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Supramolecular structures from dendrons and dendrimers☆

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Abstract

This paper reviews aspects of the association of dendrons and dendrimers into a variety of supramolecular structures. There is such a wide range of primary dendron and dendrimer chemistries that it is still difficult to predict behaviour in aqueous media, and there are few studies in non-aqueous media. The aggregation of the primary units into larger and more complex forms leads to a wider range of potential carrier systems for drugs, genes and vaccines. This review deals principally with the association structures which can be formed. These include liquid crystalline structures and dendron block copolymer aggregates, surface monolayer formation, dendrimer derived nanoparticles, micellar structures and dendrisome (vesicle) formation. Of particular interest are DNA-dendrimer complexes and dendrimer-polyanion interactions. The in vivo behaviour of dendrons and dendrimers is of course crucial and is addressed. Dendrimer vesicle solubilisation by surfactants and emulsion stabilisation by dendrimers completes the survey of secondary structures. The challenge is to understand better the processes involved and to concentrate further on the design of the synthesis of dendrons and dendrimers which will associate into specific complex structures to increase the scope of dendrimer science.

Keywords: Dendrimers; Dendrons; Monolayer; Micelles; Dendrisomes; Vesicles; Dendriplexes; DNA complexes; Aggregates; Supramolecular assembly

Contents

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1. Introduction

The origin and recent history of dendrimer chemistry has been discussed in this issue by Svenson and Tomalia [1]. There is now a growing number of publications which explore the use of dendrimers in drug, gene and vaccine delivery and the use of some dendrimers as therapeutic agents in their own right is also being investigated [2–6]. The oral absorption and organ distribution of some dendrimers has been studied [7,8] and the structure and size-related toxicity and biocompatibility of many types of dendrimers is being actively researched [4,9–13]. Dendrimers have been found to interact with several drugs and dyes providing potential applications in areas such as the solubilisation of hydrophobic molecules [14–18] and molecular inclusion formation [19,20]. Dendrimers have been designed to act as nanoscopic containers [21] or dendritic boxes [22,23] and unimolecular micelles [24] and reverse molecular micelles [25] have been described. Dendrimers have been variously proposed as pH-sensitive controlled drug release systems [26,27], catalysts [28,29] and as chromatographic materials [30].

There is a large and growing armamentarium of primary dendron and dendrimer structures, possible because of the almost limitless range of dendritic architectures that can be built around suitable multifunctional core molecules. This variety of structures has inevitably led to systems which have the ability to self-associate or to form, with agents such as surfactants and lipids, more complex secondary structures, which is the subject of this review. One of the main thrusts of work on secondary structures will be to determine which of these structures formed from what we term the 'primary' dendrons and dendrimers may be of use in the delivery of therapeutic agents.

1.1. Supramolecular assembly

The formation of supramolecular or self-assembled dendrimers induced by non-covalent interactions between dendrons and dendrimers can reduce the synthetic effort required in complex dendrimer synthesis. Such an approach generally guarantees the accuracy of the usually reversible assembly, which under the influence of particular stimuli can revert to their

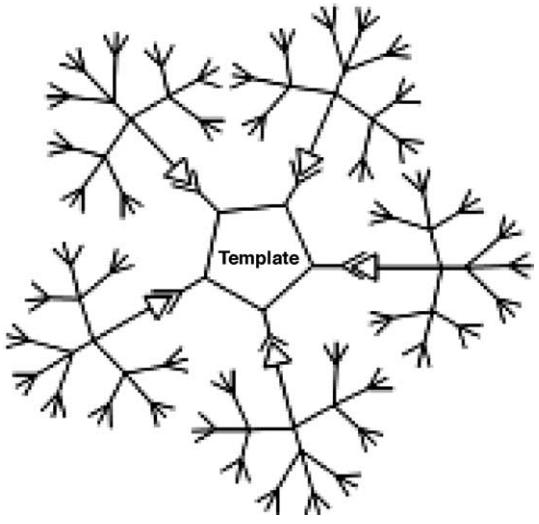

Fig. 1. Schematic representation of a supramolecular dendrimer with individual dendrons assembled around a molecular template. (Reproduced from Dykes and Smith, 2003) [34].