PREFACE

Over the past decade, applications of high-throughput technologies, such as expressed sequence tag databases, DNA microarrays, and proteome and metabolome analyses, have considerably accelerated the discovery of new components and mechanisms involved in the assembly of alkaloids in plants. Combined with an intensive worldwide research programme and using several technical breakthroughs in biochemical, molecular, cellular, and physiological research, they have contributed to impressive advancements in our understanding of alkaloid biosynthesis. In particular, many enzymes acting in alkaloid biosynthetic pathways have been identified and characterized at the molecular level and numerous regulation processes have been also deciphered, highlighting the specific roles of phytohormones in the regulation of alkaloid biosynthesis as well as in their trafficking and storage. Different approaches based on microscopy analysis have also contributed to the elucidation of the complex and original architectures of alkaloid biosynthetic pathways showing the distribution of the high number of enzymatic steps in different tissues but also in different subcellular compartments. Alkaloids classification, usually based on their chemical structure, is thus reassessed according to a new vision of their metabolism and better knowledge of their biological and ecological activities. This complex organization can explain, in part, the difficulties encountered in the attempts to improve alkaloid production *in planta* as well as the challenges to generate these products via chemical synthesis.

Alkaloids have important biological activities, many of which have medicinal properties and are used in the treatment of human ailments, explaining our great interest not only in the identification of new natural molecules but also in the development of alkaloid production processes. We still believe that these alkaloids, and drugs developed from them, could be part of our arsenal of medicines used to cure serious diseases such as cancer or AIDS. However, plants contain only low levels of alkaloids. Therefore, improving their production by chemical synthesis or by increasing natural synthesis in plants remains a challenge and motivates research in this field. One of the ultimate goals of current research is to transpose part of the recent discoveries to the development of metabolic engineering strategies to overcome the usually very low yield of alkaloid production *in planta*. In this context, we have witnessed, over the past 5 years, the emergence of new

processes including development of yeast or bacterial platforms for the fermentative production of plant alkaloids.

The understanding of alkaloid biosynthetic pathways improves every year and there are now 12,000 natural compounds recognized as alkaloids, according to the discovery and the characterization of new natural molecules. Alkaloids present a relatively large prevalence in nature and are relatively common chemicals in all kingdoms of living organisms. More than 20% of identified plants are able to produce alkaloids of one form or another. These alkaloids show a very large degree of diversity that is at least equivalent to that observed between the plant species themselves. This structural diversity is probably the result of specific biochemical differentiation over the course of evolutionary time which reflects changing interactions of molecules with biological targets leading to adaption of plants to their changing environment. Thus, in our quest to identify new bioactive molecules after having largely explored the plant kingdom, we are now greatly interested in marine organisms. Indeed, if several plant-derived alkaloids are now classed as leading drugs in the treatment of different types of cancer, marine-derived alkaloids, isolated from aquatic fungi, cyanobacteria, sponges, algae, and tunicates, have been found to also exhibit various anti-cancer activities suggesting exciting perspectives.

Alkaloids have already been the subject of many books and academic works from various scientific fields. *New Light on Alkaloid Biosynthesis and Future Prospects* is intended to present different alkaloid families displaying the best characterized biosynthetic pathways and ecological role and the most advanced biotechnological developments. The book is divided into eleven chapters. Chapters 1 to 6 focus on plant alkaloid biosynthesis with a particular emphasis on monotepernoid indole alkaloids, tropane alkaloids, purine alkaloids and isoquinoline alkaloids. This presentation is completed by the chapter 9 which aims at presenting the technological advances leading to the identification and the characterization of new alkaloids and the chapter 10 which illustrates a distinct ecological role of alkaloids. Moreover the final chapter 11 gives an overview of marine alkaloids since very interesting discoveries have been recently made. Four chapters from 5 to 8 are more dedicated to the presentation of recent biotechnological developments leading to improvement in alkaloids production. Two of them present example(s) of the biotechnological production of camptothecin and the development of plant systems adapted to the production of specialized metabolites. The two others describe the ways used to improve the production of isoquinoline alkaloids by metabolic engineering in transgenic plants

or by using an emerging concept of fermentative production of plant alkaloids by heterologous microbial systems.

In conclusion, I wanted here to acknowledge all the authors who agreed to share their knowledge on alkaloids and to contribute to this book and also the colleagues of my laboratory for their assistance in the preparation of this book. I hope it will be of interest not only for researchers but also for students or anyone who is interested in the field of specialized metabolite research.

Nathalie Giglioli-Guivarc'h
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