Natural Products
I wish to dedicate this book to honor Professor Arnold L. Demain’s 60 years experience as a pioneer and a mentor in the field of natural product-based drug discovery. In 1954, he received his PhD from the University of California, Davis and Berkeley, in Microbiology, and joined Merck and Co. as a research microbiologist. By 1965, he had become the Founder and Head of the Department of Fermentation Microbiology at Merck. In 1969, he became a full Professor at MIT. He was elected to the National Academy of Sciences in 1994. Arny is one of the world’s leading industrial microbiologists and a pioneer in research on the elucidation and regulation of the biosynthetic pathways leading to penicillins and cephalosporins. He has led the way to the development of the β-lactam industry. His current interests are in the area of industrial microbiology and biotechnology, including industrial fermentation, antibiotics, enzymes, secondary metabolism, biofuels, and bioconversions. During his tenure, Arny trained a group of visiting scholars, postdocs, and students from all over the world, which is now internationally renowned as “Arny’s Army.” Approximately every 2 years, there is a unique scientific symposium, bringing together key academic and industrial professionals in industrial microbiology and biotechnology, called “A Celebration of Arny’s Army & Friends.” Continuing the success of the four previous meetings (in 1995 in Cambridge, Massachusetts; in 1997 in Nara, Japan; in 1999 in Gent, Belgium; and in 2001 in Merida, Mexico), the fifth symposium will be held in Shanghai, China on June 27–29, 2005.

Arny is a tireless advocate who would use every possible opportunity to promote natural product-based drug discovery. His vision, inspiration, and leadership contributed significantly to the soon-to-come renaissance of natural products. As we reflect on the history, it is abundantly clear that we benefit from his wisdom to this day.

Lixin Zhang, PhD
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Lixin Zhang, PhD
Arnold L. Demain, PhD
It seems appropriate to emphasize the topic of natural products at a time when new compounds are desperately needed to combat the current problems of antibiotic resistance, emergence of new diseases, continued presence of old, unconquered diseases, and the toxicity of certain present-day medical products. Despite such needs, today’s output from the pharmaceutical industry has decreased markedly as a result of mega-mergers among the large pharmaceutical companies, and the downgrading of natural-product discovery efforts in favor of high throughput screening of synthetic compounds made by combinatorial chemistry. The latter may appear surprising because at least half of the antibiotics and antitumor agents approved by the FDA have been natural products, derivatives of natural products, or synthetic compounds inspired by natural product chemistry. However, it is a matter of economics. The extremely high costs to the large companies of purchasing or developing genomics, proteomics, and bioinformatics have left little funding available for the more tedious screening of natural products. Even so, there is some hope. The continuing success of biopharmaceutical products from the biotechnology industry points to the ever-increasing success of natural compounds, albeit that of large molecules. Some of these smaller companies are directing part of their efforts toward small-molecule natural-product screening. A few are emphasizing biodiversity by either harnessing environmental DNA in the metagenomic effort or discovering means of growing the uncultured microbes of the past and learning how to induce secondary metabolism in these organisms. Other companies are emphasizing combinatorial biosynthesis to yield new derivatives or DNA shuffling to rapidly increase the levels of production. Future success is not a matter of the old vs the new; it is dependent on learning how to apply the exciting methodologies of genomics, proteomics, combinatorial chemistry, DNA shuffling, combinatorial biosynthesis, biodiversity, bioinformatics, and high-throughput screening to rapidly evaluate the activities in extracts as well as purified components derived from microbes, plants, and marine organisms.

There have been concomitant advances and an explosion of information in the field of natural products and it is therefore timely to review both basic and applied aspects. *Natural Products: Drug Discovery and Therapeutic Medicine* addresses historical aspects of natural products and the integration of approaches to their discovery, microbial diversity, specific groups of products (Chinese herbal drugs, antitumor drugs from microbes and plants, terpenoids, and arsenic compounds), specific sources (the sea, rainforest endophytes, and Ecuadorian biodiversity), and methodology (high-performance liquid chromatography profiling, combinatorial biosynthesis, genomics, bioinformatics, and strain improvement by modern genetic manipulations). We consider past successes, the excitement of the present, and our thoughts on the future. We hope that this book will inspire industrial and academic researchers, practitioners, and developers, as well as administrators, to look again at Nature for the future gifts that will solve unmet medical needs and make the world a safer place in which to live.

*Lixin Zhang, PhD
Arnold L. Demain, PhD*
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