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Extended Abstract

Nanomedicine & Drug Delivery: Dendrimer nanotechnology for biomedical applications- Ling Peng Aix-Marseille University, France

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Abstract

Nanotechnology is widely expected to bring breakthroughs in specific delivery of the right therapeutic agent to the right patient at the right disease lesion. Dendrimers are ideal nanocarriers for drug delivery by their uniquely well-defined structures and multivalent cooperativity confined within a nano-sized volume per Se. We have established bio-inspired structurally flexible and self-assembling supramolecular dendrimers for drug delivery. These dendrimers are excellent nanocarriers for personalized medicine: They can form modular, responsive and adaptive nanosystems and effectively deliver various chemo and bio-therapeutics as well as imaging agents for precise diagnosis and personalized treatment in various diseases' models. These studies have offered new perspectives in dendrimer nanotechnology based biomedical applications.

Dendrimers are nano-sized, radially symmetric molecules with well-defined, homogeneous, and monodisperse structure consisting of tree-like arms or branches . These hyperbranched molecules were first discovered by Fritz Vogtle in 1978, by Donald Tomalia and co-workers in the early 1980s, and at the same time, but independently by George R. Newkome. The second group called synthesized macromolecules 'arborols' means, in Latin, 'trees'. Dendrimers might also be called 'cascade molecules' , but this term is not as much established as 'dendrimers' . Dendrimers are nearly monodisperse macromolecules that contain symmetric branching units built around a small molecule or a linear polymer core. 'Dendrimer' is only an architectural motif and not a compound. Polyionic dendrimers do not have a persistent shape and may undergo changes in size, shape, and flexibility as a function of increasing generations. Dendrimers are hyperbranched macromolecules with a carefully tailored architecture, the end-groups (i.e., the groups reaching the outer periphery), which can be functionalized, thus modifying their physicochemical or biological properties. Dendrimers have gained a broad range of applications in supramolecular chemistry, particularly in host-guest reactions and self-assembly processes. Dendrimers are characterized by special features that make them promising candidates for a lot of applications. Dendrimers are highly defined artificial macromolecules, which are characterized by a combination of a high number of functional groups and a compact molecular structure. The emerging role of dendritic macromolecules for anticancer therapies and diagnostic imaging is remarkable. The advantages of these well-defined materials make them the newest class of macromolecular nano-scale delivery devices. Dendritic macromolecules tend to linearly increase in diameter and adopt a more globular shape with increasing dendrimer generation. Therefore, dendrimers have become an ideal delivery vehicle candidate for explicit study of the effects of polymer size, charge, and composition on biologically relevant properties such as lipid bilayer interactions, cytotoxicity, internalization, blood plasma retention time, biodistribution, and filtration

The structure of dendrimer molecules begins with a central atom or group of atoms labeled as the core. From this central structure, the branches of other atoms called 'dendrons' grow through a variety of chemical reactions. There continues to be a debate about the exact structure of dendrimers, in particular whether they are fully extended with maximum density at the surface or whether the end-groups fold back into a densely packed interior. Dendrimers can be prepared with a level of control not attainable with most linear polymers, leading to nearly monodisperse, globular macromolecules with a large number of peripheral groups as seen in , the structure of some dendrimer repeat units, for example, the 1,3-diphenylacetylene unit developed by Moore.

Dendrimers are a new class of polymeric belongings. Their chemistry is one of the most attractive and hastily growing areas of new chemistry. Dendrimer chemistry, as other specialized research fields, has its own terms and abbreviations. Furthermore, a more brief structural nomenclature is applied to describe the different chemical events taking place at the dendrimer surface. Dendrigrafts are a class of dendritic polymers like dendrimers that can be constructed with a well-defined molecular structure, i.e., being monodisperse. The unique structure of dendrimers provides special opportunities for host-guest chemistry and is especially well equipped to engage in multivalent interactions. At the same time, one of the first proposed applications of dendrimers was as container compounds, wherein small substrates are bound within the internal voids of the dendrimer . Experimental evidence for unimolecular micelle properties was established many years ago both in hyperbranched polymers] and dendrimers.

Dendrimers are just in between molecular chemistry and

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polymer chemistry. They relate to the molecular chemistry world by virtue of their step-by-step controlled synthesis, and they relate to the polymer world because of their repetitive structure made of monomers . The three traditional macromolecular architectural classes (i.e., linear, cross-linked, and branched) are broadly recognized to generate rather polydisperse products of different molecular weights. In contrast, the synthesis of dendrimers offers the chance to generate monodisperse, structure-controlled macromolecular architectures similar to those observed in biological systems . Dendrimers are generally prepared using either a divergent method or a convergent one . In the different methods, dendrimer grows outward from a multifunctional core molecule. The core molecule reacts with monomer molecules containing one reactive and two dormant groups, giving the first-generation dendrimer. Then, the new periphery of the molecule is activated for reactions with more monomers.

Dendrimers can be synthesized by two major approaches. In the divergent approach, used in early periods, the synthesis starts from the core of the dendrimer to which the arms are attached by adding building blocks in an exhaustive and step-wise manner. In the convergent approach, synthesis starts from the exterior, beginning with the molecular structure that ultimately becomes the outermost arm of the final dendrimer. In this strategy, the final generation number is pre-determined, necessitating the synthesis of branches of a variety of requisite sizes beforehand for each generation

Another fascinating and rapidly developing area of chemistry is that of self-assembly. Self-assembly is the spontaneous, precise association of chemical species by specific, complementary intermolecular forces. Recently, the self-assembly of dendritic structures has been of increasing interest . Because dendrimers contain three distinct structural parts (the core, end-groups, and branched units connecting the core and periphery), there are three strategies for self-assembling dendrimers. The first is to create dendrons with a core unit that is capable of recognizing itself or a ditopic or polytopic core structure, therefore leading to spontaneous formation of a dendrimer. A self-assembling dendrimer using pseudorotaxane formation as the organizing force was reported by Gibson and coworkers .

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