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Polymers against Microorganisms

On the Race to Efficient Antimicrobial Materials

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Preface

Bacterial contamination is still an unresolved problem present in cases in which a biomaterial is required. This is an issue independent of the biomaterial considered and is particularly serious in those cases in which long-term implants are employed. In this context, polymers have been proposed as interesting candidates to improve the biomaterial performance in order to prevent microbial contamination. Different previous books have been published focusing their efforts on one of the aspects of antimicrobial polymers: the synthesis, in the biology of the microorganisms in contact with synthetic materials or related to their final use (e.g., food packaging). This book aims to present a complete overview of this rapidly evolving field providing a concise, clear, and precise image of the most important aspects involved in the use of polymers to combat microorganisms.

As will be depicted throughout this book, polymers' mode of action relies on physiochemical parameters such as hydrophobicity and cationic charge, rather than specific receptor-mediated interactions, so the activity of the polymers can be modulated by tuning key structural parameters. Taking into account the mechanism of action, polymers exhibit important advantages that have motivated their investigation as antibacterial materials. These include that polymers do not provide toxicity to the environment, do not develop resistance, and have an enhanced antimicrobial action. Other important advantages are their versatility; polymers are easy to process and cheap.

I hope that this text will be helpful for readers with very different backgrounds, ranging from chemists, biochemists, materials scientists, and engineers, who aim to have a general and complete overview of the use of polymers in the preparation of antimicrobial materials. This book is not presented as a manual and will not provide answers to all possible questions about polymers with antimicrobial properties. On the contrary, this book is intended to provide an introductory view highlighting important aspects including synthesis, surface functionalization and structuration, and the extension of these important aspects to the preparation of antimicrobial fibers, hydrogels, or membranes among others.

This text, devoted to the recent developments and ongoing works concerning the use of polymers as antifouling and antimicrobials for different applications, is organized as follows. The first part of this book (Chaps. 2 and 3) describes the basics of bacterial infections and the main functional groups incorporated into polymeric structures to avoid microorganism contamination. Chapter 4 depicts the use of nanostructured polymer assemblies in solution as antimicrobials.

The design and fabrication of polymer surfaces is analyzed in Chaps. 5 and 6. Chapter 5 discusses the alternatives to modify the surface chemical composition in order to introduce both antifouling and/or antimicrobial functional groups. Chapter 6 concerns those approaches that resort to both the modification of the surface topography and those that combine surface functionalization and patterning to remove bacterial contamination and biofilm formation.

Chapters 7, 8, and 9 are devoted to the use of antimicrobial polymers for the elaboration of three different materials. The approaches developed for the fabrication of nano- and microstructured fibers are depicted in Chap. 7. In Chapter 8, the synthesis and modification of hydrogels to improve the bacterial adhesion and to introduce antimicrobial moieties are described. Finally, Chap. 9 focuses on the elaboration of membranes with enhanced antifouling properties.

The last part of this book will analyze the eventual environmental concerns as well as safety issues related to the use of nanoparticles. The last chapter will summarize the future trends on the development of more sophisticated and effective antimicrobial polymer systems.

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Chapter 1
Polymers Against Microorganisms

Abstract The significant advances on the control and prevention of infectious diseases carried out during the first decades of the twentieth century produced an optimist sensation about the possibility to completely eradicate any illness. But this optimistic vision rapidly changed as a result of the reemerging of new and in some cases antimicrobial-resistant infections. Examples of the novel/old/appearing/reappearing infectious diseases include the Ebola virus, HIV, or Legionnaire's disease that are still a public health problem in the twenty-first century.

Within this context, two main aspects have deserved particular attention during the last decades. On the one hand, food-borne diseases are directly related to the emergence of microbial diseases. On the other hand, the emergence of antimicrobial resistance, recognized soon after the discovery of penicillin, has followed the introduction of most every new drug. As will be depicted in this chapter, synthetic macromolecular antimicrobials have emerged as a highly promising class of therapeutics with immense potential for combating multidrug-resistant microbes. In effect, the polymers mode of action relies on physiochemical parameters such as hydrophobicity and cationic charge, rather than specific receptor-mediated interactions, the activity of the polymers can be modulated by tuning key structural parameters. Taking into account the action mechanism, polymers exhibit in comparison with other materials, important advantages that have motivated their investigation as antibacterial materials. These include that polymers do not provide toxicity to the environment, do not develop resistance, and have an enhanced antimicrobial action.

Keywords Bacterial resistance • Infectious disease • Antibiotics • Implants • Antimicrobial polymers

1.1 Infectious Diseases: Historical Context

The significant advances on the control and prevention of infectious diseases carried out during the first decades of the twentieth century produced an optimist sensation about the possibility to completely eradicate any illness [1]. Prominent scientists of that time such as Henry Sigerist [2] and later others including William H. Stewart [3] anticipated that those advances will be the key to definitely prevent infection.

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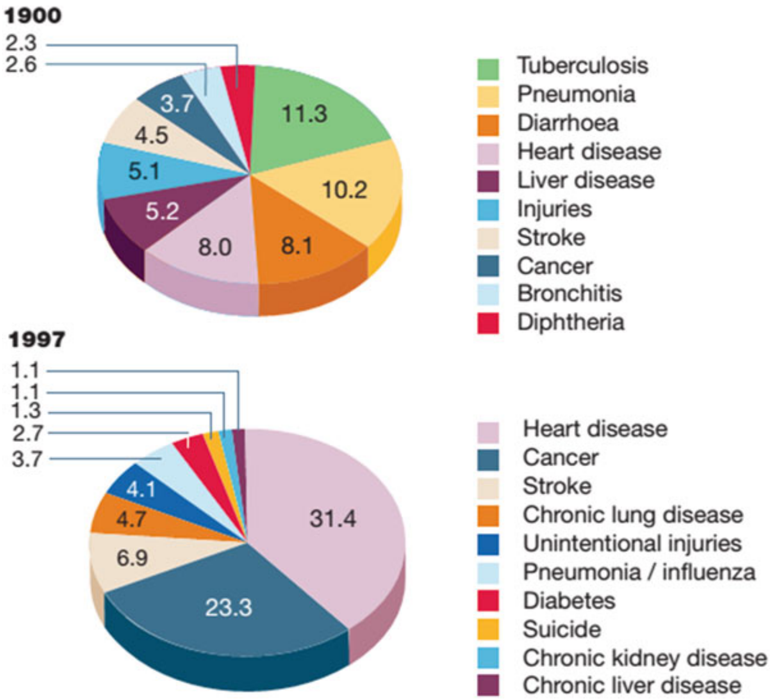

Fig. 1.1 Leading causes of deaths in the USA in 1900 and 1997. Reproduced with permission from [1]

Pioneer and priori successful studies carried out by Sigerist and coworkers during the first three decades concluded in an extermination of many illnesses and control of many others. Later developments we carried out on the fabrication of novel antibiotics. These antibiotics were successfully employed between 1940 and 1960 and further developed by pharmaceutical companies during the following decades. However, in the 1980s the tendency varied and pharmaceutical companies started to reduce the development of new drugs or redirecting it away from antibiotics [1, 4, 5].

But this optimistic vision rapidly changed as a result of the reemerging of new and in some cases antimicrobial-resistant infections. Examples of the novel/old/appearing/reappearing infectious diseases include the Ebola virus, HIV, or Legionnaire's disease that are still a public health problem in the twenty-first century. The evolution of the infectious disease patterns has been thoroughly described by Cohen [1]. As mentioned in its review, at the beginning of the twentieth century, infectious diseases were the leading cause of death worldwide. In particular, in the USA, only three diseases (tuberculosis, diarrhoeal disease, and pneumonia) were the cause of 30 % of deaths (Fig. 1.1).

However, by the end of the twentieth century, in most of the developed world, mortality from infectious diseases had been replaced by mortality from chronic illnesses such as heart disease, cancer, and stroke. This situation enhanced the average life span that had increased by about 60 % to more than 76 years [6].

While this is, a priori, true for the already developed countries, those under development do still have a serious problem with infectious diseases which are still the major cause of morbidity and mortality. According to the World Health Organization, the infectious diseases caused over 13 million deaths that correspond to a quarter of the deaths worldwide [7]. In particular, three diseases are the most common: pneumonia (3.5 million), diarrhoeal disease (2.2 million) and tuberculosis (1.5 million) [1]. Interestingly, these diseases were common on the developed world at the beginning of the twentieth century.

However, as depicted by Cohen [1] in both developed and developing worlds exhibit new microorganisms and infectious diseases have been recognized. These include toxic shock syndrome, Lyme disease, HIV, Helicobacter pylori, Nipah virus, flesh-eating bacteria, or Legionnaire's disease just to mention a few of them. Moreover, some of these infectious diseases are nowadays the origin of other chronic illnesses. For instance, Helicobacter pylori has been evidenced to be at the origin of peptic ulcers.

It is also important to note that new infectious agents had the potential for rapid international spread. This is for instance the case of Ebola or Marburg virus. Other, on the contrary, dengue fever and in spite of their apparently easier control they were reemerging. This is the case of yellow fever or malaria.

In effect, in addition to the appearance of new microorganisms, the reemerging of old infections as a result of resistance to antimicrobial agents is currently a serious global problem. This involves both developing and developed countries. For instance, in the USA from 1981 to 1995, this increase was at a rate of 4.8 % per year from 36 to 63 deaths per 100,000 [8].

Within this context, two main aspects have deserved particular attention during the last decades. On the one hand, food-borne diseases are directly related to the emergence of microbial diseases. According to the IOM [9]: "The potential for foods to be involved in the emergence or reemergence of microbial threats to health is high, in large part because there are many points at which food safety can be compromised." On the other hand, the emergence of antimicrobial resistance, recognized soon after the discovery of penicillin, has followed the introduction of every new drug. As a result, the IOM [9] reported that: "Microbes that once were easily controlled by antimicrobial drugs are, more and more often, causing infections that no longer respond to treatment with these drugs." The seriousness of this situation has increased during the twenty-first century and today antimicrobial resistance is a serious problem. Some examples of antimicrobial-resistant microbes are depicted in Table 1.1.

As mentioned above, the effect of bacterial infections significantly decreased with penicillin that became available for use in the early 1940s. In that and the following decades, small molecular weight antibiotics were used as efficient antimicrobial agents. As has been clearly explained by Ganewatta et al. [10], the targets of these antimicrobial molecules typically involved cell membranes, biosynthetic pathways, 60S ribosomes, cell wall, or genetic materials (Fig. 1.2).