Medicinal and Environmental Chemistry: Experimental Advances and Simulations

PART 2

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Bentham Books

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ISBN (Online): 978-981-4998-30-7

ISBN (Print): 978-981-4998-31-4

ISBN (Paperback): 978-981-4998-32-1

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FOREWORD

In recent years, our environment has deteriorated at an alarming rate. Be it the air we breathe, the water we drink, or the food we eat—the hazards are hitting closer to home. Consequently, there has been a deluge of diseases and disorders associated with environmental pollution, industrialization, lifestyle changes, etc. From cardiovascular diseases and growth defects to neurological disorders and stress, these environmental diseases have been coupled with other environmental threats like pollution, climate change, food shortage, and novel infections and have made the study of environmental chemistry indispensable in present times. In the development of more effective and safer therapies that would cater to diseases both old and new, the study of medicinal chemistry is vital to determine accurate knowledge of drugs, their structure, synthesis, pharmacology, and pharmacokinetics.

Environmental diseases have brought about a close association between these two branches of chemistry as well as pharmaceutical chemistry. It gives me great pleasure that this book brings them together on one platform. This book aims to provide a better comprehension of environmental problems as well as remedial strategies to amend them and includes an assorted collection of topics presented by experts from academia, research, and development.

I think that the authors can be confident that readers will gain a broader perspective of the disciplines of environmental chemistry, medicinal chemistry, and pharmaceutical chemistry as a result of their efforts.

Imran Ahmad
Jina Pharmaceuticals Inc.
USA

PREFACE

With the drastic disturbance in environmental harmony and balance, there has been a rise in global deaths and diseases, calling for the exploration of novel remediation strategies for innovative drug action mechanisms and target identification. The fine balance between human and ecological health is getting disturbed, leading to serious implications including the occurrence of new pathogens and diseases, including the novel corona virus SARS-CoV-2, being the most recent instance having gripped the entire globe.

Environmental diseases are non-communicable and are caused by chronic exposure to toxic pollutants. Other contributory causes of environmental diseases include radiation, pathogens, allergens, and psychological stress. Their increasing occurrence is due to industrialization, changes in farming protocols, and the increase in exposure to chemicals released into the environment. Lifestyle changes, including the increased use of tobacco and processed foods also greatly contribute to the environmental/lifestyle diseases burden.

Though medicinal chemistry and environmental chemistry have been widely explored separately, yet their close association and interdependence have been overlooked. By exploring the association between these two focal areas, the present book aims to provide solutions and curative strategies for the well-being of humans and the environment.

The twenty-one chapters included in the book are focused on diverse topics trying to blend the fields of environmental chemistry and medicinal chemistry and have been authored by expert scientists and academicians from renowned institutions. A wide range of topics has been explored in the book, to make it relevant to environmental chemists and students. The chapters have been designed to introduce environmental contaminants and techniques for their quantification and removal. Also, a medicinal perspective for remediation of environmental hazards, from therapeutic strategies available to the design of new and safer drugs, is introduced through experimental and simulation approaches.

Specialized chapters have been dedicated to persistent organic pollutants, heavy metals, antibiotics, and plastics, which have become a major source of pollution, along with their remediation. The biochemical aspect of Cytochrome P_{450} and its association with mitigation strategy upon the exposure of smog on the human body, the effect of environmental xenoestrogens on human health, and the potential of natural curing agents to combat ecotoxicity have also been explored. Experimental techniques like the use of quantification methods for pharmaceuticals and persistent organic pollutants, chemosensors and polymeric ceramic composite membranes, and the concept of nanotechnology for the synthesis and use of gold and silver nanoparticles from plant-based sources have also been elaborated. To further elaborate on the importance of safe chemical practise, the concept of green chemistry has been introduced.

As we are aware that drug discovery for a particular disease is a time taking endeavour, therefore, a few chapters have also been dedicated to *in-silico* predictions like molecular docking and virtual models for biological properties, the software used and their utility to make futuristic and accurate predictions to make drug discovery efficient, quicker and cost-effective. Chapters summarizing the advances of biomolecular simulations for drug designing with respect to ecotoxicity, drug degradation, use of bioisosteric groups, and advances in pharmaceutical and modelling interventions for the treatment of COPD are also included. An interesting chapter has also explained the ligand identification for effective drug development through virtual screening by taking the example of COVID-19.

The book will prove beneficial for academicians, students of environmental chemistry and pharmacy, researchers, scientists, computational chemists, pharmacologists, environmentalists, policymakers, and postgraduate students. It would also provide researchers and medicinal chemists, information about the latest research done and the modern techniques used to develop more effective and safer drugs that would not be harmful to the environment. In this way, the proposed book would be highly beneficial to the audience it hopes to cater to.

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CHAPTER 11

Novel Drug Development Strategies- A Case Study With SARS-CoV-2

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Abstract: The current epidemic of Severe Acute Respiratory Syndrome coronavirus (SARS-CoV-2) has led to a major health crisis in 2020. SARS-CoV-2 has spike protein, polyproteins, nucleoproteins, and membrane proteins with RNA polymerase, 3-chymotrypsin-like protease, papain-like protease, helicase, glycoprotein, and accessory proteins. These are probable targets to be explored for the discovery of antiviral agents, still, to date, no definite treatment or vaccine has been discovered. Virtual screening with molecular docking has its advantage to speed up the drug development procedure in an accurate manner. In this chapter, novel computational strategies for drug discovery have been elaborated. Docking tools and drug filtering rules which may efficiently assist the drug development procedure and channelize the whole process in the right direction have also been discussed. A case study with 322 natural, semi-synthetic, and synthetic derivatives of citric acid (2-hydroxy-1,2-3-propane tricarboxylic acid), in search of a potential lead molecule to combat the novel coronavirus SARS-CoV-2, has been elaborated. The derivatives were explored from the PubChem database. The obtained library of compounds was filtered through Lipinski's rules, out of which, 74 obeyed the rule and were further subjected to molecular docking investigation against the SARS-CoV-2 replicase polyprotein 1a or pp1a (ID: 6LU7), with AutoDock Vina and iGEMDOCK. Deptropine possessed the highest binding affinity, in terms of released binding energy (-7.4 kcal/mol), against the SARS-CoV-2 replicase polyprotein 1a.

Keywords: Citric acid, Computational strategies, Drug, Docking, Repurposing, SARS-CoV-2, Virtual screening.

INTRODUCTION

Three coronaviruses responsible for zoonotic diseases *viz.* Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), Middle East Respiratory Syndrome coronavirus (MERS-CoV), and SARS-CoV-2, have caused lethal

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