Based Drug Design (SBDD) 9, 15, 86, 87, 103, 104, 186, 193
Structure-Based Virtual Screening (SBVS) 66, 68, 69, 75, 76, 106, 199
Scaffold hopping 49, 60, 63, 73
Scaffolds 5, 16, 17, 58, 63, 71, 72, 77, 124, 133, 214
Schrödinger 9, 34, 38, 42, 44, 50, 65, 69, 193, 203, 219
Scoring functions 7, 66, 69, 70, 71, 73, 74, 78, 194
Selectivity 4, 8, 10, 11, 12, 15, 18, 19, 101, 102, 103, 166, 167, 168, 173, 175
Side effects 10, 66, 100, 101, 113, 114, 128, 132, 177, 207
Simulations 45, 47, 77, 78, 111, 132, 151, 152, 155, 156, 157, 158, 159, 160, 161, 162, 164, 165, 166, 168, 169, 171, 173, 174, 175, 176, 177, 188, 189, 192, 203, 217
Simplified Molecular Input Line Entry System (SMILES) 2, 92, 108, 162, 196, 200, 203, 204
Supervised learning (SL) 85, 86, 87, 88, 89, 90, 94, 100
Support Vector Machines (SVMs) 87, 88, 90, 100, 105, 106, 108, 110, 129, 213
SwissADME 199, 200, 201, 202, 216, 219

T

Target identification 75, 85, 86, 92, 98, 99, 100, 101, 123, 124, 125, 127, 128, 132, 134
Target proteins 11, 12, 33, 36, 37, 66, 95, 103, 104, 106, 107, 131, 132, 166, 168, 195, 196, 199
Targets 11, 16, 18, 19, 47, 48, 60, 66, 70, 75, 76, 85, 89, 98, 101, 104, 123, 124, 127, 128, 132, 134, 135, 136, 137, 143, 173, 187, 188
Test sets 40, 50, 205, 206, 210, 214
Therapeutics Data Commons (TDC) 97, 188
Three-dimensional structure 33, 38, 44, 45, 60, 135, 156, 161, 162, 195, 197, 207, 214, 215
Topological Polar Surface Area (TPSA) 200, 202
Toxicity prediction 88, 99, 103, 109, 187, 203
Training datasets 5, 40, 65, 97, 108, 111, 113, 145, 189, 198, 199, 205, 206, 210, 214

Transcriptomics 75, 109, 123, 124, 125, 136, 137, 138

V

Validation 6, 10, 33, 40, 47, 48, 49, 50, 59, 64, 65, 66, 68, 70, 72, 73, 75, 78, 86, 98, 112, 123, 134, 177, 195, 197, 198, 203, 205, 206, 210, 211
Variational Autoencoders (VAEs) 5, 15, 85, 89, 90, 91, 94, 102, 103, 129
Velocity Verlet 157, 158
Virtual screening 14, 33, 34, 43, 46, 47, 48, 59, 62, 63, 66, 67, 69, 70, 77, 78, 86, 104, 106, 107, 128, 168, 192, 193, 195, 196, 199

X

X-ray crystallography 3, 12, 13, 14, 15, 50, 64, 66, 77, 132, 133, 152, 161, 173

Z

ZINC database 77, 162, 196, 203, 208, 216, 218, 219
ZINCPharmer 34, 42, 65, 215

Ajmer Singh Grewal

Dr. Ajmer Singh Grewal is a Professor (Pharmaceutical Chemistry) at Guru Gobind Singh College of Pharmacy, Yamuna Nagar, Haryana (India), with 15 years of experience in pharmaceutical education and research. Dr. Grewal holds a Ph.D. in Pharmaceutical Sciences from I. K. Gujral Punjab Technical University, India with expertise in drug design, medicinal chemistry, and computational modeling. With over 150 publications in esteemed journals, a Google Scholar h-index of 27, and more than 4600 citations, Dr. Grewal is emerging as an expert in his field. Dr. Grewal has authored 30 book chapters, and edited 20 books. His research focuses on structure-based drug design for anticancer, anti-diabetic, anti-inflammatory, and Alzheimer's therapies, with extensive use of tools like Glide, AutoDock Vina, and Discovery Studio. His expertise in computer-aided drug design makes him a valuable contributor to advances in this field.

Viney Lather

Dr. Viney Lather is a distinguished Professor and Centre-Head at the Centre for Pharmaceutical Chemistry and Analysis, Amity Institute of Pharmacy, Amity University, Noida (India). With 24 years of extensive national and international experience in pharmaceutical sciences, he has made significant contributions to drug discovery and development. From 2007 to 2010, Dr. Lather worked as a Research Scientist at Universidade da Madeira, Funchal, Portugal. His research expertise spans medicinal chemistry, molecular modeling, AI-driven drug discovery, chemoinformatics and bioinformatics. He has particular proficiency in developing nanoplatforms for drug delivery and employing in silico tools for structure-based drug design. With over 170 publications, a Google Scholar h-index of 32, and more than 5000 citations, Dr. Lather is a recognized leader in his field. He has secured research grants from prominent agencies such as AICTE (New Delhi) and SERB (New Delhi) and received accolades, including the Best Scientist Award from Jubilant Biosys Ltd. Dr. Lather has delivered over 15 invited talks.

Geeta Deswal

Dr. Geeta Deswal is a Professor Head of the Department (Pharmacognosy) at Guru Gobind Singh College of Pharmacy, Yamuna Nagar, Haryana (India), since August 2022. With over 14 years of teaching experience, Dr. Deswal has mentored and guided numerous UG and PG students. She has supervised five M. Pharm. research projects and is currently guiding three Ph.D. students in pharmaceutical sciences. Her research interests include bioactivity-guided extraction and isolation of phytoconstituents, plant tissue culture, molecular modelling, and natural product-based drug discovery. She has authored over 50 articles in reputed journals, 20 book chapters, and edited 15 books.

Kumar Guarve

Dr. Kumar Guarve is a seasoned academician and Principal-cum-Professor at Guru Gobind Singh College of Pharmacy, Yamuna Nagar, Haryana (India), with over 21 years of extensive experience in pharmaceutical education and institutional leadership. Under his leadership, faculty members have achieved numerous Scopus-indexed publications and patented innovative products. Dr. Guarve has also contributed to securing copyrights for educational processes and curriculum frameworks, further solidifying his commitment to advancing the academic and research profile of the institutions he serves. Dr. Guarve has published over 90 articles in national and international journals of repute, contributed 20 book chapters and edited 5 books.