Dendrimers

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Bakalářská práce by měla obsahovat základní informace o dendrimerech, tzn. výroba, struktura, vlastnosti,použití, nově získané poznatky a aktuálně řešený výzkum v této oblasti

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Seznam odborné literatury:

1. Biron, Michel., Thermoplastics and Thermoplastic Composites (2nd Edition), Elsevier, 2013, ISBN: 978-1-4557-7898-0, 1044 p.
2. Ezrin, Meyer., Plastics Failure Guide Cause and Prevention (2nd Edition), Munich, Hanser Publishers, 2013, ISBN: 978-3-446-41684-0, 833 p.
3. Gao, C.,Yan, D., Hyperbranched polymers: from synthesis to application, Progress in Polymer Science, 29 (2004), 183-275 p, doi:10.1016/j.progpolymsci.2003.12.002
4. Lutz H. Gade, Dendrimer Catalysis (Topics in Organometallic Chemistry), Springer, 2006, ISBN: 3540344748, 202 p.
5. Nicholson, John W., Chemistry of Polymers (3rd Edition), Kent , Royal Society of Chemistry, 2006, ISBN: 0-85404-684-4, 178-189 p.
6. Cevik Emre, Senel Mehmet, Novel reagenttes glocose biosensor based on ferrocene cored asymmetric PAMAM dendrimers, Sensors and Actuators B Chemical B 176 (2013), 299-306 p, doi:10.1016/j.snb20.12.10.1072

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ABSTRACT

The work deals with dendrimers and offers basic overview of dendrimers with regards to their application. After the terms and definition there is molecular and supramolecular description. Then methods of synthesis used for the preparation of dendrimers with examples of final products that have the most frequent application. The work does not forget properties resulting from the structure and used components. Finally it introduces possible application in medicine and also in industry for research only or commercially available.

Keywords: dendrimers, divergent and convergent synthesis, application

ABSTRAKT

Práce rozebírá problematiku dendrimerů a nabízí základní přehled kategorií denrimerů s ohledem k jejich využití. Po uvedení definicí, přechází k popisu struktury jak na molekurární tak na nadmolekulární úrovni. Následuje rozdělení syntéz využívaných k přípravě dendrimerů s konkrétními příklady výsledných produktů, které jsou co do využití nejčetnější. Neopomíjí ani vlastnosti plynoucí ze struktury a složení. Na závěr uvádí možné aplikace v medicíně a průmyslu, které jsou ve fázi testování nebo přímo komerčně dostupné.

Klíčová slova: dendrimery, divergentní a konvergentní syntéza, použití

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CONTENT

INTRODUCTION

The term dendrimer is rather new concept in the field of macromolecular chemistry. The first dendritic structures were described by Vögtle in 1978 and have been coined "cascade molecules"[1].

The biggest boom in the field however is dated to the late 80s to the Tomalia's group at the Dow Chemicals Company. Donald Tomalia and his co-workers introduced a new class of macromolecules named "dendrimers" built up from two Greek words"dendros" meaning "tree" or "branch" and "meros" meaning "part"[1]. Moreover, he also took out another some tens of patents in the field and also participated in developing the polyamidoamine cascade polymers, also known as the PAMAM dendrimers, which are the first full family of dendrimers that have been synthesized, characterized and subsequently commercialized. Nevertheless, the divergent method for synthetizing dendrimers was also introducted by him.

In the intervening time second methodology was elaborated by Fréchet, the convergent synthesis.There are two approaches involved in forming dendrimers: the convergent approach and the divergent approach. Basically, both the approaches are complementary, but neither is likely to be recognized as the preferred one i.e. the convergent approach provides better overall structural control while the divergent one is more favourable in synthetizing of higher generation dendrimers.

The dendrimers are assembled mostly via covalent bonds only, however, many dendrimers have also been formed involving a variety of non-covalent self-assembly processes e. g. hydrogen bonding or supramolecular coordination chemistry resulting in the supramolecular dendrimer structure which provides the greater room for application into the practice.

The dendrimers allow for precise size, shape control as well as placement of terminal groups that highly welcomed by life science industry. In this respect, the biomimetic dendrimers are deemed to tap the potential of dendrimers as macromolecular vectors in novel drug delivery systems and biomedical, and thus discussed in the paper.

1 CLASSIFICATION, TERMS AND NOMENCLATURE

Dendrimers are special form of hyper branched polymers [1]. They are highly branched macromolecules with 3D dentritic architecture. It is fourth major class of polymer structure after linear, cross-linked and branched polymer.

Dendritic architecture consists of six subclasses (see Fig. 1) [2]

A) dendrons and dendrimers
B) linear-dendritic hybrids
C) dendrigrafts or dendronized polymers
D) hyperbranched polymers
E) multi-arm start polymers
F) hypergrafts or hypergrafted polymers

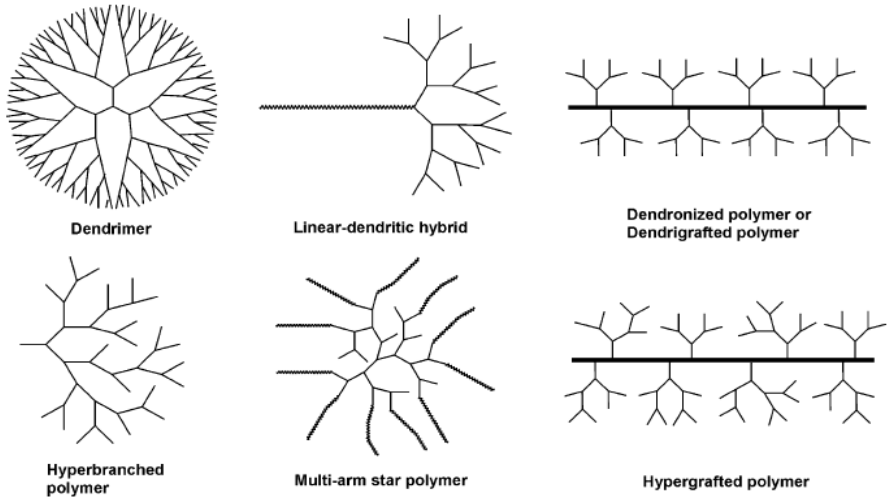

Fig. 1 Classes of branched polymers [2]

Dendrimers are family of nanosize paticles. Dimensions of differentes types of dendrimers are from 1 to 100 nm, typically 2−15 nm in diameter with a molecular weight ranging from 15 to 4 000 kDA. Comparison of weight and diameter is shown in Fig. 2. Lower generation dendrimers are floppy disk like structures, but beyond the fourth generation, they conform into the globular geometry similar to that of proteins [3].

Dendrigrafts are class of dendritic polymers however in the contrast to dedrimers are centred aroun linear polymer chain.

Dendrons is dendritic wedge without a core. Dendrimer can be prepared from assembling of two or more dendrons. Dendrons are very useful tool in the convergent synthesis. Fréchet type dendrons are dendritic wedge built up from by hyperbranched polybenzylether structure [1].

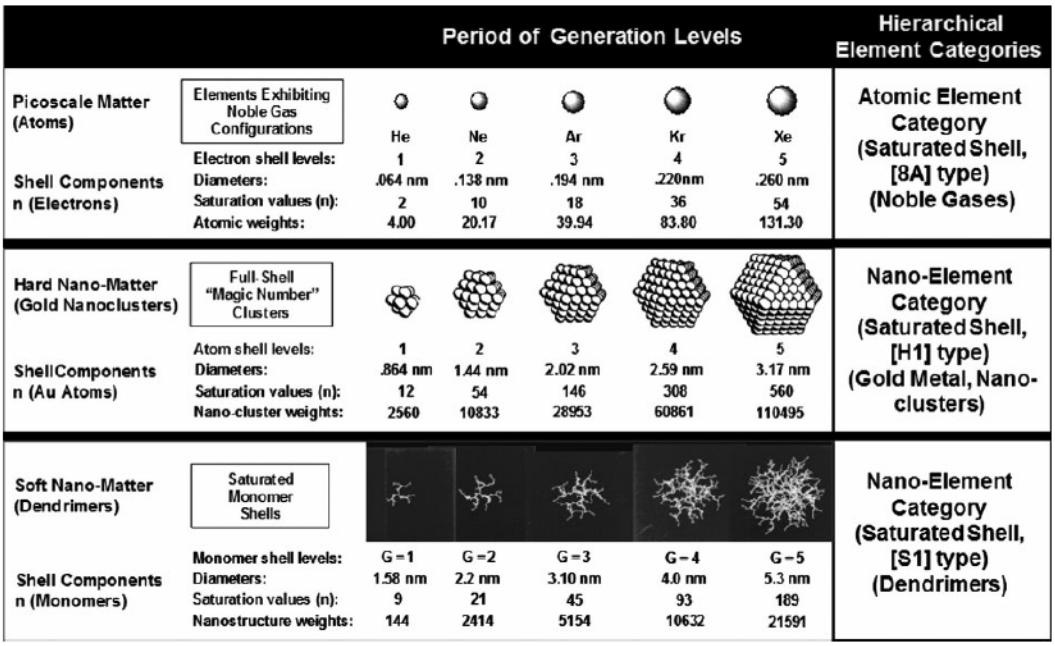

Fig. 2 Overview and comparison of the diameters and weights of atoms and nano structures [3]

Dendrimersomes are stable, monodisperse unilamellar vesicles self-assembled in water from ampiphilic dendrimers. The me mechanism of formation of vesicles is not completely elucidated [4].

2 STRUCTURE

They consist of numerous branches growing out of a central point called core. Dendrimer posses three major architectural components the core, the branching unit and end groups at the pheriphery.

Initiator core affects size, shape multiplicity and specific funtcion. It is synthetic starting point which is in the center of the denrimer. It affects size, flexibility, multiplicity, chemical composition and topology of cavities [5]. Initiator core consists of atom or more usually a multifunctional molecule such as amine or amonium.

Interior branching units are covalently bound to the core. Repetition of branching units make radially concentric layers called generation. They are made by various molecules for exemple by PMMA, PPI [6].

Exterior terminal groups affects shape, chemistry (moieties), stoichiometry, congestion (steric effects), reaction kinetics, flexibility, fractal character (clefts). They are located at the surface of the dendrimer. Depends on the requested final physical and chemical characteristics, exterioir end-groups could be hydrophilic (OH, COOH, NH_2, M), hydrophobic (CH_3, COOR), lipophilic or neutral [7].

2.1 Molecular structure

For the description of molecular structure following characteristics are used

G is the number of generations.

N_b is the branch-juncture multiplicity.

N_c is the iniciator-core multiplicity.

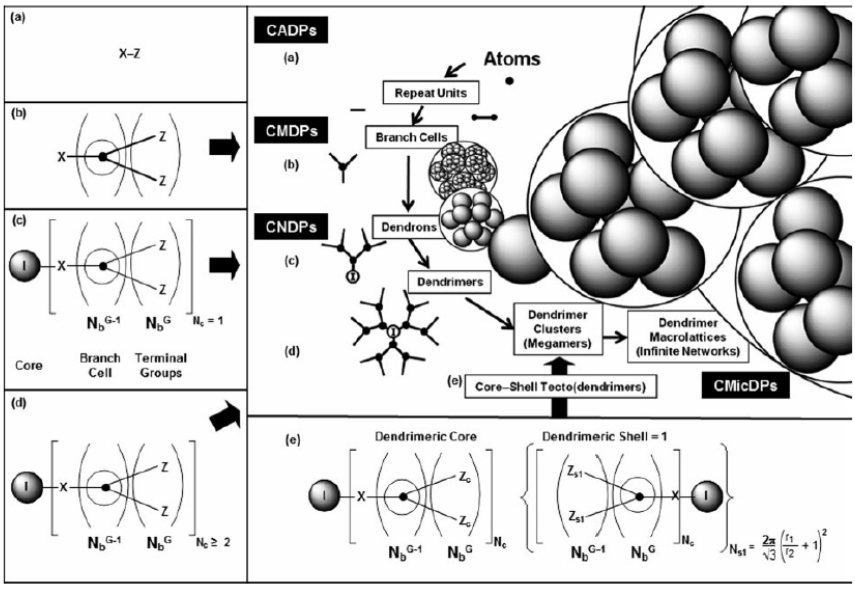

Fig. 3 Mathematical description of the structure from branch cells to Core-shell tecto(dendrimers) [8]

These values can be predicted mathematically (as shows Fig.4) for ideal systems according the following expressions [9].

Number of surface group:

$$(Z) = N_c\, N_b{}^{G} \tag{1}$$

Number of dendrimer branch cells:

$$(BC) = N_c\,(N_b{}^{G} - 1 / N_b - 1) \tag{2}$$

Number of dendrimer repeat unit (degree of polymerization)

$$(RU) = N_c\,(N_b{}^{G+1} - 1 / N_b - 1) \tag{3}$$

Molecular weight:

M_c, M_{RU}, M_{BC}, M_t are molar masses of initial core, repeat units, branch cells and terminal units [34].

$$(MW) = M_c + N_c\,[M_{RU}\,(N_b{}^{G+1} - 1 / N_b - 1) + M_t\, N_b{}^{G+1}] \tag{4}$$

$$(MW) = M_c + N_c\,[M_{BC}\,(N_b{}^{G} - 1 / N_b - 1) + M_t\, N_b{}^{G}] \tag{5}$$

The relationship between the number of terminal groups on a dendritic branch (dendron) and the number of generations of the branch can be represented as follows:

terminal groups per dendritic branch = $N_b^G/2$.

The total number of terminal groups in the dendrimer is determined by the following:

terminal groups per dendrimer = $N_c \cdot N_b^G/2$

The stoichiometric limits (N_{max}) are determined by the core shell spheroid ratios that are predicted by Mansfeld-Tomalia-Rakesh equation for calculating the maximum shell filling value when $r_1/r_2 > 1{,}2$ where r_1 is radius of core dendrimer and r_2 radius of shell dendrimer [3].

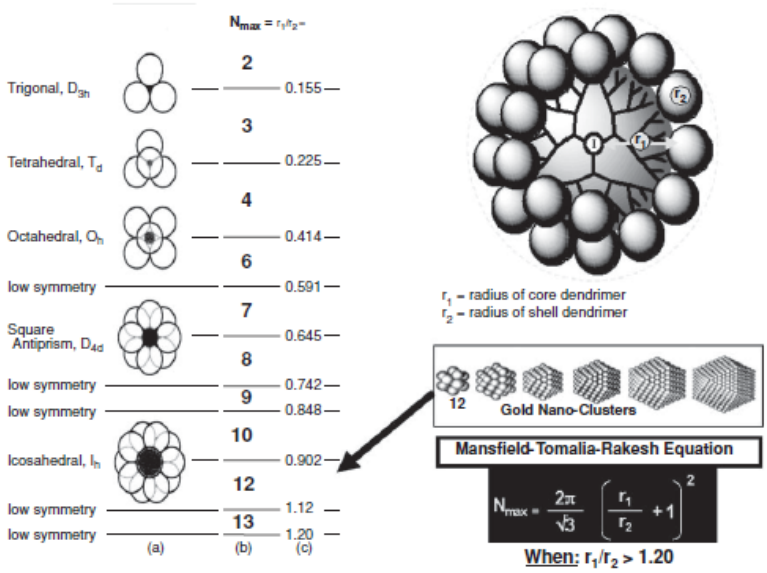

Fig. 4 a) symmetry properties of core-shell (tecto)dendrimers structure, when $r_1/r_2 < 1{,}2$ b) sterically induced stoichiometry defined shell capacities N_{max}, based on the respective core and shell radii, when $r_1/r_2 < 1{,}2$ c) Manfield-Tomalia-Rakesh equation for calculating the maximum shell filling value for $r_1/r_2 > 1{,}2$. And gold nano clusters as an exemple of $r_1 = r_2$ where $N_{max} = 12$ [10]

2.2 Supramolecular structure

The formation of supramolecular dendrimer assembly is determined by either covalent or non-covalent bonding interactions, molecular recognition and self-assembly systems. Hence, the supramolecular assembling proces involve mostly hydrogen bonding,

hydrophobic and hydrophilic binding, metal-ligand interactions, electrostatic interactions. dendrimer by ligand-metal interaction, hydrogen binding or electrostatic interactions [11].

The secondary supramolecular dendritic structure shall adopt lamellar, columnar or spherical morphologies respectively similar to that of β-sheets and α-helix (7/2 helix, 5/2 helix) structures of fibrilar proteins or pseudo-spherical structure of globular proteins [6]. G1 columnar structure form varius Φ lattices, G2 columnar structures form into the Φ_h lattice ,and the G3 would take mostly the spherical structure but would take complete spherical structure only with the G3-G5. In general, the supramolecular dendrimer assemblies pack to cubical form (Cub) type crystal lattice. But structure maz vary base on the different sterric efect [12].

The tertiary supramolecular structure are pine-tree like column, columnar, spherical generated from the conical conformation of the dendron. Much more like proteins, the primary structures of the amphiphilic dendrons determine thier tertiary structure. Regarding the tertiary sumpramolecular structure, it should be noted that the most dendrons and dendrimers do not self-assemble or self-organize. Hence, it is necessary to select dendrimers of proper properties as for exemple benzyl ether dendrons functinalized with aliphatic alkyl groups [20].

The following are the quatemary supramolecular structures the dendrimers would normally take as shows Figure 5: 2-D Interdigitated Smetic A (SAd), p2mm Simple Rectangular Columnar (¼r-s), c2mm Centered Rectangular Columnar (¼r-c), Various p6mm Hexagonal Columnar (¼h), and 3-D Ia3hd Bicontinuous Cubic, 12-Fold Quasi-Liquid Crystal (QLC), Pm3hnCubic (Cub), P42/mnm Tetragonal (Tet), and Im3hm Cubic (Cub) Lattices [12, 13].

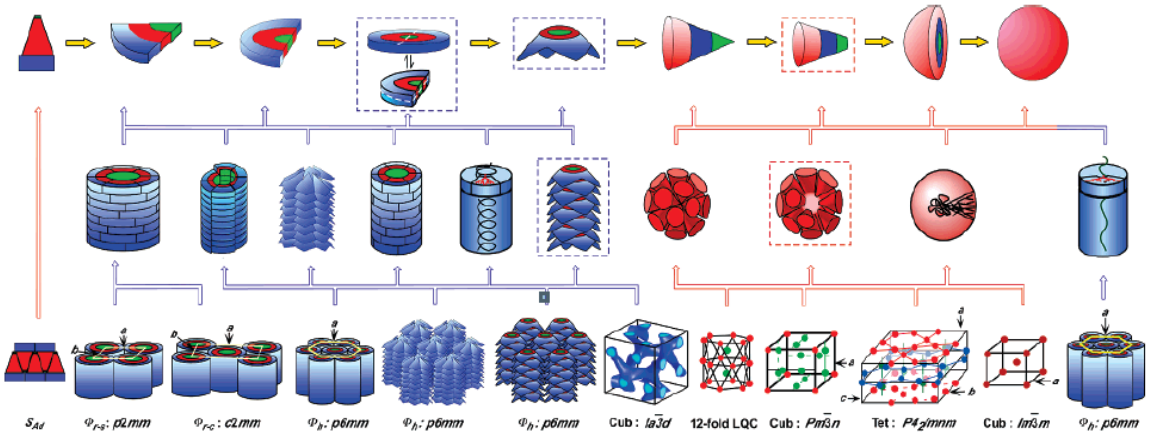

Fig. 5 Overview of tertiary and quatemary structure of dendron assemblies based on primary structure controlled dendron as a) size b) shape c) surface d) flexibilty [12]

There is rather higher degree of architectural polymorphism observed in the dendrimers due to the greater flexibility in branching. Moreover, reduced steric crowding shall also contribute to the tendencies of dendrimers to get organized into the non-cubic latices of spherical supramolecular structures at higher generations as can bee seen in Fig. 6.

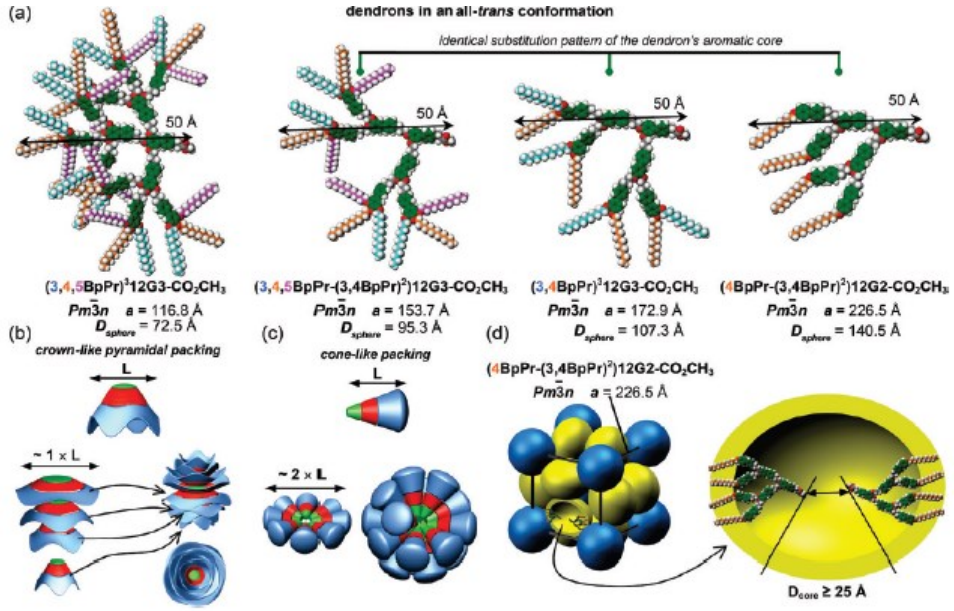

Fig. 6 Molecular models of four chosen dendrons in the all-trans conformation a) crown-like pyramidal packing b) cone-like packing [13]

The presence of internal cavities is found to be very beneficial but it doesn´t necessarily mean they are permanent and rigid. "Dendrimer box" is cosequence of flexibility to accomodate inclusion guests but they are able to collaps or fully extend depends on the type of solvent [14].

Colleration between the molecular geometry of monodedritic molecules and shape and size of supramolecular structure is determined by dendrimer generation, core, the size and aliphatic region of the structure.

The dendrons and dendrimers of higher water solubility tend to agreggated into micelle-like formations, especially if having hydrophilic peripheral terminal groups and hydrophobic interior branching units, however, unlike common micelles they are static and retain their cohesion regardless of concentration. The result of their inherent stability is encapsulation of the guest molecules with a simple precipitation approach [14].

Dendrimers together with the hyperbranched polymers are considered interesting building block for constructing of the monolayer materials because of the larger sizes and globular shapes of them. Moreover, since dendrimer molecules are rather larger than common surfactants used in manufacturing the monolayers, they can interactwith surfaces through their numerous terminal groups or inner structures [14].

3 SYNTHESIS

In general, dendrimer synthesis can be performed according to two major schemes; divergent and convergent growth. Traditional method dendrimer synthesis are Michael reaction.

Divergent growth (see Fig. 7) is based on the stepwise addition of low molecular mass building blocks starting from a multifunctional core molecule and results in a radial growth of the dendrimers [15].

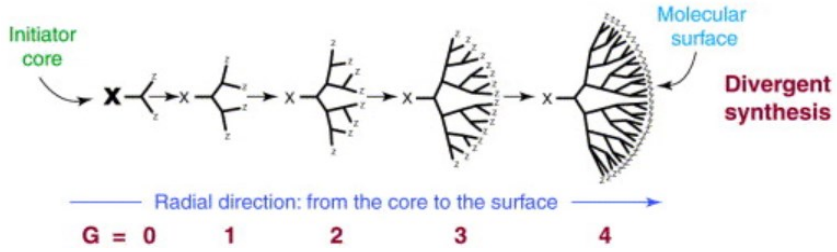

Fig. 7 Schema of divergent synthesis [16]

Convergent dendrimer synthesis (see Fig. 8), on the other hand, involves the coupling of preformed dendrons onto a central core molecule [15].

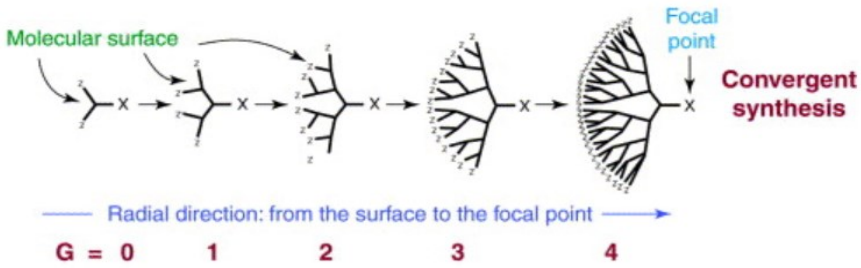

Fig. 8 Schema of convergent synthesis [16]

Michael addition, named by Arthur Michael (1855−1942), is a versatile synthetic methodology for the efficient coupling of electron poor olefins with a vast array of nucleophiles. Reaction benefit from mild reaction condition, high functional group tolerance. Reaction lends itself to both step growth and chain growth polymerization and has been employed in the systhesis of linear, graft, hyperbranched, dedritic and network polymers.

Post polymerisation modification and coupling of biological and synthetic polymers are often facilitated by the Michael reaction. This make it well suited to numerous emerging

technologies, gene transfection, cell scaffolds and tissue replacement. Furthermore, it takes benefits in synthesis of crosslinked polymers such as hydrogels, thermoset resins, and coatings, whre rapid cure and high conversion is necessary [6].

The Michael reaction refers to the base catalyzed addition of a nucleophile (Michael donor) to an activated α,β-unsaturated carbonyl-containing compound (Michael akceptor). Over the years, the scope of reactions have increased dramatically to include a broad range of acceptors and non-carbon donors [17].

The nitrogen-donor version often visible during PAMAM sythesis is called aza-Michael reaction. Since the aminne can act as both nucleophiles and bases, no additional base is needed in the reaction. The reaction tends to follow second order kinetics base on the concentration of olefin akceptor and the amine. Primary amine react with acceptor to bring secondary amines that are more nucleophilic and they are more reactive. Reaction with secondary amine is the first folowing by reaction of the primary amine, which lead to polymerization. This reaction is usualy catalysed by acids, the Lewis acids [17].

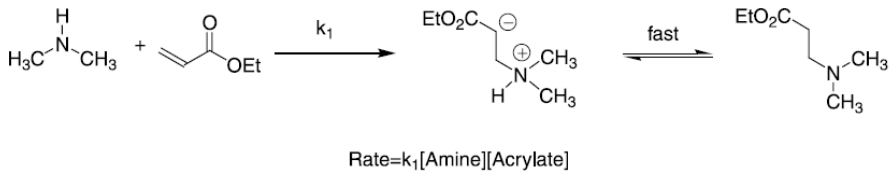

Fig. 9 Aza-Michael addition reaction of dimethylamine with ethyl acrylate [17]

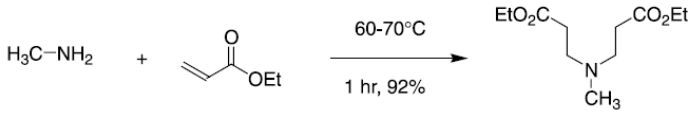

Fig. 10 Aza-Michael addition of methyl amine to ethyl acrylate [17]

3.1 Divergent approach

Divergent synthesis allows production of symetric dendrimers and specific incorporation of function into the interior.

The selection of syntehesis of the iniciator core is of great importance. It determines site, shape, multiplicity, and specialized function will clearly influence the dendrimer throughout its construction [6].

Divergent synthesis include two steps. Activation of functional terminal group and addition of branching monomers units.

Divergent synthesis takes advantage in the production of large quantities of dendrimers as the quantity of dendrimer sample essentialy doubles with each generation increment, and where demand for purification of the final product is lower [7].

In case of the number of coupling reactions increases exponentially with each generation, there is also higher possibility of incomplete functionalization or side reactions. Although removal of the monomer or any flawed molecules resulting from cyclization or incomplete reactions connot be easily removed because of the similarity to the intended product [4].

3.1.1 PMMA Polyamidoamin dendrimers

PAMAM dendrimers consist of alkyl-diamine core and tertiary amine branches

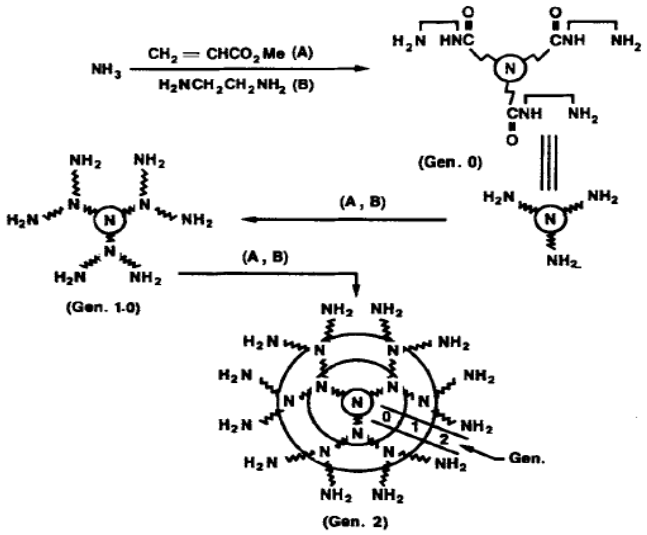

Fig. 11 Synthesis of PMMA [7]

The divergent approach initiate growth at core of the dendrimer and continues by the repetition of coupling and activation steps [18]. Synthesis may begin with a nucleophilic (ammonia, amine) or an electrophilic core.

The first step (A) in the case of nucleophilic core (see Fig. 11), involves Michael addition of metacrylate to the amine. This reaction run very rapidly and in high yield with quite complete selectivity and no amidation at room temperature [7].

The second step (B) requires addition of triester intermediate to a large excess of ethylendiamin to produce the terminal triamine core cell. Repetition of the coupling and activation steps produce higher generations of dendrimer. Ideal branching growth would produce dimensionally precise surfaces with a defined number of terminal groups as shows Table 1.

Table 1 Relative molar mass, predicted diametr (CPK model), and hydrodynamic diametr (size exclusion chromatografy) for PAMAM dendrimer [7]

Generation	M_r	Monomer units	Terminal groups	CPK	Diameters [Å]	SEC
0,0	359,0	3,0	3,0	9,6	19,2	10,8
1,0	1 043,0	9,0	6,0	12,8	28,8	15,8
2,0	2 411,0	21,0	12,0	17,6	416,6	22,0
3,0	5 147,0	45,0	24,0	24,1	51,2	31,0
4,0	10 619,0	93,0	48,0	30,6	65,6	40,0
5,0	21 563,0	189,0	96,0	38,5	81,6	53,0
6,0	43 451,0	381,0	192,0	47,5	91,2	67,0
7,0	872 227,0	765,0	384,0	61,8	104,0	80,0
8,0	174 779,0	1 533,0	768,0	78,0	117,0	92,0
9,0	349 883,0	3 069,0	1 536,0	98,0	130,0	105,0
10,0	700 091,0	6 141,0	3 072,0	123,0	143,0	124,0

PAMAM dendrimers are commercialy produced for exemple by Sigma Aldrich® are available in generations G0−10 with five different core types and ten functional terminal groups. Most PAMAM dendrimers are supplied as solutios in methanol for improved long-term storage stability. They can be dried and reconstituted in other application-specific solvents [19].

Commercially available PAMAM dendrimers prepared by divergent growth

approach are one of the most widely used dendrimer scaffolds in biology. Despite their broad applicability, it is necessary to modify their surface amine groups with neutral hydroxyl, acetyl or anionic carboxyl group to avoid the toxicity and liver accumulation associated with their polycationic surface [20].

Macromolecular vectors in novel drug delivery (PAMAM after the acytylation) can form dendrimer five fluoruracil (remarkable anti tumor activity but high toxic side effects) conjugates which upon hydrolysis release free 5FU (see Fig. 12), thus minimizing toxicity, and biomedical applications as PAMAM G5 dendrimer with the surface modified with Gd(III) complexes and folic acid as targeting agent to increase cell-specific uptake cancer cells is used by the contrast agent in MRI [20, 38].

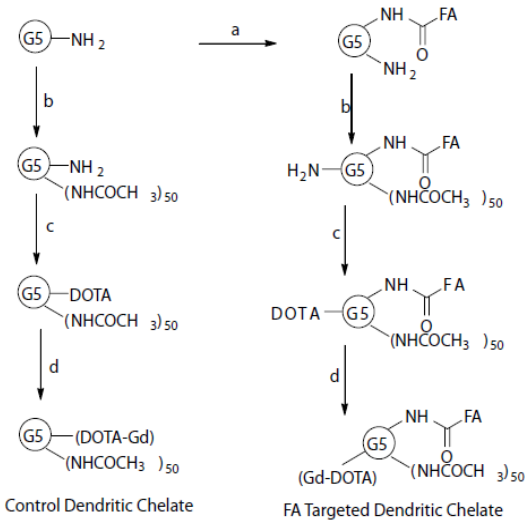

Fig. 12 Synthesis of contrast agent [20]

3.1.2 PEI Polyethylenimine denrimers

PEI is less common subclass of PPI-Polyalkylimine. They have primary amines as end groups and its interior consists of numerous tertiary trispropylen amines.

PEI dendrimers up to the third generation were prepared by divergent synthesis method from ethylenediamine (EDA) or propylendiamine (PDA) core (see Fig. 13).

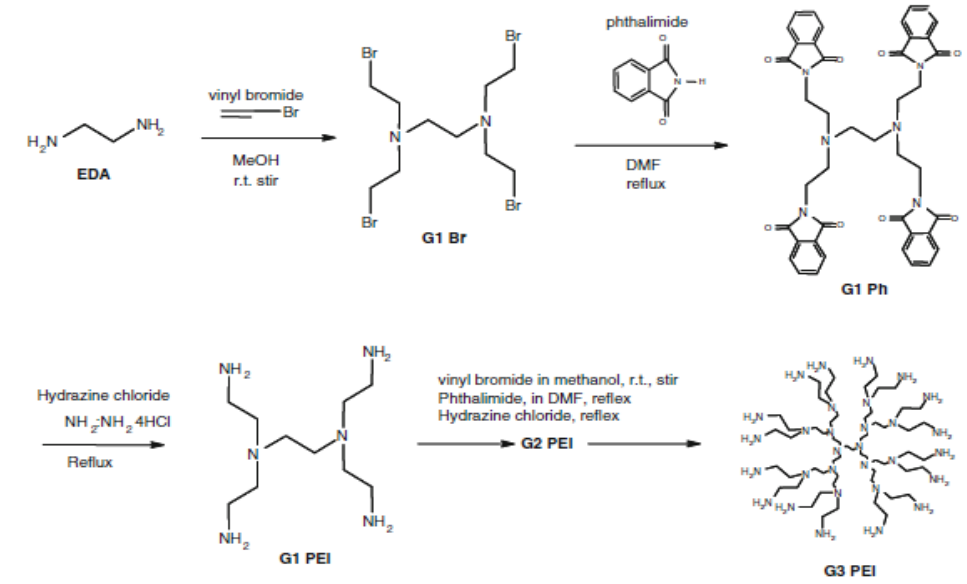

Fig. 13 Synthesis of PEI [39]

In the first step amine reminals are bonded with vynil bromide by Michael addtion reaction. Then, the bromide terminals were converted to amine groups using a Gabriel amine synthesis method where primary alkyl halids are transformed into primary amins [39].

PPE dendrimers have been commercialized and investigated for their biological application, but the presence of multiple cationic amine groups leads to significant toxicity. Studies has shown that PPI G2 dendrimer binds efficiently to DNA, has low toxicity to cells, and the in vivo gene transefr aktivity is optimized [5].

3.1.3 PAMAMOS Polyamidoamine-organosilan dendrimers

Radially layered PAMAMOS dendrimers (copolymeric amidoamine-organisilicon dendrimers) are prepared with hydrophilic polyamidoamine interior and hydrophobic organosi licon exteriors.

Synthesis of PAMAMOS are prepared from amine-terminated polyamidoamine precursors by Michael addition of silicon containing acrylates or metacrylates or haloalkylation with chloro or iodoalkylsilanes [21].

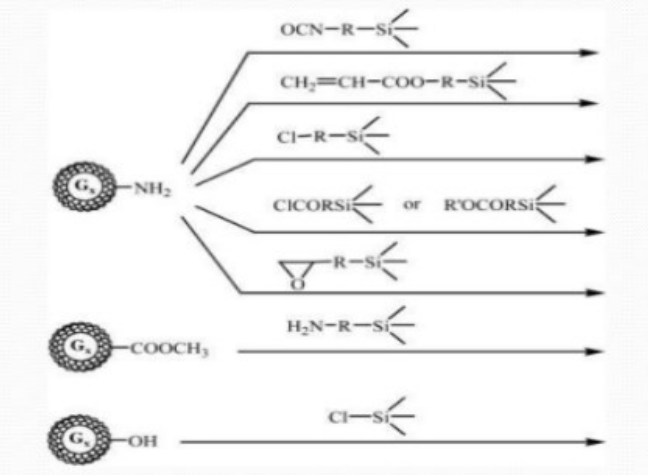

Fig. 14 Examples of interior branching units [21]

Depending on the choice of PAMAM dendrimer generation, silicon-contaning reagent, and synthetic route, the resulting PAMAMOS dendrimers differed (see Fig. 14) [21]:

a) in relative content od PAMAM and OS branches cell layers,
b) the type of OS branch cells involved,
c) the type and relative content of reactive or nonereactive end groups,
d) the degree of "coverage" of the PAMAM interior by the OS exterior.

3.1.4 Core-Shell Tecto(dendrimers)

Core-Shell Tecto(dendrimer) is covalent or non-covalent assembly of reactive monomers branch cells or dendrons around atomic or molecular core densrimer. The synthetic procedures allow the attachement of additional shell dendrimer, which would then enable the systematic construction.

Way of synthesis is divergent or convergent and result to the supramolecular core-shell assemblies (see Fig. 15). One of the exemple, with covalent assembly, is again well known PAMAM used as a core with shell of other PAMAM, typically, the generation number of the core is larger than surrounding shell dendrimers [22].

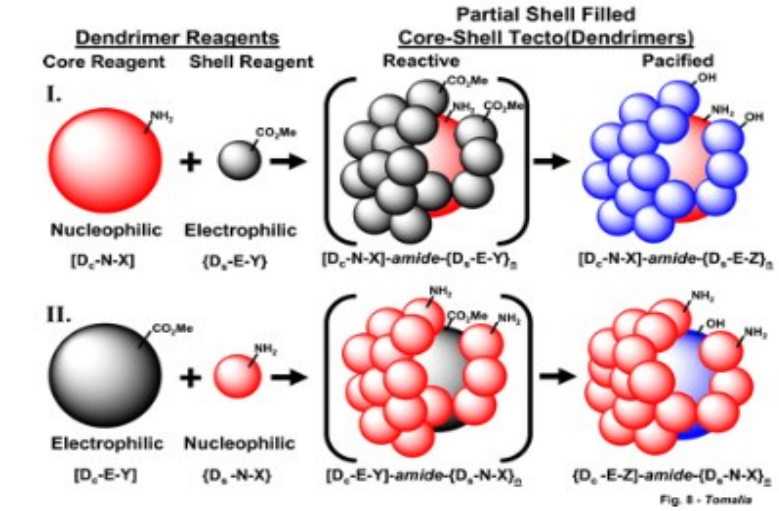

Fig. 15. Two ways of synthesis partial shell-filled tecto(dendrimers) [10]

Tecto-dendrimers made by self-assembly way from block copolymers PEO-b-PPO, PEO-B-PCL, PEO-b-PAsp have following drivig forces: hydrophobic ineteraction of the inner block, ionic interaction of a cationic block (polyapartat), complexed to a negatively charged polymer (DNA), which results to polyion micelle. The outer block is consist usualy of a polar polyethylenoxid block which form the shell of the nanocarrier and protect the core througt steric stabilization and prevents the adsorbtion of proteins. The size block copolymer micelle is deteminated by termodynmics parameters and partiall by varaition of the block length [23].

Core shell type architecture is often connected with the research of the supramolecular nanocarrier drug delivery sytem (see Fig. 16). The main advantages is good size control (5−20 nm for dendritic cire shell architectures and 10−50 nm for block copolymer micelles). Efficient encapsulation driven by noncovlent interactions with selective release base on the signal such as pH change [23].

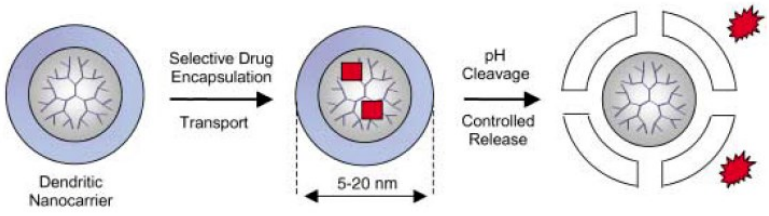

Fig. 16 Release of the encapsulated particle [23]

3.1.5 Amphiphilic dendrimers ADs

Dendrimers built with two segregated sites of chain end, one half is electron donating and the other hal fis electron withrawing, so called as diblock dendrimers or bow-tie dendrimers [3].

ADs have three subclasses. Amphiphilic layered dendrimers, amphiphilic diblock (Janus) dendrimers, segmented block dendrimers [14].

The new interesting type of dendrimers are the second ones, Janus dendimers (JDs) are different from conventional dendrimers, because they provide assymetric structure that are composed of two hemispheres (hydrophilic and hydrophobic), having different size and numerous of terminal groups [40].

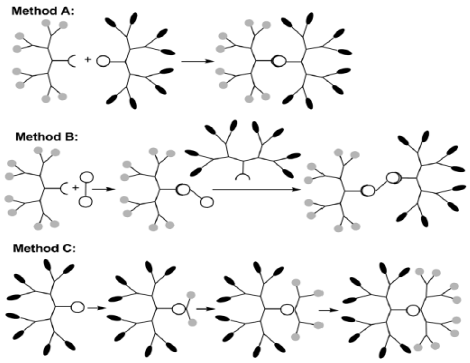

Fig. 17 Schema of main methods of synthesis of Janus dendrimers [3]

JDs dendrimers have been synthetised by both divergent and covergnent approaches, and recently by accelerated approaches such as double exponential growth, hypermonomer strategies, orthogonal and chemo-selective growth strategies [8].

During the synthesis three methods arise as can bee seen in Fig. 17. A) reaction of two dendrons having complementary functions as the core, the simpliest one, B) reaction of one dendron with in controlled manner with multifunctional core and then second dendron is grafted to the remaing structure of the core and finaly C) reaction, rare one, is using the focal point of a dendron for the growing of new branches [25].

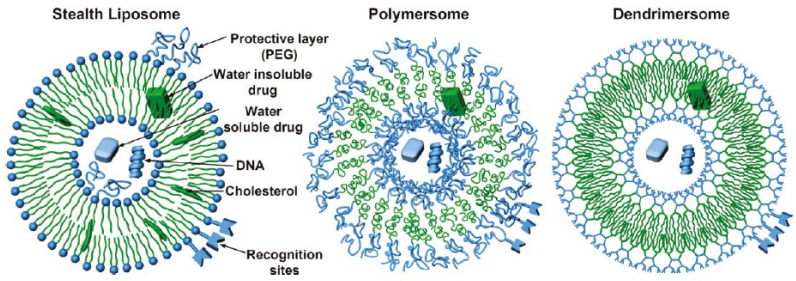

Fig. 18 Three examples of simmilar vesicals made by phospholipides, amphiphilic block copolymer and Janus dendrimers [40]

During the experiments JDs can self-assemble into differentes shapes such as vessicles (Fig. 18 and Fig. 19), cubosomes, discs, tubular vesicle, helical ribons and bilayered vesicles being called dendrimersomes [12].

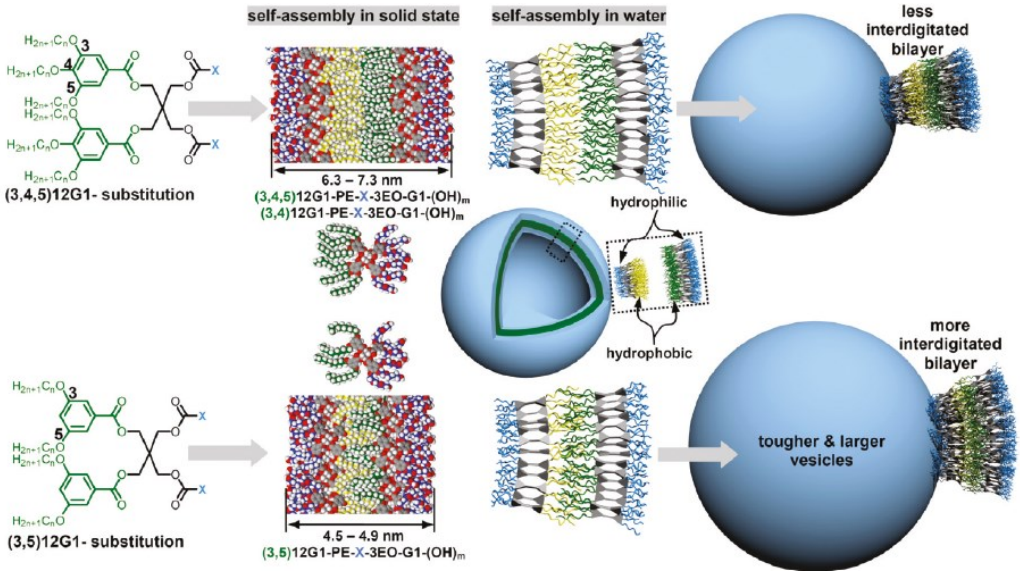

Fig. 19 Schematic of the self- assembly of Janus dendrimers into denrimersomes [40]

During the synthesis different thickness of the layer changing the branching pattern of the alkyl chain can be achieved. On the other hand the difference in te length of alkyl chain can not provide significant difference [40].

This new category of dendrimers provide wide ranges of synthetic methods with different advantages of conjugation system depends on the multiple purpose such as site specific drug delivery,enhacement of antioxidant activity and lipophility, multi drug combination therapy, micellar delivery (to reduced cytotoxicity, resistence and improve distribution), supramolecular hydrogels made by self-assemble amphiphilic molecules from

fibrous aggregates that are able to absorb large amount of water and finaly dendrimersomes-unilamelar bilayed vesicles self assembled in water from the amphiphilic JD [40, 8].

3.1.6 Liquid crystaline dendrimers

Liquid crystalline dendrimers are highly branched oligomers or polymers of dendritic structure containing mesogenic groups that can display mesophase behaviour.

Liquid crystalline dendrimers are respresentative of the class of mesogen. They provide a new types of mesophase and morphologies but thier behaviour follow general characteristic valid for liquid crystalline state between crystalline solid and the amorphous liquid visible in Fig. 20.

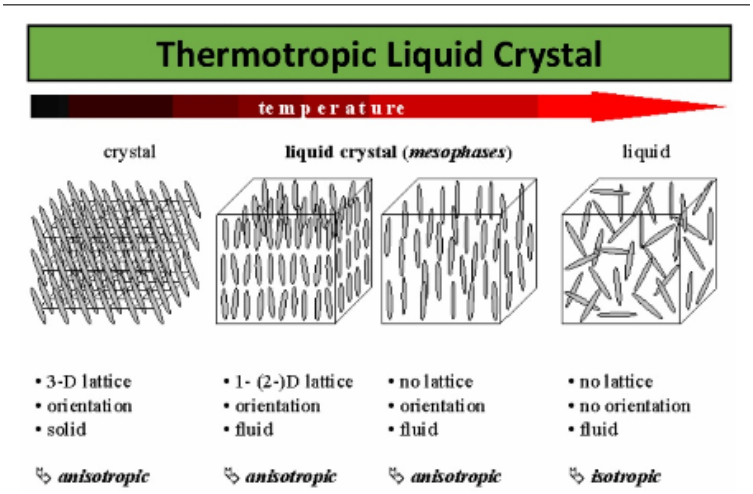

Fig. 20 The transition to the liquid crytsalline state [26]

They are orientational which result to anisotrophy of physical properties. The production of liquid crystalline state is thermotropic (LC phase is formed when the pure compund is heated) or lyotropic LC phase (forms when the moleculs are mixed with the solvent). Material with LC propreties is mesogen that form mesophase described on the basis of the mesogen shape or symetry of the different molecular arrangement [27].

Side chain liquid-crystalline dendrimers have a structure consists of mesogenic groups attached to the interior branching units laterally or terminally.These units interact with each other to give rise to anisotropic mesophases transition owing to the enthalpic gain, as we can see in conventional liquid crystals [28]. Among side LC dendrimers belogs silicone-containing LC dendrimers, PAMAM and PPI LC dendrimers, PES and polyether LC dendrimers.

Silicon-containing LC dendrimers can be derivatized to carbosilane (Si-C), siloxane (Si-O), carbosilazane (Si-N). Possible application would be as high-temperature materials, modifies for composite materials (Si-O, Si-C), rainforcers of silicon rubber, scaffolds for homogenous catalysis [29].

PES and poylether LC dendrimers are amphiphilic polyol monodendrons functionalized alkyl chains connected to a linear polethylene oxide chain self-assemble into various supramolecular archhitecture. Attaching the chiral mesogens onto amphiphilic polyester dendritic core was detected first ferroelectric LC upon the application of exteral electric field

Main-chian LC dendrimers have less conformational freedom as side-chain LC due to the anisotropic molecular moieties where anisometric branches do not radiate isotropically. This group of dendrimer is represented by willow-like dendrons.

Shape persistent LC crystalline dendrimers represent another family of mesogens. The particularity of these systems in dendritic compeletely rigid conjugaed and intrinsically discotic dentritic matrice. They have also electron rich core that have interesting photochemical and photophysical properties [27].

3.2 Convergent approach

The convergent growth method has several advatages as relatively low number of coupling reactions at each growth step, allowing acces to dendritic products of unmatched purity and functional versatility, the ability to precisely place functional group throughout the structure, to selectively modify the focal point or terminal groups, and to prepare well-definied asymmetrical dendrimers which is the most attractive feature of the convergent synthesis [14].

3.2.1 Fréchet type of dendrimers

Fréchet dendrimer is a dendrimer based on a polybenzylether hyperbranched skeleton. This type of dendrimer can be symmetric or built up asymetrically consisting of two or three parts of dendrons with different generation.These dendrimers have very often carboxylic acid groups as terminalgroups as anchor point for surface chemistry and to increase the solubility of hydrophobic dendrimer in polar solvents [1].

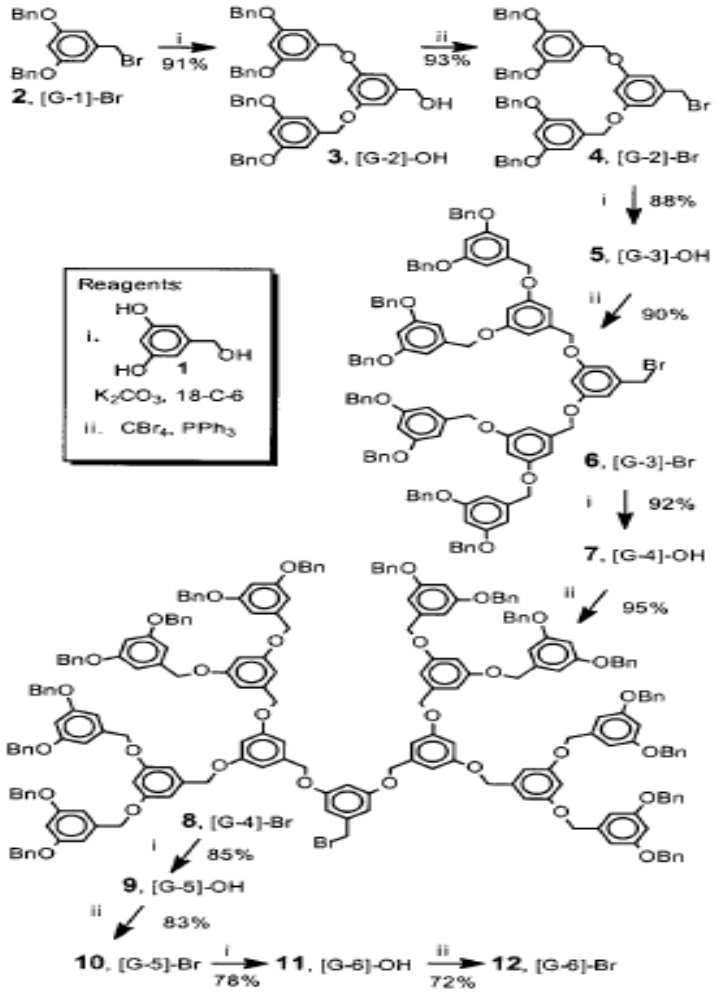

Figure 21 Convergent synthesis of Fréchet type dendrimer [1]

Phenolic groups of this monomer were coupled to the benzylic bromide and then te focal benzylic alcohol funcionality activetaed the next coupling step. Subsequent repetition of the Wiliamson coupling and bromination steps enable the production of G6. This synthesis is one of only a few convergent synthesis (see Fig. 21) that can produce dendrons and dendrimesrs in reasonable yields up to the sixth genereation due to the hight efficient that is for G1 90 %. Thanks to benzyl substrate Williamson coupling reaction eliminate side reactions that accompany nuclephilic reactions [14].

This group of denrimers have a wide range of cores which predict their applicatoion. Traditionally covalently bound (trisphenolic), chiral cores (binaphthol), host-guest core binding sites (iridium complex, porphyrin), core catalytic core (copper

complexes, tertiary amines), photochemicaly resposive cores (azobenzen undergoing a photochemical cis and trans isomerisation).

Fréchet type dendrons find application in light harvesting systems and light amplification because of their complementary behaviour in energy transfer through their mlecular frameworks. In connection of this topic a variety of systems with different chromatophores, including cumarin dyes have been investigated.

As Fréchet dendrimers tend to self assembly processes and create tubular and spherical aggregates that form cylindrical columns and cubic lattice. They are able to sterically encapsulate the core from the external enviroment that may eventually provide a syntetic mimic of enzymatic catalysis [14].

4 PROPERTIES

Dendrimers are highly monodispersing macromolecules of globular geometry reslting of the branches radiating out from the core [30].

The dendrimers are to be identified as nano-sized particles of low compressibility. And it applies the higher the generation and the steric hindrance occurs, the less the compressibility of the dendrimer. The compressibility together with shape and biodegradability are the determining factors playing the key role in the biological application of dendrimers.

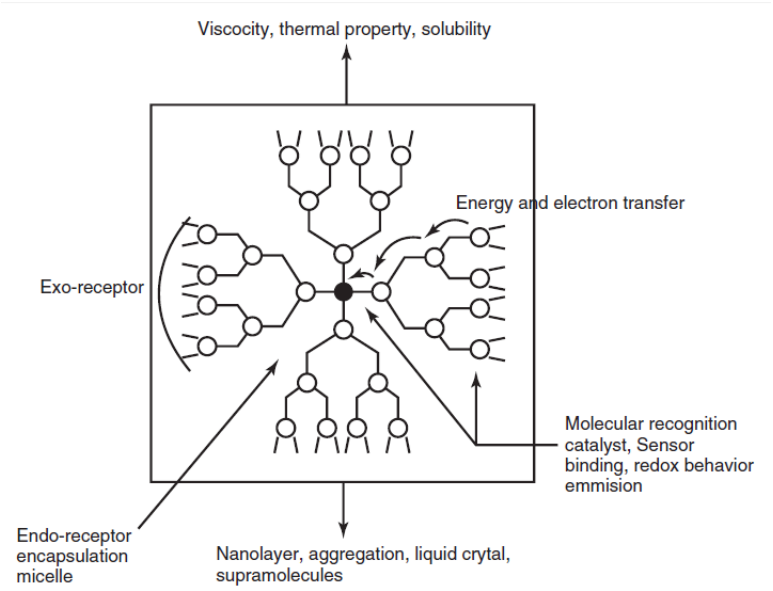

Fig. 22 Overview of properties and possible application [24]

They have ability to entrap small molecules in their core region and very low intrinsic viscosities what is the reason that dendrimers exist as tightly packed balls. A plot of intristic viskosity versus generation number shows maximum at about G4−G5. The major difference between the linear and dendritic polymer is that while the former entangles, the latter does not [31]. Dendrirtic volume increases cubically with generation, while dendritic molecular weight increases exponentially. This qrowth leads to deviation in their solution. The physical parameter which mesure this deviation is the intristic viscosity [31].

The dendrimer´s rheological behaviour as well as the dendrimer surface activities of dendrimers, especially PAMAM dendrimers, depend strongly on the location of the

terminal groups and their distributions within the molecule. The early discussions of dendrimers and usual schematic diagrams convey the idea that the terminal groups are located around the periphery of the molecule [7].

The dendrimers are futher definied as highly soluble and readily miscible because of the large number of chain ends.The level of solubility vary with different types of terminal groups e. g. the dendrimers containing either hydrophilic or hydrophbic terminal groups tend to dissolve in polar solvents. Moreover they are non-crystalline substances of low glass temperature [15]. Comparison of linear and polymer and dendrimer shows Table 2.

Table 2 Comparison of linear polymer and dendrimer [15]

	Linear Polymers	**Dendrimers**
Shape	Random coil	Spherical
Viscosity	High	Low
Solubility	Low	High
Crystallinity	Depends on polymers	Low
Reactivity	Low	High
Compatibility	Low	High
Compressibility	High	Low
Structural control	Low	Very high
Dielectric constant	Typically 4-6	Ultra low, < 2

Generally speaking, dendrimers shows unusual intrisic viscosity to molecular weight correlation. They are globular macromlecules that require charcterisitc rigidity only with high generations. The fifth generation dendrimers adopt the spherical three-dimensional structure similar to that of globular proteins, hence, such a cross-structural similarity assumes dendrimers to behave in a similar way as proteins do. However, there are many low generation dendrimers that tend to be rather malleable, especially those involving long and flexible cinnctors between branching points, and thus may even result in collapsing to ovoids or flattened pancake-like shape [25].

5 APPLICATION

5.1 Dendrimers as MRI contrast agent

Magnetic resonance imaging (MRI) is a technology used to visualize organs, blood vessels and tissues. This technique is based on the measurement of the nuclear magnetic resonance of the body water protons under a defined inhomogeneous magnetic field, which allows assigning the water signal to its place of origin.

Paramagnetic ion complexes, such as gadolinium (III) with seven unpaired electrons, are used as contrast agents for MRI imaging since they shorten the proton relaxations times. However, the dendrimers as contrast agent can significantly shorten the proton relaxation times compared to paramagnetic ion complexies (four times the standard times of large number of paramagnetic metal ions) attached to the same molecule, a diminished flexibility in the globular surface of the dendrimer and a prologed vascular retention time obtained by larger size of the dendritic molecules [31].

Moreover, the dendrimers can be prepared that gind paramagnetic ions and hence used as MRI contrast agent based on polylysine with gadolinium ion complex on the terminal groups(Gadomer 17®). The main role of the dendrimers is to prevent the gadolinum complexes from spreading out of the target area, and this providing the pictures in excellent quality. But this MRI agent is still available only for research purpose only [31].

5.2 Dendrimers and Drug delivery

The dendrimers are able to enhance water solubulity, increase half-life circulation, impove drug targeting, delivery and transit through biomembranes, and slow down drug clearance. The higher solubility and stability together with the ability to effectively encapsulate different drugs and easy-to-modify dendrimer surface are considered the pros for applying the PAMAM dendrimers into drug delivery tegnologies, though the application is rather limited due to the toxicity issues of amino peripheral terminal groups. However, the dendrimers containing only neutral or anionic terminal groups have been proven less toxic [32].

Moreover, globular shape and presence of internal cavities are considered the most significant properties of dendrimers, though, finding the ability to encapsulate the therapeutic agent into the interior of dendrimer the most striking one (the drug molecule can

be either loaded into the dendrimer´s internal cavities or attached to the peripheral terminal groups on the dendrimer as can be seen in Fig. 22). Moreover, the water-soluble dendrimers canbe also used as coating agents to protect or deliver the drug to specific sites of the body or as time-release carrier for controlled release of biologically active agents [33].

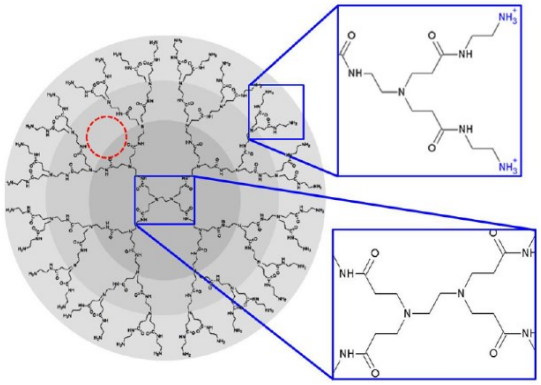

Fig. 22 Schematic structure of PAMAM dendrimer architecture [33]

5.3 Dendrimers as Vectors in Gene Therapy

Gene therapy is used to correct of the genetic defects i. e. works on principle of transferring of the active genes into target muatated cells, for exemple, it is used in cancer treatment as an alternative to tradional chemotherapy.

The dendrimers, such as widely used the PAMAM and PPI, have been studied thoroughly as for the ability of them to act as non-viral gene transfection agents, especially in case of the cancer treatment, and thus overcoming safety risks of viral vector agents, scheme of transfection leading by denrimer is visible in Fig. 23.

Such dendrimers are able to form compact polycations under physiological conditions able to complex DNA. The peripheral amino functional units are at pH 7.4 positively charged ammonium groups, which can interact with the negatively charged phosphate groups of nucleic acids. DNA is assembled to the dendrimer as a result of this ionic interaction, leading to compact toroidal structures and optimizing the entry into the cell via endocytosis, since protonated residues on these complexes favours the binding to the negatively charged cancerous cell surface. The tertiary amine groups of the dendrimer interior in the complex are available to act as a "proton sponge" in an endosomal environment (pH 5−6), and thus preventing the DNA from lysosomal degradation

because of the pH-controlled inhibition of lysosomal nucleases (endosomal buffering effect) [34].

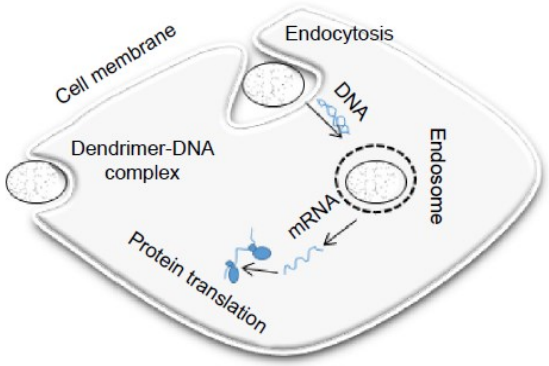

Fig. 23 Gene transfection lead by denrimer [34]

5.4 Dendrimers Antimicrobial and Antiviral Agent

The dendrimers with either a high positive or high-negative surface charge act in the same way as the covalent bound micelles of soap molecules do, thus showing anti-microbial and antiviral aktivity. Moreover, the dendrimer with cationic terminal groups seem to be more efficient than other types of cationic surfactants. Nevertheless, the well known anionic dendrimer family, also known as Vivagel® (lysine based dendrimers with napthalensulfonate groups on the surface) developed by Starpharma in Australia, is commonly used in technologies applied to prevent from the HIV and herpes simplex virus infections [30].

5.5 Dendrimers and Industry, Catalysts, Additives, Printing Inks and Paints

The combination of large surface area and high solubility makes the dendrimers to be useful also as nanoscale catalysts, and also as follows: firstly, they are able to create large well-defined dendrimer with many active sites, and secondly, they are able to encapsulate single catalytic site, the activities of which can be further enhanced by dendritic structures [31].

The dendritic catalysts are mostly applied in homogenous catalysis where metallodendrimers are most frequently used, though they can also be used in heterogenous

catalysis as molecular micelles or inverted micelles [35]. Position of metal is visible in Fig.24.

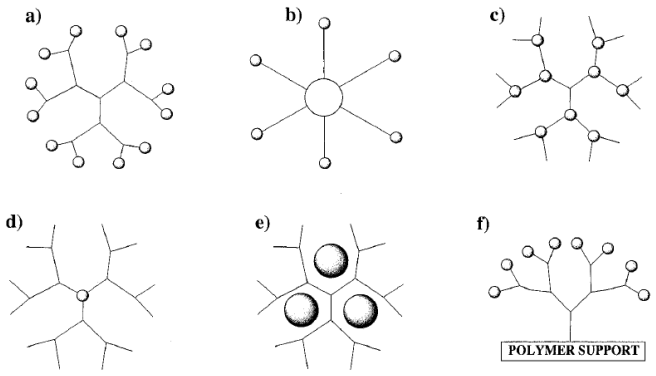

Fig. 24 Position of metall component in thedenrimer struction [35]

The dendrimers can also be used in toners as charge enhancing additives since require less material than their liquid counterparts. The Xerox® Corporation has been granted a patent for dry toner compound dendrimers as charge enhancing additives. Using of additives in printing inks, the dendritic polymers are able to promote adhesion of ink to polar and non-polar foils. First hyperbranched compound attach themselves to the pigment and they are still many free functional groups that are able to work for adhesion to the surface [31].

The dendritic polymers as additives provide more firmness but comfort for flexible polyurethane foam technologies used in automotive seating systems where they seem to substitute for conventional cross-linkers or graft co-polymer polyols of SAN type.

The dendrimers improve the Tg, flexibility of cast polyurethane elastomer product, rapid curing, durability and high performance in UV curing application, provide volatile organic compounds in coatings. paints impart hardness, scratch resistence, chemical resistence, light fastness, weathering resistence as well as high gloss which is often required in design of the furniture and automotive industry [21].

The swedish company Polymer Factory® offers commercially available dendritic polymers, such as dendrimers, dendrons and hyperbranched polymers, and provides wide range of products based on the polyalcohol monomer 2,2-bis(methylol)propionic acid (bis-MPA) as well as various types of focal points (azide, hydroxyl, carboxyl etc.). The dendrimers are available up to the G5 and are designed for use in micelle templating and

also as the drug carriers. Among them, they are the disulfide dendrimers that are considered excellent for studing enzymes and proteins. They can also depict high grafting yields from noble surfaces; for example, gold used for preparing of the polymer-modified gold nanoparticles [36].

W & D™ dispersing agents produced by the SpecialChem® company which are the acrylic resin in xylen or butyl glycol, enhance water and corrosion resistance as well as wear and abrasion resistance. They are commonly used as wetting and dispersing agents, and also to stabilize the pigment dispersions in mid-polar or polar paint systems; used as hyperdispersants in road marking, elastomeric roofing and decorative interior wall coatings; also widely used in marine (anti-corrosive) [37].

CONCLUSION

It is generally known that natural polymers such as silk, wool or cotton have been replaced with nylon and other linear synthetic polymers, such as the natural rubber that has been substituted by its synthetic alternative of cross-linked polymers. Such a growing trend in science and technology may indicate it is about time to start considering also other ways of enhancing (or replacing) of natural polymers e. g. to be used in cancer and gene therapy, prophylactic treatment.

Individual architectural components of dendrimers, which are the core, the branching units and the terminal groups respectively, make them ideal candidates for application in biological and material sciences; and it applies that while peripheral terminal groups affect solubility and chelation ability of dendrimers, varying cores impart unique properties to the cavity size, absorption capacities and encapsulation characteristics.

Dendrimers are synthesized using step-wise chemical methods to produce different generations (G0, G1, G2 etc.) of molecules of narrow molecular weight distribution, uniform size and shape, and multiple terminal groups. Dendrons are monodisperse structures with single focal .

Possible fields of application of dendrimers frequently referred to in literature are drug delivery, gene transfection, catalysis, energy harvesting, photo activity, nanoscale science and technology.

Providing such great similarity between dendrimers and globular proteins, enzymes and biomembranes as for the size and shape control and their biological and chemical properties, it allows for tapping of the dendrimers also into the newly emerging field of biomimetics. Nevertheless, the range of properties of the dendritic polymers assumes them to play a significant role also in the development of medical devices and treatment approaches.

REFERENCES

[1] Boas, U., Christensen, J. B, Heegaard, P. M., Dendrimers in Medicine and Biotechnology: New Moleculae Tools, 2006, 2-27 p, ISBN: 978-0-85404-852-6

[2] Gao, C.,Yan, D., Hyperbranched Polymers: From Synthesis to Application, Progress in Polymer Science, Vol. 29, 2004, 183-275 p, doi:10.1016/j.progpolymsci.2003.12.002

[3] Christensen, J. B., Tomalia, D. A., A Proposed taxonomy and Classification Strategy for Well-Defined, Soft-Matter Nanoscale Building Blocks,Torres, T., Bottari, G., in Organic Nanomaterials: Synthesis, Characterization, and Device Applications, Oxford, 2013, 1-23 p, ISBN: 978-1-118-01601-5

[4] Nijhuis A. CH. ter Maat J., Bisri S. Z., Weusthof M., Salm C., Schmitz J., Ravoo B. J., Huskens J., Reinhoudt N. D., Preparation of metal–SAM–dendrimer–SAM–metal Junctions by Supramolecular Metal Transfer Printing, New Journal of Chemistry, Vol. 34, No. 4, 2008, 652-661 p, doi:10.1039/b712979c

[5] Kalomiraki, M., Thermos, K., Chaniotakis, N. A., Dendrimers as Tunable Vectors of Drug Delivery Systems and Biomedical and Ocular Applications, International Journal of Nanomedicine, Vol. 11, 2016, 1-12 p, doi:10.2147/IJN.S93069

[6] Tomalia, D. A., Christensen, J. B., Boas, U., Dendrimers, Dendrons and Dendritic Polymers: Discovery, Applications, and the Future, Cambridge University Press, 2012. 359-369 p, ISBN:978-1107006935

[7] Tomalia, D. A., Nazloe, A. M., Goddard W. A., Starburst Dendrimers-Molecular Level Control of Size, Shape, Surface Chemistry, Topology, and Flexibility from Atoms to Macroskopic Matter, Vol. 29, No. 2 1990, 138-175 p, doi:10.1002/anie.199001381

[8] Sikwal, D. R., Kalhapure R. S., Govender, T., An Emerging Class of Amphiphilic Dendrimers for Pharmaceutical and Biomedical Application: Janus Amphiphilic Dendrimers, European Journal of Pharmaceutical Sciences, 97 2017, 113-134 p, dx.doi.org/10.1016/j.ejps.2016.11.013

[9] Tomalia et al., Dense Star Polymers Having Core, Core Branches, Terminal Groups, Tomalia D. A, Dewald J. R., United States of America, 4 507 466, Mar. 26, 1985

[10] Tomalia, D. A.,Dendrons/Dendrimers: Quantized,Nano-element like building blocks for Soft-Soft and Soft-Hard Nano-Compound synthesis, Soft Matter, Vol. 6, No. 3, 2010, 456-474 p, doi**:** 10.1039/b917370f

[11] Al-Jamal K. T., Ramaswamy Ch., Florence A. T., Supramolecular Structures from Dendrons and Dendrimers, Advanced Drug Delivery Reviews, Vol. 57, Issue 15, 2005, 2238-2270 p, doi:10.1016/j.addr.2005.09.015

[12] Percec, V., Won, B. C., Peterca, M., Heiney P. H., Expanding the Structural Diversity of Self-Assembling Dendrons and Supramolecular Dendrimers via Complex Building Blocks , Journal of the Amercan Chemical Society, Vol. 129, No. 39, 2007, 11265-11278 p, doi:10.1021/ja073714j

[13] Rosen M. B., Wilson D. A., Wilson J. CH., Peterca M., Won B. C., Huang CH., Lipski L. R., Zeng X., Ungar G., Paul A. Heiney A. P., Percec V., Predicting the Structure of Supramolecular Dendrimers via the Analysis of Libraries of AB3 and Constitutional Isomeric AB2 Biphenylpropyl Ether Self-Assembling Dendrons, Journal of the American Chemical Society, 2009, No. 131, Vol. 47, 2009, 17500–17521 p, doi:10.1021/ja907882n

[14] Fréchet M. J., Dendrimers and Supramoecular Chemistry, Proceeding of the National Academy of the United states of America, Vol. 99, No. 8, 2002, 4782-4787 p, doi:10.1073/pnas.082013899

[15] Nicholson, John W., Chemistry of Polymers (3rd Edition), Kent, Royal Society of Chemistry, 2006, 178 p, ISBN 0-85404-684-4

[16] Esfand, R., Tomalia, D. A., Poly (amidoamine) (PAMAM) dendrimers: from

Biomimicry to Drug Delivery and Biomedical Applications, Drug Discovery Today, Vol. 6, No. 8, 2001, 427-436 p, doi: 10.1016/S1359-6446(01)01757-3

[17] Mather, BD., Viswanathan, K., Miller, KM., Long, TE., Michael Addition Reactions in Macromolecular Design for Emerging Technologies, Progress in Polymer Science, Vol. 31, No. 5, 2006, 487-531 p, doi:10.1016/j.progpolymsci.2006.03.001

[18] Grayson, S. M., Frechet, J-M. J., Convergent dendrons and dendrimers: from synthesis to applications, Chemical Reviews, Vol. 101, No. 12, 2016, 3819-3867 p, doi:10.1021/cr990116h

[19] Sigma Aldrich [online] available from http://www.sigmaaldrich.com/materials-science/material-science-products.html?TablePage=9539880. [cit. 4.2.2017]

[20] Quintana, A. et al., Design and function of a dendrimer-based therapeutic nanodevice targeted to tumor cells through the folate receptor, Pharmaceutical Research, Vol. 19, No. 9, (2002), 1310-1316 p, doi**:**10.1023/A:1020398624602

[21] Dvornic, R .P., PAMAMOS: The First Commercial Silicon-Containing Dendrimers and their Applications, Journal of Polymer Science A: Polymer Chemmistry, Vol. 44, No. 9, 2006, 2755-2773 p , doi:10.1002/pola.21368

[22] Uppuluri, S., Swanson, DR., Piehler, L. T., Li, J., Hagnauer, G. L., Core-Shell Tecto(dendrimers): I. Synthesis and Characterization of Saturated Shell Models, Advanced Materials, Vol. 12, No. 11, 2000, 796-800 p

[23] Haag, R., Supramolecular Drug-Delivery Systems Based on Polymeric Core–Shell Architectures, Angewandte Chemie International Edition, Vol. 43, No. 3, 2004, 278–282 p, doi:10.1002/anie.200301694

[24] Dockendorff, J., Gauthier, M., Dendritic Polymers, Guerra, S. E. Lima, E. V., in Handbook of Polymer Synthesis, Characterization, and Processing, John Willey and Sons, Inc.,2013, 559-584 p, ISBN: 978-0-470-63032-7

[25] Caminade, M-P., Laurent, R., Delavaux-Nicot, B., Majoral, J-P., "Janus" Dendrimers: Synthesis and Properties, New Journal of Chemistry, Vol. 36, 2012, 217-226 p, doi:10.1039/clnj20458k

[26] Centre of molecular materials for photonics and electronic [online] available from http://www-g.eng.cam.ac.uk/CMMPE/lcintro1.html [cit. 4.2.2017]

[27] Donnio, B., Buathong, S., Bury, I., Liquid Crystalline Dendrimers, Chemical Society Review, Vol. 36, No. 9, 2007, 1495-1513 p, doi:10.1039/B605531C

[28] Marcos, M. et al., Highly Congested Liquid Crystal Structures: Dendrimers, Dendrons, Dendronized and Hyperbranched Polymers, Chemical Society Review, Vol. 36, No. 12, 2007, 1889-1901 p, **doi:**10.1039/b611123h

[29] Lang, H., Lühmann, B., Siloxan nad Carboxiloxane Based Dendrimers: Synthesis, Reaction Chemistry and Potential Application, Advanced Material, Vol. 13, No. 20, 2001, 1523-1533p

[30] Mogens B. N., Organic Synthesis and Molecular Engineering, Wiley, 2013, 361-392 p, Published Online: 25 OCT 2013 09:00PM EST, doi:10.1002/9781118736449, Online ISBN: 9781118736449

[31] Singh, U., Dar M. M., Hashmi A. A., Dendrimers: Synthetic Strategies, Properties and Applications. Oriental Journal of Chemistry, Vol. 30, No. 3, 2014, 911-922 p, http://dx.doi.org/10.13005/ojc/300301

[32] Gillies, E. R., Fréchet, J. M., Dendrimers and Dendritic Polymers in Drug delivery, Drug Discovery Today, Vol, 10, 2005, 35-43 p, doi:10.1016/S1359-6446(04)03276-3

[33] Sahoo, S. K., Labhasetwar, V., Nanotech Approaches to Delivery and Imaging Drug, Drug Discovery Today, Vol. 8, No. 24, 2003, 1112-1120 p, doi:10.1016/S1359-6446(03)02903-9

[34] Vallet-Regí**,** M., Vila, M., Advanced Bioceramics in Nanomedicine and Tissue Engineering, Trans Tech Publications Ltd., 2010, 241-242 p, Online version available at: http://app.knovel.com/hotlink/toc/id:kpABNTE006/advanced-bioceramics/advanced-bioceramics

[35] Astruc, D., Chardac, F., Dendritic Catalyst and Dendrimers in Catalysis, Chemical Reviews, Vol. 101, No. 9, 2001, 2991-3023 p

[36] Polymer factory [online] available from http://www.polymerfactory.com/hyperbranched-polymers/boltorn/ [cit. 4.12.2016]

[37] Specialchem [online] available from http://coatings.specialchem.com/product/a-k-tech-india-w-d-4444, http://coatings.specialchem.com/product/a-k-tech-india-w-d-4400 [cit. 4.2.2017]

[38] Swanson, S. D., Kukowska-Latallo, J. F., Patric, A. K., Chen, C. Y., Ge, S., Cao, Z. Y., Kotlyar, A., East, A. T., Baker, J. R., Targeted Gadolinium-Loaded Dendrimer Nanoparticles for Tumor-Specific Magnetic Resonance Contrast Enhancement, Internal Journal of Nanomedicine, Vol. 3, No. 2, 2008, 201-210 p

[39] Yemul, O., Imae, T., Synthesis and characterization of poly(ethyleneimine) dendrimers, Colloid and Polymer Science, Vol. 286, No. 6-7, 2008, 747-752 p, doi:10.1007/s00396-007-1830-6

[40] Peterca, M., Percec, V., Leowanawat, P., Bertin, A., Predicting the Size and Properties of Dendrimersomes from the Lamellar Structure of their amphiphilic Janus Dendrimers, Journal of the American Chemical Society, Vol. 133, No. 50, 2011, 20 507-20 520 p 133, doi**:**10.1021/ja208762u

LIST OF SYMBOLS

B_c	Branch cell.
bis-MPA	Dimethylolpropionic acid
C	Carboneum
cub	Cubic
DNA	Deoxyribonucleic acid
EDA	Ethylendiamine
e.g.	Exempli gratia
Etc.	Et cetera
G	Generation of dendrimer
Gd	Gadolinium
HIV	Human Immunodeficiency Virus.
i.e.	Id est
LC	Liquid crystalline
M_c	Molar masses of initial core
M_{RU}	Molar masses of repeat units
M_{BC}	Molar masses of branch cells
MRI	Magnetic resonance imaging
M_t	Molar masses of terminal units
MW	Molecular weight
N_b	Branch juncture multiplicity
N_c	Initiator–core multiplicity
N_{max}	Maximum shell filling
O	Oxygenium
OS	Organosilan

PAMAM	Polyamidoamin
PAMAMOS	Polyamidoamine-organosilan
PEG-b-PAsp	Polycationic block polymer (polyethylene glycol-b-poly{N'-[N-(2-aminoethyl)-2-aminoethyl] aspartamide})
PEO-B-PCL	Poly(ethylene oxide)-block-poly(ε-caprolactone)
PEO-b-PPO	Poly(ethylene oxide)-block-poly(propylene oxide)-
PES	Polyesther
PEG	Polyethylen oxide
PDA	Propylediamine
pH	Potential of hydrogen
PPI	Polyalkylimine
QLC	Quasi liquid crystal
R_U	Repeat unit
Si	Silicium
Tet	Tetragonal
T_g	Glass transition temperature
SAd	Integrated smectic A
SAN	Styrene acrylonitrile
UV	Ultraviolet
Z	Number of surface group

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