Fundamental Applications of Biochemistry in the Environment

Editor

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Published by

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ISBN: 978-93-5737-783-6

ISBN: 978-93-5737-783-6

First Edition
Printed at *Apex Digital Services, Manjeri, PIN 676121, Malappuram (DT), Kerala, India.*

POST GRADUATE DEPARTMENT OF CHEMISTRY

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Department of Chemistry was started in 1991 with Chemistry as subsidiary subject. Chemistry as main subject was started in 1993. 28 batches have successfully completed B.Sc. Chemistry Programme. The department conducted B.Sc. Industrial chemistry course in the vocational stream with the assistance of UGC during 1999-2004. Three batches completed the course. In 2013 the Department became a Post Graduate Department. 8 batches have successfully completed the M. Sc. Chemistry Prgramme.

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- To produce scientifically literate graduates and post graduates with a broad and deep knowledge of fundamental chemical principles.

ISBN: 978-93-5737-783-6

₹ 500

March 2023

ISBN: 978-93-5737-783-6

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ISBN: 978-93-5737-783-6

Chapter 1

HISTORY OF ANTIBIOTICS

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INTRODUCTION

Antibiotic is a chemical substance produced by a living organism, generally a microorganism. Microorganisms that produce antibiotics useful in preventing or treating disease include the bacteria and the fungi that is detrimental to other microorganisms. We usually associate the beginning of the modern "antibiotic era" with the names of Paul Ehrlich and Alexander Fleming. Ehrlich's idea of a "magic bullet" that selectively targets only disease-causing microbes and not the host was based on an observation that aniline and other synthetic dyes, which first became available at that time, could stain specific microbes but not others. This idea led him to begin a large-scale and systematic screening program in 1904 to find a drug against syphilis, a disease that was endemic and almost incurable at that time. This sexually transmitted disease, caused by the spirochete *Treponema pallidium*, was usually treated with inorganic mercury salts but the treatment had severe side effects and poor efficacy. In his laboratory, together with chemist Alfred Bertheim and bacteriologist Sahachiro Hata, they synthesized hundreds of organoarsenic derivatives of a highly toxic drug Atoxyl and tested them in syphilis-infected rabbits. In 1909 they came across the sixth compound in the 600th series tested, thus numbered 606, which cured syphilis-infected rabbits and showed significant promise for the treatment of patients with this venereal disease in limited trials on humans . Despite the tedious injection procedure and side effects, the drug, marketed by Hoechst under the name Salvarsan, was a great success and, together with a more soluble and less toxic Neosalvarsan, enjoyed the status of the most frequently prescribed drug until its replacement by penicillin in the 1940. Amazingly, the mode of action of this 100-year-old drug is still unknown, and the controversy about its chemical structure has been solved only recently.

STAGES OF DEVELOPMENTS IN ANTIBIOTICS

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The systematic screening approach introduced by Paul Ehrlich became the cornerstone of drug search strategies in the pharmaceutical industry and resulted in thousands of drugs identified and translated into clinical practice, including, of course, a variety of antimicrobial drugs. During the earlier days of antibiotics research, this approach led to the discovery of sulfa drugs, namely sulfonamidochrysoidine which was synthesized by Bayer chemists Josef Klarer and Fritz Mietzsch and tested by Gerhard Domagk for antibacterial activity in a number of diseases. Prontosil, however, appeared to be a precursor to the active drug, and the active part of it, sulfanilamide, was thus not patentable as it had already been in use in the dye industry for some years. As sulfanilamide was cheap to produce and off-patent, and the sulfanilamide moiety was easy to modify, many companies subsequently started mass production of sulfonamide derivatives. The legacy of this oldest antibiotic on market is possibly reflected in one of the most broadly disseminated cases of drug resistance: sulfa drug resistance, which is almost universally linked with class 1 integrons. Moreover, once the sulfa drug resistance is established on a mobile genetic element, it may be difficult to eliminate because the resulting construct confers a fitness advantage to the host even in the absence of antibiotic selection . Despite this, many continuously modified derivatives of this oldest class of synthetic antibiotics are still a viable option for therapy, and the action of and resistance to sulfanilamide is one of the best examples for the arms race between man and microbes. Two other classes of synthetic antibiotics successful in clinical use are the quinolones, such as ciprofloxacin, and oxazolidinones, such as linezoild.

Unknown to many, however, is the fact that the first hospital use of a drug that we would name an antibiotic today was the so-called Pyocyanase prepared by Emmerich and Löw from *Pseudomonas aeruginosa* (formerly *Bacillus pycyaneus*). Importantly, Emmerich and Löw noticed that the bacterium as well as the prepared extracts were active against a number of pathogenic bacteria and thus tried to use the extract for treatment of various diseases. As the results of these treatments were not consistent and the preparation itself was quite toxic for humans, the treatment was eventually abandoned. Further investigations confirmed the production of antibiotic substances by *Pseudomonas aeruginosa* , which appeared to be the quorum sensing molecules, 2-alkyl-4 quinolones, in this bacterium .

Even before the extensive use of penicillin, some observations suggested that bacteria could destroy it by enzymatic degradation. In general, though, the outlook was more or less optimistic. One of the earlier studies of possible resistance emergence under laboratory conditions concluded that: “Syphilis has now been treated with arsenicals for about 40 years without any indications of an increased incidence of arsenic-resistant infections, and this work gives grounds for hoping that the

ISBN: 978-93-5737-783-6

widespread use of penicillin will equally not result in an increasing incidence of infections resistant to penicillin.

CURRENT STATUS OF ANTIBIOTICS

The current state in the field of antimicrobials, resistance, and chemotherapy is certainly not limited to clinical microbiology as it was in the early years of the antibiotic era. Thus, it is not a single grand challenge; it is rather a complex problem requiring concerted efforts of microbiologists, ecologists, health care specialists, educationalists, policy makers, legislative bodies, agricultural and pharmaceutical industry workers, and the public to deal with. In fact, this should be of everyone's concern, because, in the end, there is always a probability for any of us at some stage to get infected with a pathogen that is resistant to antibiotic treatment. Moreover, even the behavioral patterns, such as hygienic habits or compliance with antibiotic treatment regimens, may have consequences that are not limited only to individual health issues but, on a larger scale, contribute to the interaction with the resistomes around us. In the following sections I will briefly touch upon some of the areas ranging from research to regulations to the cultural patterns that are important in dealing with the challenges of the antimicrobials, resistance, and therapy fields.

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Chapter 2

METAL COMPLEX INTERACTIONS WITH DNA

Dr. Deepa K

ISBN: 978-93-5737-783-6