

SYNTHESIS, PROPERTIES AND APPLICATIONS OF DENDRIMERS IN CHEMISTRY, MATERIALS SCIENCE AND NANOTECHNOLOGY

Abstract

Dendrimers are monodispersing, well-defined, and uniform macromolecules with symmetrical branched units constructed around a small molecule or a linear polymer core. They have a core that is typically symmetric, an outer shell, and an inner shell. It discusses the divergent and convergent methods of synthesis, explaining their advantages and challenges. The concept of dendrimers, such as polyamidoamine (PAMAM), Polypropylenimine (PPI), and L-lysine-based dendrimers, showcases their distinct characteristics and applications ranging from drug delivery, gene therapy, and imaging to sensing, catalysis, and optoelectronics, underscoring the versatility of dendrimers. Dendrimers could be a wonderful choice in pharmaceuticals because of their diverse abilities and various applications.

Keywords: Dendrimer; Nanoscale; PAMAM; PPI

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I. INTRODUCTION

The Greek word "Dendrons," which meaning "tree," is where the word "dendrimers" originates [1]. Tree-like arms or branches make up the well-defined, homogenous, monodisperse structure of dendrimers (Figure 1), which are nanoscale, radially symmetric molecules [2]. In 1978, Fritz Vogtle made the initial discovery of these hyperbranched molecules. The early 1980s and concurrently and independently by George R. Newcome as well. "Arborols," which translate to "trees" in Latin, are the second group of synthesised macromolecules [3]. Although this term is not as well-established as dendrimers, it may also be referred to as "cascade molecules." Almost monodispersed macromolecules known as dendrimers are composed of symmetric branching units encircling a linear polymer core or small molecule. The term "Dendrimer" refers to an architectural motif, not a compound. The size, shape, and flexibility of polyionic dendrimers can vary with successive generations and they do not have a stable shape. Dendrimers are hyperbranched macromolecules with an architecture that is precisely designed. Their end-groups, or the groups that reach the outer periphery, can be functionalized to change their biological or physicochemical characteristics. Applications for dendrimers in supramolecular chemistry are numerous, especially in host-guest reactions and self-assembly mechanisms. The unique properties of dendrimers make them attractive candidates for a wide range of applications. The combination of a large number of functional groups and a compact molecular structure characterises dendrimers, which are highly defined artificial macromolecules. Dendritic macromolecules are playing an amazing new role in diagnostic imaging and anticancer therapies [4]. These materials are well defined and represent the newest class of macromolecular nano-scale delivery devices because of their advantages. With an increase in dendrimer generation, dendritic macromolecules typically exhibit a linear diameter growth and a more globular morphology [5].

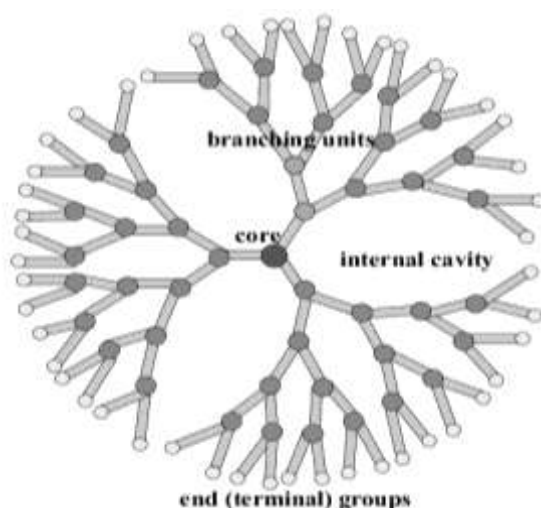


Figure 1: Common structure of dendrimer.

Consequently, dendrimers have emerged as a prime candidate for delivery systems in the explicit investigation of the effects of polymer size, charge, and composition on biologically significant characteristics like lipid bilayer interactions, cytotoxicity, internalisation, and blood plasma retention time. The dendrimers' shapes, stability, solubility,

rigidity or flexibility, and viscosity vary depending on the end groups they contain [6]. Changes to the branching units alter the dendrimer's molecule's density. This holds significant importance for the host-guest chemistry, which utilises lower density regions to enable suitable branching module selection without requiring premade unoccupied cavities.

II. BIOCOMPATIBILITY STUDIES OF DENDRIMERS

Dendrimers have some specific properties that are capable of them in biological usage and drug delivery vehicles in vivo or drug design. For this reason, they must be safe, able to pass through biological barriers, and able to circulate throughout the body for the duration of time required for a therapeutic impact [7-8].

- 1. Permeability:** It can pass across cell membranes and the blood-brain barrier (BBB). Their homogeneity and size within the nanometre range may improve their capacity to pass cell membranes [9-10].
- 2. Sustained release:** Dendrimers are also capable of releasing drugs over an extended period [11].
- 3. Stability:** They demonstrate good conjugated stability [12].
- 4. Solubility:** Most of the dendrimers display very low solubility [13].

III. SYNTHESIS OF DENDRIMERS

A relatively recent area of polymer chemistry called dendrimer synthesis is characterised by regular, highly branching monomers that result in a monodisperse, tree-like, or generational structure. A strong synthetic control is necessary for the synthesis of monodisperse polymers, and this is accomplished via stepwise processes that create the dendrimer one monomer layer, or "generation," at a time. Every dendritic site on a dendritic wedge-attached core molecule makes up a dendritic dendrimer. The term "generation" refers to the central molecule [14–15].

- 1. Divergent Method:** The multifunctional core from which the dendrimer is assembled is expanded outward by a series of reactions, most often a Michael addition reaction. To avoid errors in the dendrimer, which might produce trailing generations (some branches are shorter than the others), each step of the reaction must be decided to completion. Because there is relatively little difference in size between perfect and defective dendrimers, these impurities may disrupt the dendrimer's functioning and symmetry, making them very challenging to remove [16].
- 2. Convergent Method:** Dendrimers are made up of tiny molecules that start at the sphere's surface and are subsequently joined to a core by processes that occur before the inmost construction occurs. This process greatly simplifies the process of removing contaminants and shorter branches along the way, resulting in a more mono-disperse final dendrimer. However, because of the constrictive crowding caused by the steric characteristic along the core, dendrimers produced in this manner are not as big as those created by divergent approaches. The dendrimer's convergent growth response is being shown in Figure 2 [17].

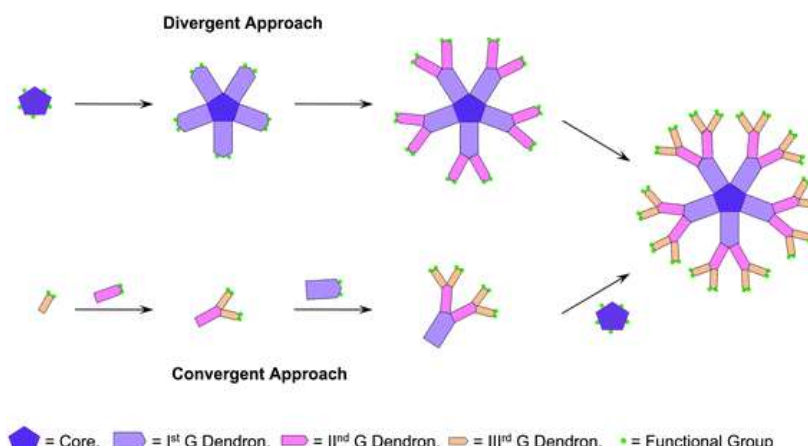


Figure 2: Synthetic approach of dendrimer by divergent and convergent method.

IV. CHEMISTRY AND CLASSIFICATION OF DENDRIMERS

A generalized structural formula of dendrimers is shown in Figure 3. Starting material represented structurally as $-\text{[CH}_2\text{N(CH}_2\text{CH}_2\text{CO)}_2\text{]}_2$ is ethylenediamine. The functionality of core N_c is 4, the functionality of branched function N_b is 2. G is the number of generations surrounding the central core and the repeating units $[\text{NHCH}_2\text{CH}_2\text{N(CH}_2\text{CH}_2)]$. Z represents the terminal functional groups, which dendrimers are $-\text{OCH}_3$ or $-\text{NHCH}_2\text{NH}_2$ [18].

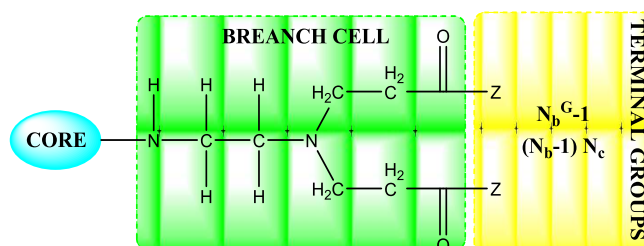


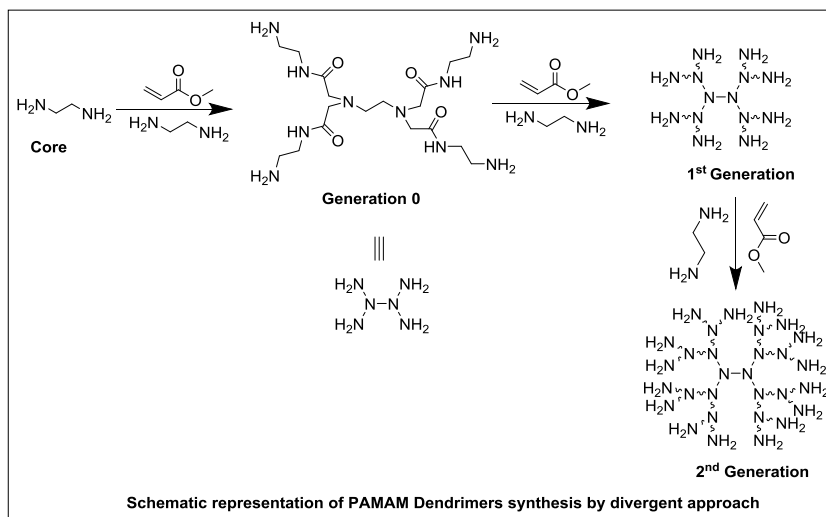
Figure 3: A generalized structural formula of dendrimers.

It can be divided into the following classes based on their form, end functional groups, and interior cavities is being shown in Table 1.

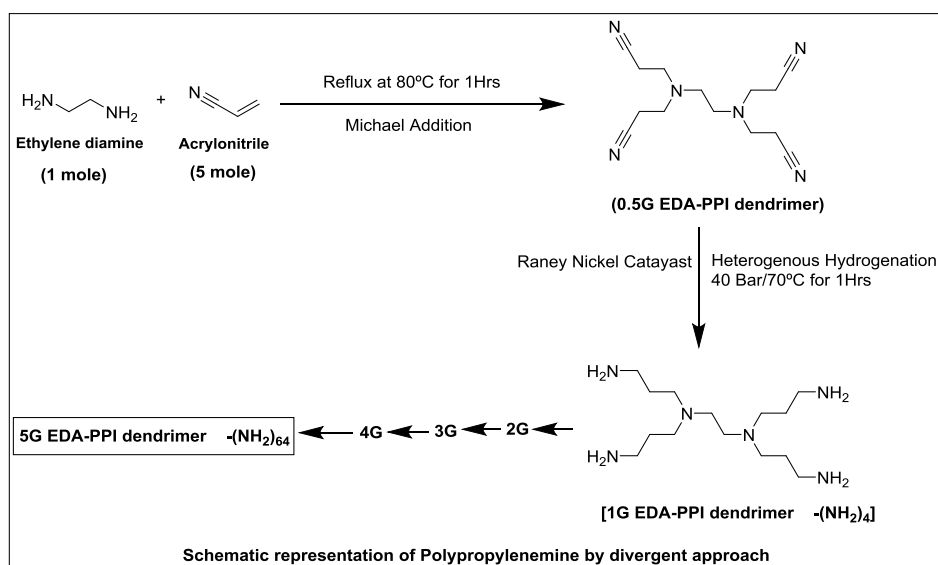
Table 1: Classification of Dendrimer.

S. No.	Chemical Classification	Physical Classification	Miscellaneous
1.	Polyamidoamine (PAMAM) dendrimers.	Simple dendrimer	Dendrophanes
2.	Polypropylenimine (PPI) Dendrimers.	Liquid crystalline dendrimer.	Metallo dendrimers
3.	Polyether (PE) dendrimers	Chiral dendrimer	Polyamino phosphine
4.	L-lysine based Dendrimers	Micellar dendrimers	Dendritic box
5.	Phenyl acetylene dendrimers.	Hybrid dendrimers	Carbohydrate vaccine dendrimers

- 1. Polyamidoamine (PAMAM) Dendrimer:** It is a specific type of dendrimer that consists of a central core, interior branches, and an exterior surface. They are synthesized through a stepwise reaction process, resulting in a well-defined and highly branched polymer structure [19, 20].

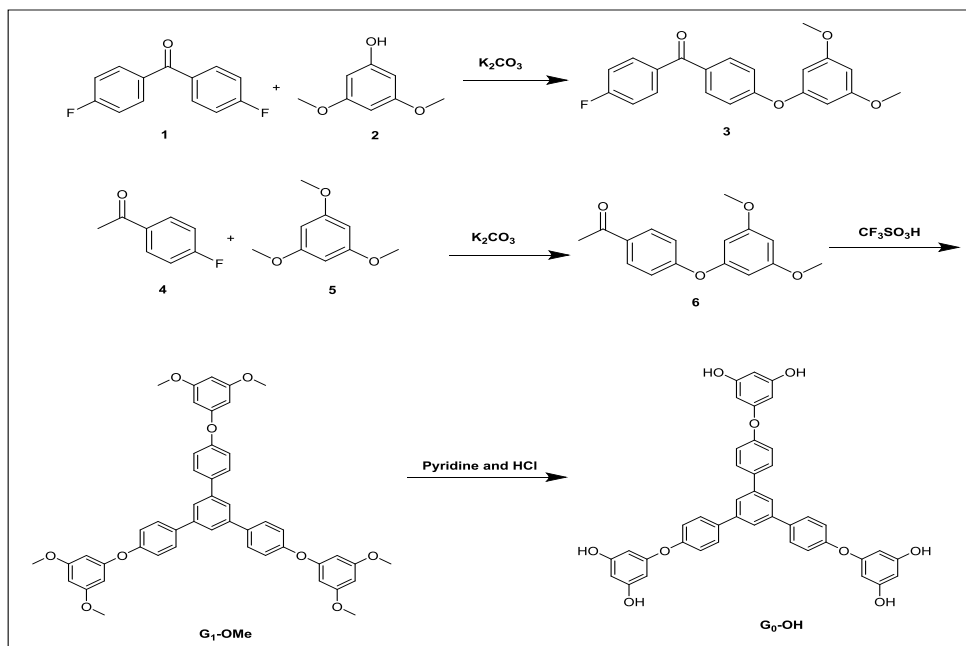


- 2. Polypropylenimine (PPI) Dendrimer:** It has increased significant interest in various fields due to their exclusive properties. PPI dendrimers are synthesized from PPI, a branched polymer with primary amine groups. Here are some key characteristics and applications of PPI dendrimers [21].



- 3. Polyether (PE) Dendrimers:** To make branched polyether ketone dendrimers, aromaphilic nucleophilic substitution reactions were used. Bis(4-fluorophenyl)methanone **1** reacted with the 3,5-dimethoxyphenol **2** in the presence of potassium carbonate to get (4-(3,5-dimethoxyphenoxy)phenyl)(4-fluorophenyl)methanone **3**. On the other hand, 1-(4-fluorophenyl)ethan-1-one **4** reacts with 1,3,5-trimethoxybenzene **5** in the presence of potassium carbonate to produce 1-(4-(3,5-dimethoxyphenoxy)phenyl)ethan-1-one **6**.

Compounds **3** and **6** were used as building blocks and starting cores. The reaction between compound **6** and trifluoromethanesulfonic acid ($\text{CF}_3\text{SO}_3\text{H}$) gave the first-generation dendrimer ($\text{G}_1\text{-OMe}$). $\text{G}_1\text{-OMe}$ having a methoxy group was converted into hydroxy groups ($\text{G}_1\text{-OH}$) treated pyridine and hydrochloric acid. These steps repeat to get a second and third generation of dendrimers [22].



4. L-lysine based dendrimer: L-lysine-based dendrimers are a type of dendritic polymer that is synthesized using L-lysine, an essential amino acid. They have a central core, interior branches, and an outer shell that can be functionalized with various groups for specific applications. L-lysine-based dendrimers are particularly interesting because L-lysine is a natural amino acid found in proteins and has well-established biocompatibility. This makes these dendrimers attractive for numerous biomedical uses. The synthesis of L-lysine-based dendrimers involves building layers of L-lysine units around a central core molecule. The repetitive nature of dendrimer synthesis allows for precise control over their size, structure, and surface functionalities. This controlled design is crucial for tailoring dendrimers to specific applications [23].

V. APPLICATION OF DENDRIMER

Dendrimers are branched, well-defined, nanoscale polymers along with a broad range of uses across several areas. Their unique structure and properties make them valuable in areas such as medicine, materials science, catalysis, and electronics. Here are some notable applications of dendrimers-

1. Gene Delivery: Dendrimers may potentially be used in gene therapy as non-viral vectors. Their surface can be modified to carry DNA or RNA molecules, facilitating their transport into cells and enhancing gene delivery efficiency. Dendrimers offer advantages such as high loading capacity, protection of genetic material, and the ability to control the release of genes [24].

- 2. Imaging Agents:** To improve contrast in medical imaging methods like magnetic resonance imaging (MRI) or fluorescence imaging, dendrimers may be functionalized with imaging agents like magnetic nanoparticles or fluorescent dyes. These modified dendrimers can help visualize specific tissues or monitor the biodistribution of drugs [25].
- 3. Sensors and Biosensors:** Dendrimers' well-defined structure and functionalize surface make them suitable for sensing applications. They can be tailored to detect specific molecules or ions by incorporating recognition sites into their architecture. Dendrimer-based sensors have been used for environmental monitoring, detection of biomarkers, and medical diagnostics [26].
- 4. Catalysis:** Dendrimers with catalytically active groups can be employed as efficient catalysts for various chemical reactions. Their large surface area and precisely controlled structure enable the creation of catalytic sites with high activity and selectivity. Dendrimer-based catalysts have found applications in organic synthesis, fuel cells, and environmental remediation [27].
- 5. Optoelectronics:** Dendrimers possess unique electronic and optical properties that make them useful in optoelectronic devices. They may be used as organic solar cells, organic light-emitting diodes (OLEDs), or organic photodetectors. Dendrimers offer advantages such as tuneable emission wavelengths, high charge mobility, and ease of processing [28].
- 6. Coatings and Adhesives:** Dendrimers can enhance the performance of coatings and adhesives by providing improved adhesion, mechanical strength, and resistance to environmental factors. They can be incorporated into paints, coatings, and adhesives to enhance their properties, such as corrosion resistance, scratch resistance, and anti-fouling capabilities [29].
- 7. Drug Delivery:** Dendrimers can be used as carriers for drug molecules. The careful control of their dimensions, form, and surface chemistry enables the targeted administration of medications to certain bodily locations. Dendrimers can encapsulate drug molecules within their internal cavities or conjugate them to their surface, improving drug solubility, stability, and bioavailability [30].

VI. CONCLUSION

Dendrimers represent a remarkable class of polymers that have captivated researchers across disciplines due to their precisely controlled architecture and versatile properties. Numerous applications that take use of dendrimers' special properties have been made possible by the ability to design them at the molecular level. Dendrimers find extensive use in the field of drug delivery, where their well-defined structure allows for precise encapsulation and controlled release of therapeutic agents. Their multifunctional nature enables the incorporation of targeting moieties, enhancing drug delivery to specific tissues or cells while minimizing side effects. Additionally, dendrimers' tunable surface chemistry facilitates the attachment of imaging agents, enabling real-time tracking of drug distribution within the body. In gene therapy, dendrimers serve as promising vectors for the delivery of genetic material. Their ability to compact and protect nucleic acids, such as DNA and RNA, while enabling controlled release in the cellular environment, holds great potential for treating

genetic disorders and various diseases at the molecular level. Dendrimers' applications extend into nanotechnology, where they contribute to the fabrication of nanoscale devices and structures. Their precisely controlled size and shape make them valuable components for building nanoscale assemblies, which have implications in electronics, sensors, and catalysis.

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