

Ajmer Singh Grewal, PhD • Ashwani K. Dhingra, PhD
Kunal Nepali, PhD • Geeta Deswal, PhD
Arun Lal Srivastav, PhD
Editors



Emerging Strategies in Antibacterial Drug Resistance Management

Mechanisms, Challenges,
and Novel Interventions

NOVA
Complimentary Copy

Ajmer Singh Grewal
Ashwani K. Dhingra
Kunal Nepali
Geeta Deswal
Arun Lal Srivastav
Editors

Emerging Strategies in Antibacterial Drug Resistance Management

Mechanisms, Challenges, and Novel Interventions



No part of this digital document may be reproduced, stored in a retrieval system or transmitted in any form or by any means. The publisher has taken reasonable care in the preparation of this digital document, but makes no expressed or implied warranty of any kind and assumes no responsibility for any errors or omissions. No liability is assumed for incidental or consequential damages in connection with or arising out of information contained herein. This digital document is sold with the clear understanding that the publisher is not engaged in rendering legal, medical or any other professional services.

Complimentary Copy

Copyright © 2024 by Nova Science Publishers, Inc.

DOI: <https://doi.org/10.52305/SKIQ7023>

All rights reserved. No part of this book may be reproduced, stored in a retrieval system or transmitted in any form or by any means: electronic, electrostatic, magnetic, tape, mechanical photocopying, recording or otherwise without the written permission of the Publisher.

We have partnered with Copyright Clearance Center to make it easy for you to obtain permissions to reuse content from this publication. Simply navigate to this publication's page on Nova's website and locate the "Get Permission" button below the title description. This button is linked directly to the title's permission page on copyright.com. Alternatively, you can visit copyright.com and search by title, ISBN, or ISSN.

For further questions about using the service on copyright.com, please contact:

Copyright Clearance Center

Phone: +1-(978) 750-8400

Fax: +1-(978) 750-4470

E-mail: info@copyright.com.

NOTICE TO THE READER

The Publisher has taken reasonable care in the preparation of this book, but makes no expressed or implied warranty of any kind and assumes no responsibility for any errors or omissions. No liability is assumed for incidental or consequential damages in connection with or arising out of information contained in this book. The Publisher shall not be liable for any special, consequential, or exemplary damages resulting, in whole or in part, from the readers' use of, or reliance upon, this material. Any parts of this book based on government reports are so indicated and copyright is claimed for those parts to the extent applicable to compilations of such works.

Independent verification should be sought for any data, advice or recommendations contained in this book. In addition, no responsibility is assumed by the Publisher for any injury and/or damage to persons or property arising from any methods, products, instructions, ideas or otherwise contained in this publication.

This publication is designed to provide accurate and authoritative information with regard to the subject matter covered herein. It is sold with the clear understanding that the Publisher is not engaged in rendering legal or any other professional services. If legal or any other expert assistance is required, the services of a competent person should be sought. FROM A DECLARATION OF PARTICIPANTS JOINTLY ADOPTED BY A COMMITTEE OF THE AMERICAN BAR ASSOCIATION AND A COMMITTEE OF PUBLISHERS.

Additional color graphics may be available in the e-book version of this book.

Library of Congress Cataloging-in-Publication Data

ISBN: 979-8-89530-060-2 (hardcover)

ISBN: 979-8-89530-140-1 (e-book)

Published by Nova Science Publishers, Inc. † New York

Complimentary Copy

Chapter 2

Mechanisms of Antimicrobial Drug Resistance

Arun Kumar^{1,*}

Mohd. Mursal¹

Sahil Hussain¹

Kuldeep Singh¹

Sana Ahmad¹

Deepshikha Singh¹

and Kaynat Fatima²

¹Faculty of Pharmacy, Integral University, Kursi Road, Lucknow, Uttar Pradesh, India

²Department of Molecular Biology, Staffordshire University, Stoke on Trent, United Kingdom

Abstract

Antimicrobial resistance occurs through enzyme-driven drug breakdown, bacterial protein modifications, and alterations in antibiotic permeability, and can be transmitted through plasmids or ingrained within the bacterial chromosome. The primary mechanism responsible for resistance to cephalosporins and penicillin is the enzymatic hydrolysis of these antibiotics by the bacterial enzyme β -lactamase. The presence of chromosomal β -lactamase can be influenced by exposure to β -lactam drugs, leading to either induced expression or sustained inhibition. Strategies to counteract resistance to β -lactam antibiotics involve two main approaches: first, the development of novel antibiotics that are resistant to β -lactamase degradation; and second, the concurrent use of β -lactamase inhibitors alongside β -lactam drugs. Methicillin resistance, which remains unaffected by gram-positive β -lactamase, arises due to modifications in penicillin-binding protein. The main mechanisms of resistance for other classes of antibiotics, encompassing trimethoprim, sulphonamides, aminoglycosides, chloramphenicol and quinolones, involve two key processes: the creation of enzymes that modify the antibiotics, and the development of bacterial targets that are resistant to the effects of these antibiotics. For several antibiotic families, including quinolones, aminoglycosides, β -lactams and chloramphenicol, decreased antibiotic penetration acts as an additional resistance mechanism.

* Corresponding Author's Email: arun.mpharm@gmail.com.

Keywords: antibiotic resistance, β -lactamase, enzyme, target, antimicrobial, bacteria

Abbreviations

AR	Antibiotic Resistance,
GN	Gram-Negative,
GP	Gram-Positive,
GTP	Guanosine Triphosphate,
MFS	Major Facilitator Superfamily,
MGEs	Mobile genetic elements,
MRSA	Methicillin-Resistant <i>Staphylococcus aureus</i> ,
PBPs	Penicillin-Binding Proteins,
PG	Peptidoglycan,
WHO	World Health Organization.

Introduction

Antibiotics have played a crucial role in combating various infectious diseases for the past century. Paul Ehrlich, often credited as the pioneer of modern chemotherapy, is known for his discovery of the first antibiotic named Salvarsan in 1909. Syphilis is a sexually transmitted infection brought on by the bacterium *Treponema pallidum*. This ground-breaking medication was used to cure it. A “magic bullet” was Ehrlich’s term for a chemical he said might kill germs without affecting the host. In the 1930s, sulfa medicines were introduced by Gerhard Domagk, while Alexander Fleming’s discovery of penicillin in the 1940s. Fleming also cautioned about the potential development of resistance due to penicillin’s overuse, emphasizing the need for careful usage (Aminov, 2010). The discovery of antibiotics played a crucial role in eliminating previously fatal infectious diseases. Due to these advancements, medical professionals anticipated that many infections would become obsolete over time. While the introduction of antibiotics significantly reduced illness and death rates compared to the era before their existence, the emergence of antibiotic-resistant bacterial strains consistently followed each new drug discovery (Yao et al., 2021). Bacterial resistance to antibacterial agents dates back as far as the existence of bacteria itself. Even before the widespread use of penicillin following its discovery, it was observed that certain bacteria could break down penicillin through enzymatic processes (Aminov, 2010). Antibiotic resistance (AR) and its global expansion are among the top three major concerns of the twenty-first century, according to the World Health Organization (WHO) (Aminov, 2010). Understanding the factors that contributed to the development of AR is crucial. It is well acknowledged that AR is brought on by the improper and excessive use of antibiotics to treat bacterial illnesses as well as non-bacterial reasons. Overuse of antibiotics in human and veterinary medicine, as well as a lack of immunisation, which is essential in avoiding various diseases, have all been linked to the development of bacterial resistance. In the present era, there is a notable increase in bacterial strains that exhibit MDR. These MDR bacterial infections raise considerable concern due to their association with prolonged patient hospitalization, and extended courses of treatment involving broad-spectrum

Complimentary Copy