Preface

Dendrimers are a new class of synthetic polymers based on a well-defined cascade motif. These macromolecules may be synthesised to reach the size of nanoobjects having dimensions similar to proteins. Dendrimers allow a highly multivalent presentation of a given molecular motif in a highly defined fashion.

This book concerns the use of this new class of macromolecules in the interdisciplinary field between synthetic organic chemistry, biology, medicine and biotechnology. Dendrimers have initially been applied extensively and studied thoroughly in polymer and material science, but the use of dendrimers as biologically useful compounds, for example in drug delivery or drug construction, is a new research field still in its infancy.

For these new applications of dendrimers, new and important questions need to be answered; how do subtle changes in the molecular motif affect the biological behaviour of a dendrimeric compound comprising multiple copies of that motif? What is the reason some dendrimers are toxic whereas others are not, although their molecular motif is similar?

The ability to construct dendrimers in a highly defined way opens up for the synthetic fine-tuning of molecules fulfilling the desired delicate balance between different biological properties. Furthermore, the ability to construct definite dendrimer architectures opens up for the thorough understanding of the exact nature of interactions taking place between biological entities and a fully synthetic macromolecule.

The present book gives a short and "popular" introduction (Chapter 1) to the dendrimer field, introducing various types of dendrimers, and some general approaches in dendrimer synthesis *e.g.* the divergent and convergent strategy, together with definitions of some common terms (dendrimer generation, shell, *etc.*) applied in this field. Importantly, our definition of dendrimer generations is in accordance with the generation definition initially applied for poly (propylene imine) dendrimers, although the generation numbering of the structurally similar polyamidoamine dendrimers seems to follow another trend. This implies that the generation numbering of the cited literature will follow the definition put out in the book and not in the associated papers. Furthermore, the introducing chapter treats some basic principles in the physicochemical behaviour of some of the common dendrimer classes.

The second chapter covers the interactions between dendrimers and biological systems both *in vitro* and *in vivo*. Important molecular factors affecting the toxicity and biopermeability of these compounds *in vitro* and *in vivo* are described, together with their ability to be transported across membranes (*e.g.* transfection) and tissue barriers

(epithelia/endothelia crossing). Biopermeability properties are of crucial importance for the pharmaco-chemical fate of a dendrimer-based drug or drug vehicle.

The subsequent chapters look into the use of dendrimers as drug-delivery devices and drugs. Chapter 3 deals with the development and chemical design of drug transport and delivery vehicles such as host–guest complexes, covalently dendrimer attached drugs (*e.g.* dendrimer prodrugs), self-immolative dendrimer drug systems and targeted drug delivery based on dendrimers.

Chapter 4 concerns the application of dendrimers as drugs and therapeutics in the treatment of antiviral or antibacterial infections as well as for antitumour and anticancer therapy. In addition this chapter goes into the interactions between dendrimers and the immune system, *i.e.* the use of dendrimers as scaffolds in vaccines and/or the use dendrimers as immune-stimulating or immune-suppressing compounds. Just recently dendrimers have been applied in the destabilisation of misfolded prion aggregates responsible for prion-associated diseases *e.g.* Alzheimer's, Diabetes or Mad Cow Disease. These aggregate destabilising dendrimers may constitute an important class of compounds in prion therapeutics and diagnostics.

The final chapter describes the use of dendrimers as mimics for naturally occurring macromolecules or even larger objects, for example, microbial or cellular surfaces, taking advantage of the fact that dendrimers can be synthesised into nanosized structures. As the mode of action of *e.g.* dendrimer antibacterial and antiviral drugs relies on their ability to mimic cellular surfaces of the infected host, there is consequently some "overlap" with Chapter 4 however, in order not to tire the reader, this overlap is kept to a minimum.

Although the main topic of this book concerns dendrimers, the book may apply for polymers having physicochemical properties similar to dendrimers (*e.g.* the larger class of hyperbranched polymers).

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Good luck!

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