Chapter 3

Dendrimers: A New Class of Nanopolymers

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Abstract

Dendrimers are nanosized, radially symmetrical molecules that possess a well-defined, uniform, and monodisperse structure. They generally consist of a central core, an inner branching layer, and an outer functional surface. Traditional macromolecular architectures often produce polydisperse molecules with different molecular weights, whereas dendrimers provide a more controlled structure. Various types of dendrimers have been developed, exhibiting biological properties such as polyvalency, self-assembly, electrostatic interactions, chemical stability, low cytotoxicity, and good solubility. Due to these unique properties, dendrimers have gained significant attention in the medical field. This review highlights the different applications of dendrimers in medicine and drug delivery.

Keywords: Dendrimers, polydisperse, solubility, medicine, drug delivery.

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1. Introduction

Dendrimers are nanosized, highly branched macromolecules that possess a well-defined and uniform structure. They consist of a central core, repetitive branching units forming the interior layers, and multiple functional groups on the outer surface. Because of their controlled architecture and monodisperse nature, dendrimers exhibit unique physicochemical and biological properties.

The concept of dendrimers was first introduced by Fritz Vogtle in 1978. Later, Donald Tomalia and his co-workers developed these molecules further in the early 1980s. Around the same time, George R. Newkome independently synthesized similar structures called “arborols,” meaning tree-like molecules.

Dendrimers are characterized by their symmetrical branching pattern, high number of surface functional groups, and compact molecular structure. These molecules show important properties such as polyvalency, self-assembly, electrostatic interactions, good solubility, and relatively low cytotoxicity. Because of these unique features, dendrimers have attracted significant attention in many scientific fields, especially in drug delivery, diagnostic imaging, and anticancer therapy.

As the dendrimer generation increases, their size and molecular weight also increase, resulting in a more globule structure. Due to their tunable size, surface functionality, and ability to interact with biological systems, dendrimers are considered promising nanoscale carriers for various biomedical and pharmaceutical applications.

1.1 Types of dendrimers

It includes structures with phenylacetylene subunits where third-generation branches may occupy the same space and fourthgeneration layers can overlap with second-generation layers. Another type is parquette-type dendrons, which are chiral and non-racemic molecules that exhibit intramolecular folding mainly driven by hydrogen bonding interactions.

2. Structure and Chemistry

Dendrimers are highly branched molecules that start with a central atom or group called the core. From this core, branches known as dendrons grow outward through repeated chemical reactions. Their structure is still discussed by researchers, especially whether dendrimers remain fully extended with dense outer surfaces or fold inward forming a compact interior. Unlike many linear polymers, dendrimers can be synthesized with high structural control, producing nearly uniform, globular macromolecules with many surface functional groups. Examples include repeat units such as 1,3-diphenylacetylene, developed by Moore. Dendrimers are a new class of polymeric materials and represent a rapidly developing area in modern chemistry. Dendrimer chemistry has its own specific terms and abbreviations used to describe structural features and reactions occurring on the dendrimer surface. Dendrigrafts are a type of dendritic polymer similar to dendrimers and can be synthesized with a well-defined, nearly monodisperse molecular structure. Due to their unique branched architecture, dendrimers provide excellent opportunities for host–guest interactions and multivalent binding. One of their earliest proposed uses was as container molecules, where small compounds can be trapped within internal cavities. Studies have also shown that dendrimers can exhibit unimolecular micelle-like behavior, similar to hyperbranched polymers.

2.1 Synthesis

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Dendrimers represent a link between molecular chemistry and polymer chemistry. They are synthesized through a controlled step-by-step process similar to molecular chemistry, while their repetitive monomer units relate them to polymer chemistry. Unlike traditional macromolecules such as linear, cross-linked, and branched polymers that often produce polydisperse products, dendrimers can be synthesized as monodisperse and well-defined structures similar to biological macromolecules. Dendrimers are mainly prepared by two methods: divergent synthesis and convergent synthesis. In these methods, dendrimers grow outward from a multifunctional core. The core reacts with monomers containing one active and two protected groups to form the first-generation dendrimer, and further reactions with additional monomers produce higher generations.

3. Properties

3.1 Pharmacokinetic Properties

Pharmacokinetic properties are important for the successful biomedical use of dendrimers. They influence applications such as drug delivery, imaging, photodynamic therapy, and neutron capture therapy. Dendrimers can be modified at their surface groups to form conjugates such as antibody–dendrimer and peptide–dendrimer complexes. They can also form dendritic boxes that encapsulate guest molecules, increasing their usefulness in medical applications.

3.2 Covalent Conjugation Strategies

Covalent conjugation is a method used to attach small drug molecules to polymeric carriers in order to improve their pharmacological properties. In many cases, dendrimers act as prodrugs, where the drug is linked to the dendrimer structure and released after entering the target cell. This controlled release helps improve drug activity and therapeutic effectiveness.

3.3 Polyvalency

Polyvalency is an important property of dendrimers that allows multiple functional groups to be attached to their surface. This feature enables strong and multiple interactions with biological receptors. Such multivalent interactions are especially useful in designing antiviral drugs and other therapeutic agents.

3.4 Self-Assembling Dendrimers

Self-assembly is the spontaneous and organized association of molecules through specific intermolecular forces. Dendrimers have attracted attention in this field because they contain three structural components: a central core, branched units, and surface end groups. These features allow different strategies for dendrimer self-assembly. One approach involves designing dendrons with core units capable of recognizing each other, leading to the spontaneous formation of dendrimer structures. Self-assembling dendrimers based on pseudorotaxane interactions have also been reported.

3.5 Electrostatic Interactions

Electrostatic interactions occur due to the presence of many identical functional groups on the surface of dendrimers. When these surface groups carry charges, the dendrimer behaves like a polyelectrolyte and can attract oppositely charged molecules through electrostatic forces. Examples include the aggregation of methylene blue on the dendrimer surface and the binding of charged species such as copper complexes and nitroxide cation radicals used in EPR studies.

4. Application of Dendrimers

Dendrimers have many important applications in medicine and

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pharmaceutical sciences due to their unique structure and high functionality.

4.1 Biomedical Applications

Dendrimers are widely used in the biomedical field because their structure is similar to biological molecules such as proteins and enzymes. Drugs and other molecules can be attached to the surface of dendrimers or encapsulated inside their internal cavities. They are also studied as potential blood substitutes.

4.2 Anticancer Drug Delivery

Dendrimers are promising carriers for anticancer drugs. They improve drug properties such as solubility, stability, and circulation time in the body. Drug–dendrimer conjugates can accumulate selectively in tumor tissues through the enhanced permeability and retention (EPR) effect, reducing toxicity to normal cells.

4.3 Drug Delivery Systems

Dendrimers can act as molecular containers that carry drug molecules inside their internal spaces. Their host–guest properties allow drugs to bind with dendrimers and be delivered effectively to target sites in the body.

4.4 Transdermal Drug Delivery

Dendrimers help improve the penetration of drugs through the skin. They are particularly useful for hydrophobic drugs with poor water solubility and help maintain therapeutic drug levels for a longer period.

4.5 Gene Delivery

Dendrimers are used as carriers for delivering DNA or genetic material into cells. They protect DNA from degradation and help in efficient gene transfer, making them useful in gene therapy research.

4.6 Magnetic Resonance Imaging (MRI) Contrast Agents

Dendrimer-based metal complexes are used as contrast agents in MRI because their structure allows multiple imaging molecules to be attached, improving imaging quality.

4.7 Dendritic Sensors

Dendrimers can function as chemical sensors due to the large number of functional groups on their surface. These groups can interact with metal ions or other molecules, producing detectable signals such as fluorescence.

4.8 Enhancement of Drug Solubility

PAMAM dendrimers are widely used to improve the solubility of poorly soluble drugs. Their hydrophilic surface and internal cavities give them a unimolecular micelle-like structure. Because of this property, dendrimer-based nanocarriers can increase drug solubility and improve oral bioavailability, especially for drugs with low water solubility or those affected by efflux transporters.

4.9 Photodynamic Therapy (PDT)

Photodynamic therapy involves the activation of a photosensitizing drug using visible or near-infrared light. This activation produces reactive singlet oxygen that can destroy tumor cells through necrosis or apoptosis. Dendrimers are used as carriers for PDT agents to improve tumor targeting, drug retention, and pharmacokinetic properties.

4.10 Miscellaneous Applications

Dendrimers also have several other applications in biological and

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chemical fields. They are used in cellular drug delivery, water purification by removing toxic metal ions and inorganic contaminants, and in cosmetic products. In addition, dendrimers are applied in highly sensitive analytical devices, MRI contrast agents, prion research, burn treatment, and EPR imaging.

5. Conclusion

Dendrimers are unique macromolecules with well-defined structures, numerous surface functional groups, and compact architecture. These properties make them promising candidates for many applications, especially in medicine and drug delivery systems. Since their discovery, research on dendrimers has grown rapidly, focusing on their synthesis, properties, and potential uses. Although significant progress has been made, the multistep synthesis process of dendrimers is still complex and requires considerable effort. Further research may improve their synthesis methods and expand their practical applications in various scientific fields.

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