Review Article

DENDRITIC POLYMERS: AN INNOVATIVE STEP TOWARDS GREEN FUTURE

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ABSTRACT

Dendrimers referred as the “Polymers of the 21st century” have advanced from a concept to become a new category of polymers with a novel architecture, high loading capacity and versatile chemical structures. The key factors that facilitate steady increase of its application are non-toxicity, multifunctionality, Biodegradability, and non-immunogenicity of dendrimers. Recent advances have generated avid studies at the frontiers of organic, inorganic, supramolecular and polymer chemistry. This review covers physico-chemical properties, classification, approaches for dendrimer synthesis, characterization, along with their potential application in areas of research, technology and treatment like dendrimers for targeted drug delivery, gene delivery, printing inks and paints, cosmetics, light harvesting materials, and waste water treatment. This review clearly demonstrates the various applications of dendrimer and indeed substantiates the high hopes for green future.

Keywords: Dendrimer, polymer, targeted drug delivery, green future

INTRODUCTION

Dendrimers are three-dimensional, highly branched, monodispersed macromolecules obtained by a repetitive sequence of reaction steps. The functional groups can be placed on the core, surface groups, or branching units of dendrimer [1]. The name dendrimer is derived from Greek word "Dendron", meaning tree. Sometimes additionally known as asborols and cascade-molecules. The first dendrimers were made by divergent synthesis approach by Fritz Vogtle[2], Donald Tomalia at Dow Chemical[3,4], and by George Newkome[5]. Dendrimer may be spheroid or nanostructures that are capable of carrying molecules encapsulated within the void spaces or connected to the surface. The chemical composition and generation of the surface and core functionalities aids in the verification of dimension, shape, and reactivity. They have very low polydispersity and usually have a size in the range of 1-10 nm. Dendritic copolymers are a specific group of dendrimer. There are generally two different types of copolymer as Segment-block Dendrimer are obtained by attaching completely different wedges to one poly functional core molecule and Layer-block Dendrimer comprise coaxial spheres of differing chemistry [6].

Synthesis

Dendrimer composition is one of the newly fields of polymer chemistry. They are synthesized by a stepwise repetitive reaction succession which builds the dendrimer up one generation (or one monomer layer) at a time [7], with topology radiating from a central core and grown generation by generation. The molecular design parameters such as surface/interior chemistry, dimension, shape, topology and flexibility can be controlled during the time of synthetic procedures. Some of the efficient Synthetic techniques include the Starburst divergent strategy [8, 9], the convergent growth strategy [10], and the self-assembly strategy [11]. The idea of the dendrimer synthesis is simple. Various methods used for the synthesis of dendrimer are as follow:

Divergent method: The molecule is congregated from the core to the periphery, initiated by the coupling reaction of the core and a dendron monomer, which most often has one reactive group for coupling with the core, and more than one deactivated group at the outside to prevent random polymerization. In this way, the obtained first generation dendrimer has deactivated functional groups at their peripheral, that are changed over to reactive species by deprotection or changing functional groups for the next stage reaction.Convergent method: In the convergent method, the opposite approach i.e. synthesis starting from the periphery to the core, developed by Hawker and Fre´chet restructured the synthetic advances to monodisperse dendrimers. In this approach, the reactive species resides on the focal point of the dendritic wedge. Due to steric hinderance, this strategy hinders the reactivity of focal point when increase of the generation takes place.Hyper cores and branched monomers growth: In this approach the core reacts with two or more moles of reagent containing at least two protecting branching sites, followed by removal of the protecting groups. Double exponential growth: It is a mixed growth approach, where monomers for both convergent and divergent approaches are reacted together to give an orthogonally protected trimer.

Chemistry Behind Dendrimers

Click chemistry tailored to generate substances rapidly and reliably by joining small units together was first completely depicted by K. Barry Sharoless of the Scripps Research Institute in 2001. Amalgamation of dendritic units is based on the principles of Click chemistry. This reaction is clearly a breakthrough in conceptualization of dendrimers and their synthesis. A preferable Click chemistry reaction should be: measurable; wide in scope; stereospecific; generate only inoffensive byproducts; Give very high chemical yields; physiologically stable; exhibit a large thermodynamic driving force (>84 kJ/mol) to favor a reaction with a single reaction product; and have high atom economy.

Properties

The properties of dendrimers are mainly influenced by the type of functional groups on its surface. They show better physical and chemical properties than linear polymer due to their molecular structure. Intrinsic viscosity is found to be less in case of dendrimers when compared to linear polymers.

Solubility: The dendrimer with hydrophilic end group is soluble in water whereas a dendrimer with hydrophobic end group is soluble in non-aqueous solvents. It is hypothetically practicable to project a water dissolvable dendrimer with intrinsic hydrophobicity, which would allow it to capture a hydrophobic drug in its interior.Monodispersity: Systematic synthesis and proper purification of dendrimers lead to very low polydispersity. The dendrimers synthesized by the convergent method are found to have very high monodispersity.Size and Shape: The diameter of the dendrimer increases as the generation increases. Lower generation dendrimers have ellipsoidal shape and higher generation have a spherical. Cytotoxicity: Dendrimer having $-NH_2$ end groups have cytotoxic properties which are usually found to be concentration or generation dependent. Malik et al confirmed the fact that dendrimers with amine terminal groups show a hemolytic effect at concentrations as low as 10 microgram/ml[12].

Types

The dendrimer can be classified on the basis of their branching, chirality, shape, structure and attachment as follow:

1. PAMAM dendrimers

The auxillary aspects of dendrimers became an exuberant scope of research intrigued at the Winter Polymer Gordon Conference in first described the composition of PAMAM dendrimers[1]. This led to the paper set forth the dendrimer superficial-congestion attribute presently alluded to as the de Gennes dense packing phenomenon [13]. This was succeed by the first molecular level modeling contemplation by Goddard and co-worker[14] of the structural properties of NH_3-cored poly(amidoamine) (PAMAM) dendrimers (up to generation 6) and polyether dendrimer (up to the self-limiting generation 4). Polyamidoamine dendrimer has applications extending from drug delivery, molecular encapsulation, gene therapy, building blocks for nanostructures to micelle mimics as decontaminating agents.

2. Radially layered poly (amidoamineorganosilicon) Dendrimers(PAMAMOS)

This unique dendrimer with silicon[15] consists of hydrophilic, nucleophilic polyamidoamine (PAMAM) interiors and hydrophobic organosilicon (OS) exteriors. Excellent cobweb regularity, efficiency to intricate and encapsulate various guest species offer phenomenal possibilities for new applications in nanolithography, electronics, photonics, chemical catalysis etc. and useful precursors for the preparation of honeycomb like networks with nanoscopic PAMAM and OS domains.

3. Poly (Propylene Imine) dendrimers(PPI)

Poly (Propylene Imine) dendrimers (PPI) generally have poly-alkyl amines as end groups, and numerous tertiary trispropylene amines present in the interior portion. It is commercially available up to G5.0 and has wide applications in material science as well as in biology.

4. Liquid Crystalline Dendrimers

These are made of mesogenic monomers e.g. mesogen functionalized carbosilane dendrimer. Liquid Crystalline dendrimers containing silicone are the most studied and the most important type because they have excellent chemical and thermal stability.

5. Carbosilane Dendrimers

Carbosilane Dendrimers are among the most widely used because of their high flexibility, catalytic inertness, and accessibility. They are kinetically and thermodynamically steady owing to the low polarity of the Si–C bond and its high bond strength (306 kJ/mol), which is comparable to that of C–C bond (345 kJ/mol). They are built stepwise from the central core that has alkenyl groups through the reiteration of successive hydrosilylations with chlorosilanes and alkenylations with Grignard reagents.

6. Tecto Dendrimers

Tecto dendrimers are prepared by arranging nucleophilic or electrophilic core reagents.

7. Photoresponsive Dendrimers

When the divergent approaches are used for the photoresponsive dendrimer synthesis, the additional potential issues would emerge; especially the photoresponsive molecules are used as dendrimer core. That is; the photosensitive core moiety will have a chance to be exposed to room light throughout the amalgamation because the divergent method is started with a core molecule. It is a real and substantive problem because once the photoresponsive moiety reacts to give another isomer or photo products, all dendrimers prepared will be seriously damaged. On the other hand, the photoresponsive molecules are used as the end groups, this undesirable opportunity will be dimished. In this case, the reaction of dendrimer with photoresponsive molecules ought to proceed effectively and completely because of the difficulty of purification. There are few examples of the photoresponsive molecules which can be used for photoresponsive dendrimers: photoisomerizable molecules like stilbenes or azobenzenes, phototautomerizable chalcones, quinolines exhibiting excited-state intramolecular proton transfer, and the combination of the photo-induced electron donor-acceptor molecules. Some of the commercially reported photoresponsive dendrimers was azobenzene dendrimers having up to 32 azobenzenes in the periphery[16].

8. Chiral Dendrimers

In chiral dendrimers, the chirality is based on the building of 4 constitutionally grouped but chemically alike branches to an achiral core e.g. chiral dendrimers obtained from pentaerythritol.

9. Micellar Dendrimer

These are aromatic; water soluble dendrimers forming a collection of the aromatic polymeric chain which able to generate an environment that resembles some micellar structures, which forms a complex with small organic molecules in water.

10. Hybrid Dendrimer

These are the preparation of a dendritic and linear polymer in hybrid block or graft copolymer form, which provide an opening to use them as surface active agents, compatibilizers or adhesives, e.g. hybrid dendritic linear polymers.

11. Amphiphilic Dendrimer

These are the class of globular dendrimers that have an asymmetrical but highly controlled division of chain end chemistry. These may be oriented at interface forming interfacial liquid membranes for neutralizing aqueous organic emulsion.

12. Organometallic Dendrimers

Organometallic dendrimers have been considered due to their interesting optical, electronic and magnetic properties. The majority of organometallic dendrimers contain metallic species located at the periphery or at the core.

13. Multilingual Dendrimers

Multilingual Dendrimers include manifold copies of a specific functional group on the surface.

APPLICATION

1. Dendrimer as magnetic resonance imaging contrast agent

To make strides the pharmacokinetic properties of dendrimer contrast agents, the introduction of target-definite moieties to the dendritic MRI contrast agents have been examined. Dendrimer-based metal chelates simulate as magnetic resonance imaging contrast agents, which are exceedingly consistent because of their properties.

2. Dendrimer in drug delivery

Currently there are some dendrimer based formulations available in the world market shown in Table1.

Table 1: Table showing some marketed formulations with dendrimer along with their manufacturer's name and use

Trade Name	Manufacturer	Use
VivaGel™	Starpharma	Topical microbicide to prevent sexually transmitted diseases
Alert Ticket™	US Army Research Laboratory	Used to detect Anthrax
Stratus CS Acute Care™	Dade Behring	For cardiac diagnostic testing
SuperFect™	Qiagen	Gene transfection agent applicable to a broad range of cell lines.
Riofect™, Priostar™, and STARBURST	Starpharma	Targeted diagnostic, therapeutic delivery for cancer cells

3. Dendrimer as Gene Transfer Reagent

Dendrimers can also play major role in gene therapy. Administration of surface modified PPI (Poly(Propyleimine)) dendrimer complexed with DNA resulted in liver-targeted gene expression.

4. Dendrimer in targeted drug delivery

Using dendrimers conjugated target drug moieties instead drug molecule alone, the shortcomings like moderate bioavailability, insolubility, toxicity and the decomposition of the drug under biological circumstances can be overcome. The methotrexate and PAMAM dendrimer conjugates were prepared by two different methods and compared the cytotoxicity and selectivity towards cancer cell lines [17]. The dextran conjugated dendrimer was found to have the slower release, lower toxicity and higher accumulation in cancerous cells [18] whereas conjugation with different biofunctional moieties such as folic acid linked to complementary DNA to form molecules capable of targeting to the cancerous cells expressing the folate receptors [19, 20].

5. Dendrimer in transdermal drug delivery

To enhance the penetration of drugs through the skin many organic solvents are used which may cause dermatotoxicity and/or immune response. PAMAM dendrimers administered along with polyalkanoate were found to increase the penetration of model drug tamsulosin hydrochloride in comparison to when it was administered alone. The same effect was observed for various NSAIDs like ketoprofen and ibuprofen[21].

6. Dendrimer in oral drug delivery

The major problems associated with the oral dosage of drugs are first pass metabolism and insolubility of hydrophobic drugs. Dendrimer help in increasing solubility of hydrophobic drugs and offer a good protective coating of drugs to minimize the effect of enzymes. Dendrimer has unimolecular micelle and do not possess a critical micelle concentration. These properties provide the opportunity to soluble poorly drugs by encapsulating them within the dendritic structure. Oral drug delivery studies using the human colon adenocarcinoma cell line, Caco-2, have indicated that low-generation PAMAM dendrimers cross cell membranes, presumably through a combination of two processes, i.e. paracellular transport and adsorptive endocytosis.

7.Dendrimer in ocular drug delivery

The surface-modified dendrimers provide unique solutions to complex delivery problems for ocular drug delivery, as they are predicted to enhance pilocarpine bioavailability. The important compensation of dendrimer in ocular drug delivery is preservance in corneal residence time, which can provide better bioavailability of the drug, and initiate in the form of eye drops.

8.Dendrimer in pulmonary drug delivery

Administration of dendrimer through IV route is safe and nontoxic. More than 60% of cationic dendrimer get accumulated in the liver and slow rate of clearance is observed in the case of anionic dendrimers. Anticancer drugs like cisplatin and 5-Fluorouracil if administered using dendrimer show detectable blood levels for 12 hrs. Fernandez et al used first generation dendrimer to deliver anti-chagasic agents intravenously. They found dendrimers to be a perfect carrier for such type of drugs since the dendrimers showed absolutely no hemolytic effect and did not produce damage to the cellular membrane. The relative bioavailability of Enoxaparin was found to increase by 40% due to G2 and G3 generation positively charged PAMAM dendrimers.

9. Dendrimer for additives, printing inks, and paints

Dendrimers can be used in toners material with additives which require less material than their liquid counterparts. Xerox Corp. Patented a dry toner compound dendrimers as charge enhancing species in the form of an additive. Use of Dendrimer additives is effective for modifying the surface characterization of the thermoplastic resin after molding. One example for this is polycarbonates, which are broadly used as an engineering thermoplastic for providing a unique combination of toughness, stiffness, high softening temperature and processibility.

10. Dendrimer in the Sustained release of drug

The prepared ketoprofen-PAMAM dendrimer complex and compared the in-vitro release profile of this complex with the release profile of ketoprofen alone. It was found that the drug dendrimer complex showed sustained release of ketoprofen thereby also showing a prolonged effect when given in vivo to model mice. Preparatio of PAMAM dendrimer conjugated with sulfamethoxazole was tested for the in vitro release, solubility enhancers and anti-bacterial activity.

11. Dendrimer as blood substitution

Their steric bulk surrounding a heme-mimetic center significantly slows degradation compared to free heme and prevents the cytotoxicity exhibited by free heme. Therefore, they can also be investigated for use as blood substitute.

12. Dendrimer in photodynamic therapy

Photodynamic therapy (PDT) relies on the activation of a photosensitizing agent with visible or near-infrared (NIR) light. Upon excitation, an exceedingly energetic state is formed which, upon reaction with oxygen, manages a highly reactive singlet oxygen competent of inducing necrosis and apoptosis in tumor cells. Dendritic delivery of PDT agents has been investigated to make strides upon tumor selectivity, retention, and pharmacokinetics.

13. Dendritic sensors

The fluorescence of a fourth-generation poly (propylene amine) dendrimer decorated with 32 dansyl units at the periphery was examined. Since the dendrimer contains 30 aliphatic amine units in the interior, suitable metal ions are able to coordinate. It was observed that when a $Co2+$ ion is incorporated into the dendrimer, the strong fluorescence of all the dansyl units is quenched. Low concentrations of $Co2+$ ions ($4.6 \times 10-7$ M) can be detected using a dendrimer concentration of $4.6 \times 10-6$ M. The numerous fluorescent groups on the surface serve to amplify the affectability of the dendrimer as a sensor[22].

14. Dendrimer as Catalyst

Catalysis is one of the promising applications of all, since it is simple to tune the structure, size, and locations of the catalytically active site, and most importantly, dendrimers have the potential to combine both heterogeneous and homogeneous catalysis. A number of catalytic reactions involving composite mettalo dendrimers have been reported thus far, and are not limited to Suzuki coupling, oxidation, hydroformylation, hydrogenations, alkene metathesis, and the Heck reaction.

In the majority of fuel cells, the catalysts used are platinum and platinum alloy colloidal particles that are either supported or unsupported. Recently, there has been growing interest in devising wet chemical alternatives for physical deposition methods for applications involving thin films. Deposition of platinum on thin gold films is often a challenging issue leading to fragmented scope and improper adhesion. The films formed without dendrimers cannot sustain the electro-oxidation currents due to the instability of the films whereas the films formed with dendrimers can sustain currents for longer duration and for several cycles. The dendrimer-derived Pt films exhibit higher catalytic activity compared to other methods.

Characterization

Some of the techniques for the determining of dendrimer are discussed in table 2

Table 2:characterization methods of dendrimer

S. No.	Techniques
1	NMR Most widely used for dendrimers characterization. To examine the size, morphology, dynamics of dendrimers for organic dendrimers such as PPI, Polyphenylester. 1H, 1H COSY: For polyphenyacetylene or polyaryldendrimers 1H,1H NOESY: For PPI dendrimers 1H,1H EXSY: For polyamide dendrimers 1H,1H TOCSY: For melamine dendrimers
2	UV-Vis method Used to track the composition of dendrimers. The intensity of the absorption band is essentially corresponding to the number of chromophoric units.
3	Infra-red spectroscopy For monotonous analysis of the chemical transformations Occurring at the periphery of dendrimers.
4	Near Infra-red spectroscopy Used to characterized delocalize π-π stacking interaction between terminal group of modified PANAM.
5	Fluorescence The high sensitivity of fluorescence has been used to quantitate deficiency during the composition of dendrimers
6	Mass spectroscopy Chemical ionization or fast atom bombardment can be used only for the characterization of small Dendrimers whose mass is below 3000 Da. Electrospray ionization can be used for Dendrimers efficient to form constant multicharged species.
7	X-ray diffraction This technique allows definite resolution of the chemical consistency, structure, size, and shape of the dendrimer.
8	Microscopy Electron or light propagate images that enlarge the primary, with a resolution eventually confined by the wavelength of the origin.
9	Scanning microscopy The image is produced by touch contact Q at a few angstroms of a precise cantilever arm with the specimen. Ex. Atomic force microscopy.
10	Chromatography Size exclusive or gel permeation chromatography concede the separation of molecules accordingly to size.
11	Electrical techniques A. Electron paramagnetic resonance B. Electrochemistry It gives information concerning the possibility of interaction of electroactive terminal groups.
12	Electrophoresis Used for the assessment of purifying and homogeneity of several types of water dissolvable dendrimers.
13	Rheology Used as an analytical probe of the morphological structure of dendrimers.
14	Differential scanning calorimetry Depending upon the chain composition, entanglement and molecular weight of polymers it is used to perceive the glass transition temperature.
15	Dielectric spectroscopy Gives information about molecular dynamic procedure.

15. Dendrimer as a separating agent

Dendrimer with a high density of functional moiety is able to form micelle structure which can be effectively isolated and recovered by the ultrafiltration membrane. These micelles provide high functional density at the surface of the particle, high surface area and ease of separation for isolation and regeneration of the compound. It was found that unmodified commercial dendrimeric compounds containing amine and hydroxyl groups are generally more effective for boron absorption. Polyamidoamine (PAMAM) dendrimers are used as chelating agents for the removal of certain metal ions from waste water[23] and from contaminated soil[24]. Other modified chelating PAMAM and poly (propylene imine) dendrimer are also reported to be good ligands for various hard metal cations or can be described as "nanosponges" for the removal of Polycyclic aromatic hydrocarbons and other particles.

16. Dendrimer in light harvesting material

A study on σ-conjugated dendrimers family based on truxene and thienylethynylene was done. These synthesized dendrimers show intrinsic energy gradient from periphery to the core along with broad absorption in the UV-visible range and proficient energy transfer to the lower energy centre. Hence, they are highly potential as light harvesting materials [25].

17. Dendrimer nanofibres

It has been reported that polyphenylene dendrimers with various cores (such as tetraphenylmethane, biphenyl, and azobenzene) and of different generations can self-assemble into micrometer long nanofibers in addition to the formation of globular dendrimer aggregates, on hydrophobic surfaces such as HOPG and silanized mica[26, 27].

18.Dendrimer as a solubility enhancer

The use of dendrimers as the solubilizing agent for poorly soluble drugs has allure the consideration of many scientists due to its distinctive stable micelle resembling properties, which are dissimilar from those of conventional micelles. Dendrimers vanquished the obstacles to their solubilisation through either chemical or mechanical modification of the environment surrounding the drug molecule or physically modify the macromolecular characteristics of collective drug particles.

19.Dendrimer in cosmetics

Dendrimer encompasses an incredible contribution in cosmetics. Various cosmetic industries used dendrimers in their formulation. L'oreal has a patent for utilizing dendrimers for the production of cosmetics like mascara or nail polish. Some formulations of Unilever like gels, spray, and lotion are also patented for utilizing dendrimers in their formulation [28].

20.Dendrimer in Waste Water Treatment

The purification of water maculated by toxic metal ion, inorganic solute and organic solutes can be done by using dendritic polymers.

21.Dendrimer for siRNA Delivery

In current ages, dendrimers have been deliberately searched for their probable relevancy as carriers for nucleic acid therapeutics, which exploit the cationic charge of the dendrimers for efficient dendrimer-nucleic acid concentration. siRNA is considering a promising, variable tool amongst diverse RNAi-based therapeutics, which can efficiently methodize gene appearance if deliver effectively within the cells.

Advantages

Complex molecular frameworks, which combine characteristics of distinct moderate molecular weight materials(monodisperse) with those of polymers (uncertain degrees of conformational flexibility, magnitude modulated viscosity, glass transition etc.) depict an alluring passage of adding functionality (e.g., multifunctional and high control of functional specificity and hierarchy) and scheming "multitask material" with tunable properties.

Future Prediction

Future applications of dendrimers rely on effective and practical synthetic procedures. Future work is inevitable to find out cost effective synthetic strategies with least exertion and the relationship between dendrimer- drug molecules for efficacious commercial utilization of this technology.

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Conflict Of Interest

The authors declare no conflict of interest.

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References

1. Tomalia, D. A., Naylor, A. M., & Goddard, W. A. (1990). Starburst Dendrimers: Molecular-Level Control of Size, Shape, Surface Chemistry, Topology, and Flexibility from Atoms to Macroscopic Matter. *Angewandte Chemie International Edition in English*, 29, 138–175.
2. Buhleier, E., Wehner, W., & Vögtle, F. (1978). Cascade and Nonskid-chain-like Synthesis of molecular cavity topologies. *Synthesis*, 2, 155-158.
3. Tomalia, D. A., (Jan 13, 1996). Treelike molecules branch out. *Science News*, 17-32.
4. Tomalia, D. A., Baker, H., Dewald, J., Hall, M., Kallos, G., Martin, S., Roeck, J., Ryder, J., & Smith, P. (1985). A New Class of Polymers: Starburst-Dendritic Macromolecules. *Polymer Journal*, 17, 117-132.
5. Newkome, G. R., Yao, Z., Baker, G. R., & Gupta, V.K. (1985). Micelles. Part 1. Cascade molecules: a new approach to micelles. A [27]-arborol. *The Journal of Organic Chemistry*, 50(11), 2003-2004.
6. Trivedi, V., Patel, U., Bhimani, B., Daslaniya, D., Patel, G., & Vyas, B. (2012) Dendrimer: Polymer of

21st Century. *International Journal of Pharmaceutical Research Bio Sciences*, 1(2), 1-2.
7. Momatake, A., & Arai, T. (2004). Synthesis, excited state properties, and dynamic structural change of photoresponsive dendrimers. *Polymer*, 45, 5369-5390.
8. Tomalia, D. A. (1996). Starbust dendrimers-Nanoscopic supermolecules according to dendritic rules and principles. *Macromolecular Symposia*, 101, 243-255.
9. Tomalia, D. A. (1994). Starbust/Cascade dendrimers: Fundamental building blocks for a new nanoscopic chemistry set. *Advanced Material*, 6, 529-539.
10. Frechet, J. M. J. (1994). Functional Polymers and Dendrimers: Reactivity, Molecular Architecture, and Interfacial Energy. *Science*, 263, 1710-1715.
11. Zimmerman, S. C., Zeng, F. W., Richert, D. E. C., & Kolotuchin, S. V. (1996). Self-Assembling Dendrimers. *Science*, 271, 1095-1098.
12. Malik, N., Wiwattanapatapee, R., Klopsch, R., et al. (2000). Dendrimers: Relationship between structure and biocompatibility in vitro and preliminary studies on the biodistribution of 125I-labeled polyamidoamine dendrimers in-vivo. *Journal of Controlled Release*. 65(1-2), 133-148.
13. De Gennes, P. G., & Hervert, H. (1983). Statistics of Starbust polymers. *Journal de Physique Letters*, 44, 351.
14. Naylor, A. M., Goddard, W. A., Keiffer, G. E., & Tomalia, D. A. (1989). Starbust Dendrimers. 5. Molecular shape control. *Journal of the American Chemical Society*, 111, 2339-2341.
15. Dvornic, P. R., & Owen, M. J. (2002). Poly (amidoamine organosilicon) Dendrimers and Their Derivatives of Higher Degree of Structural Complexity, Synthesis and Properties of Silicones and Silicone-Modified Materials. *ACS Symposium Series*, 236-259.
16. Archut, A., Azzellini, G. C., Balzani, V., Cola, L. D., & Vo¨gtle, F. (1998). Toward photoswitchable dendritic hosts. Interaction between azobenzene-functionalized dendrimers and eosin. *Journal of the American Chemical Society*, 120, 12187–12191.
17. Patri, A. K., Lattalo, J. F., & Baker, J. R. (2005). Targeted drug delivery with dendrimers: Comparison of the release kinetics of covalently conjugated drug and non-covalent drug inclusion complex. *Advanced Drug Delivery Reviews*, 57, 2203-2214.
18. Agarwal, A., Gupta, U., Asthana, A., et al. (2009). Dextran conjugated dendritic nanoconstructs as potential vectors for anti-cancer agent. *Biomaterials*, 30, 3588-3596.
19. Choi, Y., Thomas, T., Kotlyar, A., et al. (2005). Synthesis and Functional Evaluation of DNA-Assembled Polyamidoamine Dendrimer Clusters for Cancer Cell-Specific Targeting. *Chemical Biology*, 12, 35-43.
20. Najlah, M., Freeman, S., Attwood, D., et al. (2006). Synthesis, characterization and stability of dendrimer prodrugs. *International Journal of Pharmaceutics*, 308, 175-182.
21. Cheng, Y., Xu, Z., Ma, M., et al. (2007). Dendrimers as drug carriers: Applications in different routes of drug administration. *Journal of Pharmaceutical Sciences*, 97, 123-143.
22. Balzani, V., Ceroni, P., Gestermann, S., Kauffmann, C., Gorka, M., & Vögtle, F. (2000). Dendrimers as fluorescent sensors with signal amplification, Chemical Communications. 853–854.
23. Diallo, M., Christie, S., Swaminathan, P., Johnson, J., & Goddard, W. (2005). Dendrimer Enhanced Ultrafiltration. 1. Recovery of Cu(II) from Aqueous Solutions Using PAMAM Dendrimers with Ethylene Diamine Core and Terminal NH_2 Groups. *Environmental Science and Technology*, 39(5), 1366–1377.
24. Xu, Y. H., & Zhao, D.Y., Removal of copper from contaminated soil by use of poly (amidoamine) dendrimers. *Environmental Science and Technology*, 39, 2369–2375.
25. Peng, H., Chen, Y., Zhao, Y., Yang, Q., Wu, L., Tung, C., Zhang, L., & Tong, Q. (2012). Artificial Light-Harvesting System Based on Multifunctional Surface Cross-Linked Micelles. *Angewandte Chemie International Edition in English*, 51, 2088–2092.
26. Liu, D., Zhang, H., Grim, P. C. M., De Feyter, S., Wiesler, U. M., Berresheim, A. J., Mu¨llen, K., & De Schryver, F. C. (2002). Self-assembly of polyphenylene dendrimers into micrometer long nanofibers: An atomic force microscopy study. *Langmuir*, 18, 2385.
27. Gupta, U., Agashe, H. B., Asthana, A., & Jain, N.K. (2006). Dendrimers: Novel polymeric Nanoarchitectures for solubility enhancement. Journal *of the American Chemical Society*, 7(3).
28. Allard, D., & Forestier, S., inventors; (2002). Self-tanning cosmetic composition. US Patent 6399048.