Review Article

Evaluation on characterization, properties and applications of Dendrimer: A new class of polymer

VINOD S. UNDAL*
**Department of Botany, Ghulam Nabi Azad College, Barshitakali Dist- Akola, Maharashtra, India.*

Abstract

The biomedicine correspond to one of the major study areas for dendrimers, which have demonstrated to be significances together in diagnostics and therapy, since to their competence for improving solubility, assimilation, bioaccessibility and targeted dispersal. The dendrimers are the budding polymeric structural designs that are famous for their defined organizations, flexibility in drug carrying and high concern whose properties look like with biomolecules. Their impending capability of nanostructured macromolecules have exposed in entrapping and/or conjugating the high molecular mass hydrophilic /hydrophobic entities by host-guest dealings and covalent attachment respectively. The drug entrapment and release from dendrimers can be controlled by transforming dendrimer exteriors and productions. This assessment will concentrate primarily on the distinctive properties, synthetic approach, physicochemical characterization of dendrimers and their use in biomedical applications, antitumor, diagnostic agents and many more. The evaluation will furthermore emphasize the essential and related properties of dendrimers which supply headed for drug solubilization.

Keywords: *Biomedicine, assimilation, polymers, molecular mass, solubilization*

Introduction

The word ‘dendrimers’ arrives from twice Greek words “dendron” which indicates tree and “meros” which means pieces, as a result referring to the representative tree-like emergence of these compounds[1]. The dendritic compound are documented as the fourth main architectural category of polymers subsequent to the three well recognized kinds (linear, cross-linked and branched polymers). They have developed significantly over their about 27 years account. Currently, more than 50,000 official document and literature records connected to this significant category of polymers have materialized[2]. The dendritic organizations are broad spread motifs in nature that are repeatedly employed where a specific purpose desires to be improved or exposed. These compound are enormously branched, globular, polyvalent, mono-dispersed fragments with synthetic flexibility and several promising applications [3].

The arrangement of a usual dendrimer is characterized by three divergent features specifically; a inner multifunctional ‘core’ creations or tiers of multifunctional replicating elements which are closed to the core and the terminal or end clusters (Figure 1). Controlling these structural facets of dendrimers permits controlled separation of a entire chains of vastly branched end-functionalized macro fragments that are drawing enlarged attention for several impending applications[4].The dendrimers are illustrated by an preferably branched arrangement and the occurrence of a high number of functional clusters, which can have a considerable consequence upon the physical properties together in the solid condition and in solution[5]. The controllable and flexible range, the relations with cell membranes and several dynamic drug molecules and the characteristics of their interior organizations and cavities, formulates dendrimers admirable candidates for drug delivery schemes (DDS)[6].

There are two common synthetic strategies used to produce dendrimers: (i) divergent, and (ii) convergent. Both the synthetic approaches acquires relative benefits and shortcomings and the suitable direction depends generally on the type of monomer employed and the target polymer arrangements. A variety of dendrimers have been developed and useful as drug delivery mediums for natural inventions such as polyamidoamine (PAMAM), polylysine (PLL), polypropylene (PPI), and polyglycerol (PG)[7]. The dendrimers can be employed for targeting drug release through a range of techniques, such as intravenous, subcutaneous, intraperitoneal injection, oral, and ocular delivery[8]. However the advantages of several drugs cannot be exploited since of their reduced solubility, toxicity or stability difficulty. The use of dendrimers as transporters of these compounds can resolve these problems, consequently improving their medical applications[9].

It has been observed that as soon as a dendrimer achieves a precise production (a inconsistent factor according to the dendritic organization however in common equal to or bigger than 4) a significant conformational alteration take place, and the arrangement assumes a compactly packed spherical nature. This modifications in conformation connects with a decline in chain entanglements and molecular portion relation[10], therefore conferring diverse solution and mass properties to dendrimers when compared with their linear analogues. An significant area where linear and dendritic polymers display various features is their stickiness actions. It is well recognized that the intrinsic viscosity of a linear polymer enlarges with the enhance of molecular mass according to the Mark–Houwink–Sakurada correlation. However, dendrimers reveal a linear association at lesser production numbers and a highest that corresponds to the transform in shape, followed by a smooth decline in central viscosity at superior molecular weight [11,10,12].

The dendrimers are very much branched polymers which have special characteristics resembling diverse functional terminal groups, superior compactness and lesser viscosity[13, 14,15,16,].Due to such distinctive characteristics, this class of polymeric nanomaterial have several applications in various fields like as drug release[17,18,19,20,21], dendrimer based nanomedicine[22], gene delivery[23], light harvesting[24], dendritic nanomaterials[25], electrode design[26], solubility enhancers[27] and for various biotech applications[28]. Additionally several latest studies connecting DDS (drug delivery systems) by means of dendrimers have been in the field of neoplastic diseases. The dendrimers are also reported as DDS in other therapeutic fields: anti-inflammatory, antiviral, antibiotic remedies, and in cardiovascular diseases, etc.[29] .

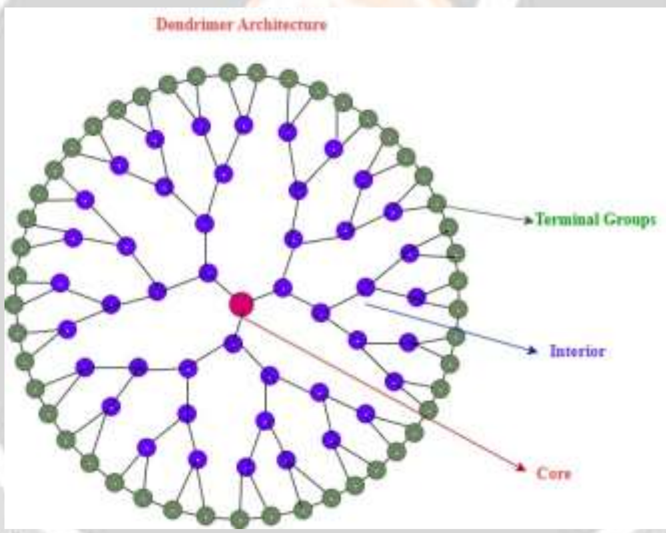

Fig. 1 Component of dendrimer

History of Dendrimers

In the outline of plants and animals nature frequently ends up producing dendritic elucidations to recover particular properties as evidenced in the respiratory organization of animals. Similarly, over the soil plants create use of their dendritic features to enhance the coverage of their foliage to sunbeams, additionally lower the land they have the maximum requirement to expose a enormous functional surface when gathering water from the soil. Consequently a dendrimer is both a covalently assembled fragments and a divergent nanoparticle[2]. The very initial prosperous effort to build and blueprint dendritic compositions by differing creation was accomplished by Fritz Vögtle and collaborators in 1978, followed by R.G. Denkewalter at Allied corporation in 1981, Donald Tomalia at Dow Chemicals in 1983 and George Newkome in 1985. Later on Jean Frechet in 1990, recognized the convergent synthetic approach. Although a several of research worker have accomplished attempt in revision the divergent properties and applications of dendrimers, however another school of concern believes the exploration on the distinctive and applications of dendrimers is still in its infancy. From 1979 to 1985, Donald A. Tomalia and his collaborators at the Dow Laboratories prepared a breakthrough in the expansion of dendrimers[30]. They produced polymers througha inner, vacant core and tendrils that divided superficial, one from another, in a defined, predictable approach, which Tomalia called dendrimers [31] (Table 1).

Table 1. Type of Dendrimers and their discoverers

S/no	Type of Dendrimer	Inventor	Year
1	Poly(Propylene Imine) PPI dendrimer	Vögtle*et al*.	1978
2	PolyAmido-Amine PAMAM dendrimer	Tomalia*et al*.	1983, 1985
3	Arbosols	Newkome*et al*.	1985
4	Poly(aryl ether) dendrimer	Frechet and Hawker	1990
5	Polylysinedendrimer	Denkewalter*et al*	1981
6	Polyether dendrimer	Frechet and Grayson	2001

Structure of Dendrimers:

Fundamentally, the dendrimers are spheroid or globular nano compositions that are specifically engineered to carry fragments encapsulated in their central void gaps or connected to the exterior. The dendrimers acquires three well-known architectural constituents (32, 33) specifically;

(i) The innercenter which is either a distinct atom or an atomic group having at least twice the same chemical functions,

(ii) Divisions emerging from the core, comprising of replicate elements having at least single branch connection, whose recurrence is controlled in a geometrical progression that outcome in a chain of radially concentric deposits known as generations, and

(iii) Several terminal functional clusters, usually situated in the outside of the macromolecule, which cooperate a means job in the properties.

The dendrimers develop into compactly packed as they expand out to the margin, which forms a closed membrane-like organization. The dendrimers cannot produce since of a lack of space, when a critical branched situation is attained. This is called the “starburst effect”. For PAMAM (poly (amidoamine)) dendrimer production it is observed subsequent to tenth generation. The speed of reaction falls rapidly and further reactions of the terminal clusters cannot take place.

SYNTHESIS OF DENDRIMERS

Typically dendrimers are structured via both a divergent or a convergent methods. There is an crucial distinction among those two design techniques(34, 35, 36, 37, 38).

Divergent method

Dendrimer build up from a multifunctional central molecule in this approach. The reaction of the core and with monomer molecules, which integrates one reactive and resting cluster, twisted the initial production dendrimer. Afterward this new surface periphery of the first-generation is then activated for reactions with additional monomers. The technique continual for numerous productions and a dendrimer is raised following several layers of response. The production of massive quantities of dendrimers, the divergent method is of superior use. The structural concerns may arise from side reactions and imperfect reactions of the terminal groups. The huge excess of reagents is requisite; to prohibit surface reactions and to force reactions for achievement. However it causes several barriers in the refinement of the closing product.

Convergent method

As to decline the concerns of the divergent synthesis, the convergent methods have been sophisticated. The dendrimer is built stepwise, opening from the terminal groups and succeeding inwards, in this convergent methods. After the dendrons are build up, they may be joined to a multi efficient central molecule. There are a number of advantages of convergent expansion approach. It is more appropriate to the preferred produce with refinement and the occurrence of defects within the final makeup is minimized. Additionally by this process formation of superior engineering into the dendritic nature through definite placement of determined productions on the margin of the macromolecule is possible. The approach does now not allow the development of high productions due to the fact steric concerns happen inside the reactions of the dendrons and the central molecule.

Physicochemical Characterization of Dendrimers

The well-defined nanometric structural design of dendrimers is the outcome of controlled production of these moieties at every step with chemical reaction. The characterization of dendrimers is consequently a crucial step in the designing and engineering of these flexible nanoscopic carriers[39,40]. Several analytical methods have been accounted in literature to explore the physicochemical constraints of dendrimers (Fig. 2; Table 2). It comprises dynamic light scattering (DLS), spectroscopic, microscopic, chromatographic, rheological, calorimetric and electrophoretic characterization: Nuclear magnetic resonance (NMR), infrared, ultraviolet (UV)-Visible, fluorescence and mass spectroscopy; small angle X-ray scattering, small angle neutron scattering, laser light scattering; atomic force microscopy (AFM), transmission electron microscopy (TEM); size exclusion chromatography, high performance liquid chromatography (HPLC); DSC, temperature modulated calorimetry and dielectric spectroscopy; Polyacrylamide gel electrophoresis (PAGE) and capillary electrophoresis[39,40]. In general, all these dendrimer characterization methodologies can furthermore be used to assess the dendrimer-drug conjugates/complexes. The encapsulation of drug molecules or nanoparticles by dendrimers can be characterized by TEM, UV-Visible and Fourier transform infrared spectroscopy.

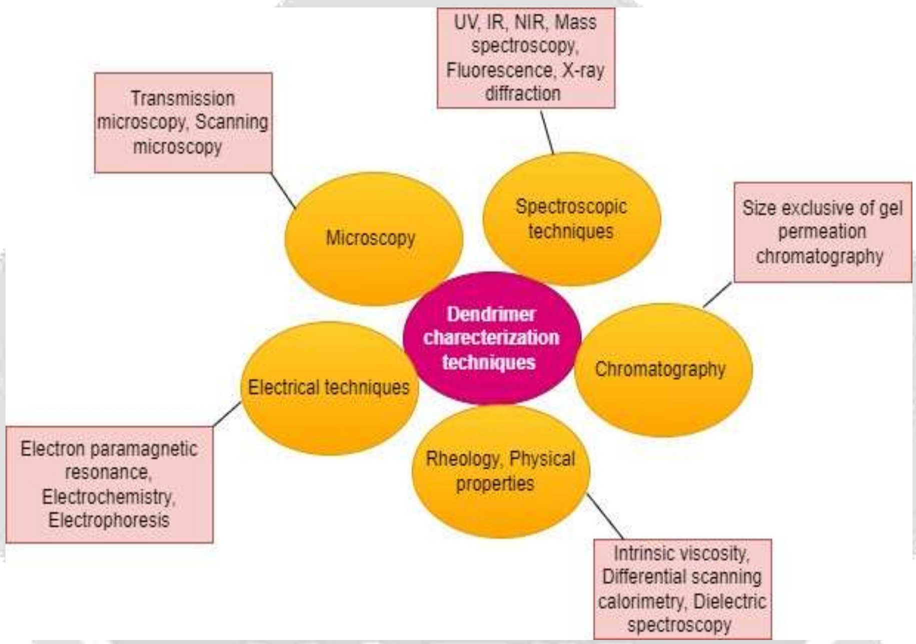

Fig. 2 Techniques of characterization of dendrimers.

Table 2. Techniques of characterization of dendrimers.

S.N.	Analytical techniques	Characterization constraint
1	Nuclear magnetic resonance (NMR)	It assists in formative chemical change undergone by terminal groups and appropriate to configrational study of dendrimers and sequential characterization of synthesis
2	Infrared and Raman spectroscopy	It learns the chemical change occurs throughout the production or peripheral engineering of dendrimers
3	UV–visible spectroscopy	Assisting determination the alteration in chemical makeup and synthesis process via identifying chromophores and auxochromes. Furthermore to check the transparency of dendrimers
4	Fluorescence	Applicable to distinguish the organization and production of dendrimers with photochemical clusters and to enumerate shortcomings take place at the time of synthesis
5	Circular dichroism	Characterization of configuration of dendrimers with optical activity
6	Atomic force microscopy	Dimension, outline and arrangement
7	TEM, Electron paramagnetic resonance	Exterior constitution
8	X-ray diffraction	Chemical constitution, dimension and outline

9	X-ray photoelectron spectroscopy	Chemical structure and dimension
10	Electrochemistry	Getting information on arrangement of dendrimers
11	Electrophoresis	To check the transparency and homogeneity of water-soluble dendrimers
12	Small-angle X-ray scattering (SAXS)	Assisting common radius of gyration in mixture, used further for calculating standard particle size, outline, distribution, and surface-to-quantity proportion
13	Small-angle neutron scattering (SANS)	Measuring standard radius of gyration (Rg) in mixture as well as complete information on the interior arrangement of intact dendrimer
14	Laser light scattering (LLS)	Detecting hydrodynamic radius
15	Mass spectrometry (FAB-MS, ESI-MS, FT-ICR MS, MALDI-TOF MS)	Resolving molecular mass and several arrangement knowledge
16	Size exclusion chromatography (SEC) (GPC)	Molecular mass and extent
17	Intrinsic viscosity	Physical description and morphological makeup
18	Differential scanning calorimetry (DSC)	Glass transition temp. (Tg), influenced by the molecular mass, entanglement and chain-terminal constitution of dendrimer
19	Dielectric spectroscopy	Learning of molecular dynamics

PROPERTIES OF DENDRIMERS

1. The dendrimers are nanoscale ranges which have analogous dimensions to vital bio-building blocks as an example, proteins, DNA.
2. The numbers of peripheral surface groups suitable for bio-conjugation of drugs, indication corporations, concentrated on moieties or biocompatibility businesses.
3. Exterior that can be designed with determined organizations to emphasizes or face up to trans-mobile, epithelial or vascular bio-permeability.
4. To encapsulate small-molecule pills, metals, or imaging moieties, an central void gap may be used. Encapsulating in that void space condenses the drug toxicity and assists administered release.
5. Positive biocompatibility outlines, which are coupled with lesser phase anionic or neutral polar terminal surface clusters, compared to superior production impartial polar and cationic exterior clusters.
6. Non- or low-immunogenicity connected with most dendrimer exteriors altered with little efficient groups or polyethylene glycol (PEG).
7. Exterior groups that may be altered to optimize bio-allotment; receptor-mediated focused on, treatment measure or controlled release of drug from the in the central gap[41,42].

Table 3. Properties of Dendrimer [43]

S. N.	Properties	Dendrimer
1	Arrangement	Compact and Globular
2	Outline	Spherical
3	Structural design	Regular
4	Structural control	Very high
5	Production	Stepwise growth
6	Crystallanity	Non-crystalline and amorphous materials minor glass temperatures
7	Reactivity	High
8	Aqueous solubility	High
9	Nonpolar solubility	High
10	Viscosity	Non linear relationship with molecular weight
11	Ionic conductivity	High
12	Compressibility	Low
13	Polydispersity	Monodisperse

Applications of Dendrimers

In analysis of the truth that every three structural design components; specifically the core, interior dividing units and the exterior groups of dendrimers can be adapted to assemble distinctive properties. These exclusive properties counting unparalleled molecular homogeny, multifunctional marginal groups and existence of several internal voids provide dendrimers apposite for prospective pharmaceutical relevance including different therapeutic and biomedical values. The applications of dendrimers have been assessed thoroughly by several scientists(44,45). Specific purposes of dendrimers in drug delivery are schematically presented in Fig. 3.

1) Remediation of environmental problems:

Dendrimers structural design i.e. high compactness of functionalities at outside edge and central voids is appropriate for entrapping little gas molecules and low molecular mass organic complexs as well as metal cations. This property make possible the dendrimers to be used in the field of environmental remediation(46,47). The PAMAM dendrimers with amine, carboxyl, and hydroxyl terminal clusters have been used to eliminate the toxic metal ions from waste water and polluted soil(48,49). Several ultrafiltration membranes supported with dendrimeric architecture have also been designed with impending application in soft water.

2) Dendritic sensors:

Due to huge number of marginal functional groups contained in single a molecule of a dendrimer, may valuable for covalent connections or closeness of a high number of species. It have been documented the fluorescence of a G4 poly(propylene amine) dendrimer elaborated with thirty two dansyl units at the outside edge(50). Therefore the amine cluster allocate the balanced number of a metal ions to coordinate. With the incorporation of Co^{2+} in the interior of dendrimer, it was observed that the strong fluorescence decreased.It has been stated that little concentrations of Co^{2+} ions can be recognized using dendrimer concentration of 4.6 × 10–6 M. Thus the dendrimers containing fluorescent may possibly use full as a sensors(51).

3) Dendrimers in biomedical field:

The application of dendrimers in biomedical field in the current era, has increase much interest from the researchers. The molecule are attractive candidates for biomedical uses since of their unique characteristics counting: hyper branching, volume, form i.e. globular organizations, expanding length/thickness, marginal functionalities, reliability, multivalency and high normal comparability. In particular, the 3D construction of dendrimers can connect an arrangement of naturally distinctive administrators to form generally prevailing conjugates. These molecules and allied species can be simply functionalized and can perform as synthetic equivalent of enzymes, proteins and viruses. The dendrimers and other molecules can either be coupled to the periphery or can be exemplified in their indoor voids(52). An variety of such materials are being used in current medicines, for instance, polyamidoamine (PAMAM) dendrimers can be utilized as prospective blood alternates(53). The improvement of precise outlines with accurate volumes and characters may showed the way to curative purposes like drug progress(54), superiority transfection (44), and imaging (55, 56).

4) Dendrimers in vaccine development:

There is forever a rising requirement for novel productions of vaccines with optimal individuality to target the infectious diseases(57). Since the best possible physical characteristics, dendrimers have capability to act as competent resistant influencing compounds (adjuvants) that can improve the usefulness of vaccines. Furthermore, dendrimers can supply well-defined multivalent scaffolds to generates conjugates by way of immune stimulators and/or antigens(58). These conjugates supposed to be outstanding exporters of little antigens upon management exclusive of any side effect. With this respect, peptide dendrons assembled up exclusively from lysine have gaina lotconcern from the researchers(59,60). The lysine molecule consist of two amino groups (R and ε) present and can act as dividing spots for logarithmic improvement. Consequently, two-layer and three-layer dendrons may have four and eight open amino clusters, correspondingly. The Tam make up word “multiple antigenic peptide” (MAP) for such a organization. Wang et al.(61) have reported the vaccine utility of a MAP which was achieved by union the V3 loop (third variable section of packet glycoprotein gp120 of HIV) chain to lysine dendrimer by Tam and his fellows (62,63). It was reported that elicitation of comparatively high and persistent levels of HIV-1-specific neutralizing antibodies in animals. The production of first glycopeptides dendrimer-type AIDS vaccine form composing of a V3 loop peptide–succinyl–maltose–proline– poly(lysine) dendrimer scaffoldas accounted by Baigude et al.(63). Furthermore these vaccine model has been declared to have superior water solubility, little cell toxicity, and antigenicity of dendrimer itself, since the presence of sugar moieties(64). Numerous investigations have been conducted using dendrimeric species mainly PAMAM dendrimers as adjuvants against a variety of pathogens. Superior usefulness and decline in undesirable consequence on host expressed that dendrimers in conjugation with vaccines/ antigens can be employedproductively (65,66).

5) Dendrimers used for enhancing the solubility:

The PAMAM dendrimers are conventional to have impending advantages in increasing the solubility for drug delivery schemes(67). It had hydrophilic peripheral and hydrophilic centers that are reliable for its uni molecular micelle nature, which are liable for its solubility conduct(68). Due to unimolecular micelle and do not acquire a critical micelle concentration. These properties offers the prospective to soluble weakly soluble drugs by encapsulating them within the dendritic configurations(69). Dendrimer base transporters intend the opportunity to get better the oral bioaccessibility of difficult drugs. Consequently, dendrimer nano-tansporters recommend the feasible means to improve the bioaccessibility of drugs which are weakly soluble or substrates for efflux carriers.

6) Dendrimers as Catalyst:

The dendritic polymers have been employed in huge quantity as catalyst. There are two mainly significant reasons for the advantage of using dendrimers. One of the basisis chance of generating a huge dendrimer through several dynamic positions. These kinds of medium are an in-between both heterogeneous and homogeneous catalyst which can be eliminated straightforwardly by separations[70]. The next significant cause is that, there is alternative of encapsulating a distinct catalytic position whose conductance can be superior by dendritic best configuration[71]. Cooper and co-workers[72] producing fluorinated dendrimers which are soluble in supercritical CO_2 that can be utilized to take out effectively hydrophilic compounds from water into fluid CO_2.

7) Dendrimers as molecular probes:

Suitable to their perfect morphology and definite features, use as molecular probes.The immobilization of sensor elements at the periphery of dendrimers is a entirely competent way to produce an integrated molecular probe, due to their enormous exterior area and extreme thickness of exterior functionalities[73].

8) Dendrimers in gene delivery:

Several of investigations is currently accessible on the significance of dendrimers in gene transfection, predominantly amino terminated dendrimers such as PPI, PAMAM, arginineand ornithine conjugated dendrimers. It boost the transfection competence into nucleus by endocytosis with the amino terminated dendrimers[44,74,75]. The complexes of dendrimers (i.e. dendriplexes) and nucleic acids displayed superior transfection competence and thus investigated for the release of genetic materials together with oligonucleotides, genes, aptamers, siRNA and others[76]. Dendrimers with configuration flexibility and hyper deviational structure designs are appropriate candidates for gene delivery functions owing to development of additional condensed complexes with DNA, recognized to superior flexibility of dendrimers. Principally in the primary step dendrimer–DNA composite is in use by cells by endocytosis, and accordingly endosomal destabilization of electrostatically accumulated dendrimer–DNA composite produced, which is followed by free of DNA. Afterward the DNA is in use up by nucleus where it replicates in host DNA. Consequently transcription occurs, and as a outcome, mRNA is discharged as bio indication, which is followed by translation of target protein [77].

9) Diagnostic applications:

The distinctive morphology and individual makeups of dendrimers formulates them capable candidate for investigative purposes. It have been used competently as imaging mediator, in radio analysis, as X-ray and MRI contrast mediator as well as molecular probes[78,79]. Dendrimers connected to diverse ligands have been employed for molecular recognition, partition, radio analysis and as imaging mediator. Wu et al. utilized the antibody associated metal–chelate–dendrimers for radio immune analysis and imaging intentions[80]. Likewise FITC labeled PAMAM dendrimers has been reported for resolving the cellular uptake[81]. The variety of the investigative relevances of dendrimers is probable to expand in near upcoming.

10) Anticancer drugs:

Possibly the most capable prospective of dendrimers is in their chance to conduct controlled and precise drug release, which regards the subject of nanomedicine. One of the main basic troubles that are set in the direction of current medicine is to develop pharmacokinetic properties of drugs for cancer[53]. The drugs conjugated through polymers are distinguished by prolonged half-life, superior strength, water solubility, declined immunogenicity, and antigenicity[82]. The distinctive pathophysiological characters of growths such as widespread angiogenesis consequential in hyper vascularization, the enlarged permeability of tumor vasculature, and restricted lymphatic discharge permit passive targeting, and as a outcome, selective gathering of macromolecules in cancer tissue. This incident is identified as 'enhanced permeation and retention' (EPR)[53,18]. Forming the drug-dendrimer conjugates displayed maximum solubility, condensed systemic toxicity, and selective gathering in solid tumors. To include within the dendrimer organization drug fragment, genetic materials, targeting mediators, and dyes either by encapsulation, complexation, or conjugation, different approaches have been projected.

11) Dendrimers in drug delivery:

The applications of these extremelydivided molecules as molecular containers recommended for the first time in 1982, by Maciejewski[83]. The host-guest characteristics of dendritic polymers are presently under systematic research and have expanded fundamental situation in the field of supramolecular chemistry. The host-guest chemistry is reliant on the response of connecting of a substrate molecule (guest) to a receptor molecule (host) [84].

12) Transdermal drug delivery:

The clinical use of NSAIDs is inadequate due to difficult responses like GI side produces and renal side effects when specified orally. The transdermal drug release overcomes these shocking outcomes and also preserves restorative blood level for extended period of time. The transdermal delivery suffers reduced speeds of transcutaneous release because barrier function of the skin. The dendrimers have found significances in transdermal drug delivery systems. Commonly, in bioactive drugs contains hydrophobic moieties in their constitution with little water solubility, dendrimers are a superior alternative in the field of competent delivery system(85).

13) Therapeutic applications of dendrimers

The molecules are being growing as topical antimicrobial mediators following investigation of efficiency of polylysine dendrimers against herpes simplex virus (HSV), presently under stage II medical testing for its value against vaginal infection. The Starpharma Pty Ltd, Australia, developed VivaGel® and is a vaginal microbicide for the avoidance of HIV and HSV infections(86). The dynamic constituent of the gel is a dendrimer that impart hydrophobicity, and a high anionic charge to the dendrimer exterior(87). The process of antimicrobial action of PAMAM dendrimers in guinea pig form of chorioamnionitis against *E. coli* stimulated ascending uterine infection was reported by Wang et al.,(88). It recognized the antimicrobial action to the dealings of poly cationic dendrimers with polyanionic lipopolysaccharide occurred in bacteria. Further it was studied that molecule glycosylated with glucosamine displayed anti-inflammatory action by restraining composite of lipopolysaccharide, Toll-like receptor, which intervene the pro inflammatory cytokine responses(89). The action of moderately glycosylated dendrimers can offer a platform for investigation of dendrimers in the dealing of malignancies, inflammatory diseases and transmittable diseases.

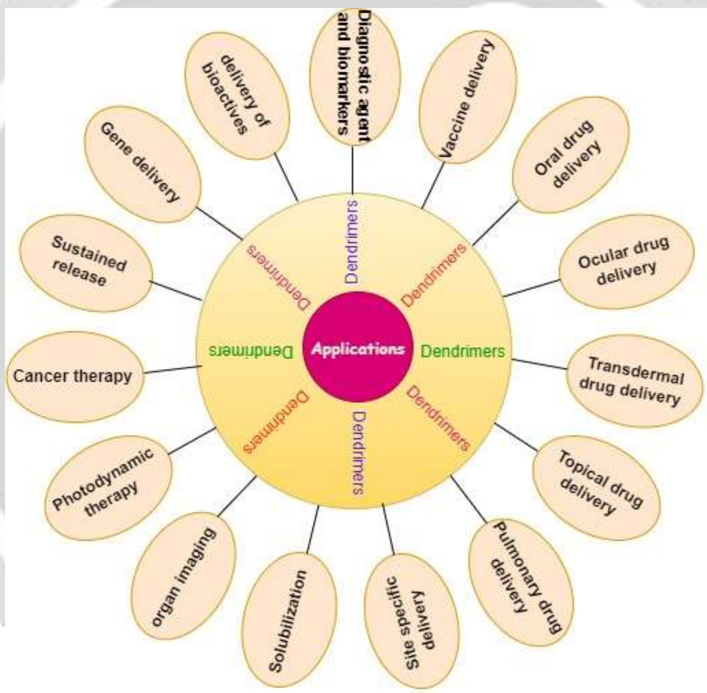

Fig. 3 An overview of denderimers applications

Conclusion

The perfect choice of the delivery method is a solution aspect in the arena of drug release. The relevance of nanotechnology in drug delivery has witnessed exponential development in the history of few years. It is a scientific breakthrough, which is being recognized extremely quick, from idea to authenticity. The dendrimers materialize as a impending macromolecule for bio remedial, pharmaceutical and biopharmaceutical uses in the 21st century, in the field of nanotechnology. The dendrimers holds several purposes because of their functional and structural flexibility. The dendrimers and hyper branched polymers characterize a comparatively novel category of materials with superior solubility properties and a elevated extent of control over molecular structural designs and dimensions contrast with conventional linear polymers. Moreover, the capability to form host–guest compounds with several organic and inorganic compounds has been exposed to be interrelated to their designand has permissible the use of dendritic polymersin liquid/liquid extraction, liquid/scCO_2 separations, and as release methods for the controlled release of dynamic compounds. The toxicity of divergent dendrimers comprises a constraint of their relevancies in biomedicine, and has triggered the progress of divergent toxicity declining approaches.

The dendrimers are distinguished by individual aspects that build them promising candidates for a bundle of applications. However the dendrimers are greatly defined synthetic macromolecules, which are characterized by a arrangement of a high number of efficient groups and a condensed molecular organization. A speedy increase of significance in the chemistry of dendrimers has been documented since the earliest dendrimers were prepared. Unless there is a significant breakthrough in this field, only a little applications for which the distinctive dendrimer configuration is necessary will pass the cost-benefit trial.

References

1) Filho D. L. and Paim L. L. (2013) Synthesis and a preliminary characterization of Poly(Proppylene) Imine Hexadecylamine Dendrimer (DAB-Am-16) modified with methyl Acrylate, American Chemical Science Journal, 3(3): 314-324.
2) Tomalia D. A. (2016) Special Issue: "Functional Dendrimers" Molecules, 21: 1035. https://doi.org/10.3390/molecules21081035.
3) Tomalia D. A. (2004) Birth of a new macromolecular architecture: dendrimer as quantized building blocks for nanoscale synthetic organic chemistry, Aldrichimica Acta, 37(2): 39-57.
4) Biag T., Nayak J., Dwivedi V., Singh A., Srivastava A. and Tripathi K. P. (2015) A review about dendrimers: synthesis, types, characterization and applications. International Journal of Advances in Pharmacy, Biology and Chemistry, 4(1):44-59.
5) Hay G., Mackay M. E. and Hawker C. J. (2001) Thermodynamic properties of dendrimers compared with linear polymers: general observations. J Polym Sci: Part B: Polym Phys., 39:1766-1777.
6) Cojocaru F. D., Botezat D., Gardikiotis I., Uritu C. M., Dodi G., Trandafir L., Rezus C., Rezus E., Tamba B. I. and Mihai C. T. (2020) Nanomaterials designed for antiviral drug delivery transport across biological barriers. Pharmaceutics, 12: 171.
7) Mignani S., Shi X., Rodrigues J., Tomás H. and Majoral J. P. (2022) Dendrimer nanoplatforms for veterinary medicine applications: A concise overview. Drug Discov Today, 27:1251-1260.
8) Sathe R. Y. and Bharatam P. V. (2022) Drug-dendrimer complexes and conjugates: detailed furtherance through theory and experiments. Adv. Colloid Interface Sci., 303:1026-1039. https://doi.org/10.1016/j.cis.2022.102639
9) Sherje A. P., Jadhav M., Dravyakar B. R. and Kadam D. (2018) Dendrimers: A versatile nanocarrier for drug delivery and targeting. Int. J. Pharm., 548:707-720.
10) Bosman A. W., Janssen H. M. and Meijer E. W. (1999) About Dendrimers: structure, physical properties, and applications. Chem Rev., 99(7):1665-1688. https://doi.org/10.1021/cr970069y
11) Tomalia D. A., Naylor A. M. and Goddard III (1990) Starburst dendrimers: molecular-level control of size, shape, surface chemistry, topology, and flexibility from atoms to macroscopic matter. WA. Angew Chem Int Ed Engl., 29:138-175.
12) Hobson L. J. and Feast W. J. (1999) Poly(amidoamine) hyperbranched systems: synthesis, structure and characterization. Polymer, 40:1279-1297.
13) Fréchet J. M. J., Hawker C. J, Gitsov I. and Leon J. W. (1996) Dendrimers and hyperbranched polymers: two families of three-dimensional macromolecules with similar but clearly distinct properties. J. Macromol. Sci. Pure Appl. Chem., A33:1399-1425.
14) Jikei M. and Kakimoto M. (2001) Hyper branched polymers: a promising new class of materials. Prog. Polym. Sci., 26: 1233-85.
15) Aulenta F., Hayes W. and Rannard S. (2003) Dendrimers: A new class of nanoscopic containers and delivery devices. Eur Polym J., 39: 1741-1771.
16) Voit B. I. and Lederer A. (2009) Hyper branched and highly branched polymer architecture synthetic strategies and major characterization aspects. Chem. Rev., 109 (11): 5924-5973.
17) Florence A. T. (2005) Dendrimers: a versatile targeting platform. Adv. Drug Delivery Rev., 57: 2101-2286.
18) Gillies E. R. and Fréchet J. M. J. (2005) Dendrimers and dendritic polymers in drug delivery. Drug Discovery Today, 10: 35-43.
19) Emanuele D A. and Attwood D. (2005) Dendrimer-drug interactions. Adv. Drug Delivery Rev., 57: 2147-62.
20) Wolinsky J. B. and Grinstaff M. W. (2008) Therapeutic and diagnostic applications of dendrimers for cancer treatment. Adv. Drug Delivery Rev., 60: 1037-55.
21) Medina S. H. and El-Sayed M. E. H. (2009) Dendrimers as carriers for delivery of chemotherapeutic agents. Chem. Rev., 109: 3141-57.
22) Majoros I. J. and Baker J. R. (2008) Dendrimer based nanomedicine. Singapore: Pan Stanford Publishing.
23) Mintzer M. A. and Simanek E. E. (2009) Nonviral vectors for gene delivery. Chem. Rev., 109: 259-302.
24) Adronov A. and Frechet J. M. J. (2000) Light Harvesting Dendrimers. Chem. Commun, 1701-1710.

25) Grimsdale A. C. and Mullen K. (2005) The chemistry of organic nanomaterials, Angew. Chem., Int. Ed., 44(35): 5592-629.
26) Guldi D. M. and Prato M. (2004) Electrostatic interactions by design. Versatile methodology towards multifunctional assemblies/ nanostructured electrodes. Chem. Commun., 2517-2525.
27) Gupta U., Agashe H. B., Asthana A. and Jain N. K. (2006) Dendrimers: novel polymeric nanoarchitectures for solubility enhancement. Biomacromolecules, 7(3): 649-58.
28) Grinstaff M. W. (2008) Dendritic macromers for hydrogel formation: Tailored materials for ophthalmic, orthopedic, and biotech applications. J. Polym. Sci., Part A: Polym. Chem.,46(2): 383-400.
29) Patel V., Rajani C., Paul D., Borisa P., Rajpoot K., Youngren-Ortiz S. R. and Tekade R. K. (2020) Dendrimers as novel drug-delivery system and its applications. In Drug Delivery Systems; Elsevier: Cambridge, MA, USA, 333-392.
30) Tomalia D. A., Baker H., Dewald J., Hall M., Kallos G., Martin S., Roeck J., Ryder J. and Smith P. (1985) A new class of polymers: Starburst-dendritic macromolecules. Polymer J., 17:117.
31) Tomalia D. A. and Frechet J. M. J. (2002) Discovery of dendrimers and dendritic polymers: A brief historical perspective. J Polym Sci A Polym Chem., 40:2719-2728.
32) Pushkar S., Philip A., Pathak K. and Pathak D. (2006) Dendrimers: nanotechnology derived novel polymers in drug delivery. Indian J. Pharm. Educ. Res., 40 (3): 153-158.
33) Sakthivel T. and Florence A. T. (2003) Adsorption of amphipathic dendrons on polystyrene nanoparticles. Int. J. Pharm., 254: 23-26.
34) Dwivedi D. K. and Singh A. K. (2014) Dendrimers: A novel carrier system for drug delivery. Journal of Drug Delivery and Therapeutics, 4(5):1-6.
35) Svenson S. and Tomalia D. A. (2012) Dendrimers in biomedical applications-reflections on the field. Advanced drug delivery reviews, 64:102-115.
36) Barbara K. and Maria B. (2001) Review Dendrimers: properties and applications. Acta biochimica polonica., 48(1):199-208.
37) Hawker C. and Fréchet J. M. (1990b) A new convergent approach to monodisperse dendritic macromolecules. Journal of the Chemical Society, Chemical Communications., 15:1010-1023.
38) Crampton H. L. and Simanek E. E. (2007) Dendrimers as drug delivery vehicles: non-covalent interactions of bioactive compounds with dendrimers. Polymer international., 56(4):489-496.
39) Caminade A. M., Laurent R. and Majoral J. P. (2005) Characterization of dendrimers. Adv Drug Deliv Rev., 57(15):2130-2146. https://doi.org/10.1016/j.addr.2005.09.011
40) Biricova V. and Laznickova A. (2009) Dendrimers: analytical characterization and applications. Bioorg Chem., 37:185-192. https://doi.org/10.1016/j.bioorg.2009.07.006
41) Nanjwade B. K., Bechra H. M., Derkar G. K., Manvi F. and Nanjwade V. K. (2009) Dendrimers: emerging polymers for drug-delivery systems. European Journal of Pharmaceutical Sciences,38(3):185-96.
42) Tolia G. T. and Choi H. H. (2008) The role of dendrimers in topical drug delivery. Pharmaceutical Tech., 32(11):88-98.
43) Hawker C. J., Farrington P. J., Mackay M. F., Wooley K. L. and Frechet J. M. J. (1995) Molecular ball bearings: The unusual melt viscosity behavior of dendritic macromolecules. J. Am. Chem. Soc., 117(15): 4409-4410.
44) Svenson S. and Tomalia D. A. (2005) Dendrimers in biomedical applications-reflections on the field. Adv. Drug Deliv. Rev., 57(15): 2106-2129. https://doi.org/10.1016/j.addr.2005.09.018.
45) Menjoge A. R., Kannan R. M. and Tomalia D. A. (2010) Dendrimer-based drug and imaging conjugates: design considerations for nanomedical applications. Drug Discovery Today, 15:171-185.
46) Lard M., Kim S.H., Lin S., Bhattacharya P., Ke P. C. and Lamm M .H. (2010) Fluorescence resonance energy transfer between phenanthrene and PAMAM dendrimers. Phys. Chem. Chem. Phys., 12: 9285-9291.
47) Wei X.-Z., Zhu L.-P., Deng H.Y., Xu Y. Y., Zhu B.-K. and Huang Z.-M. (2008) New type of nanofiltration membrane based on crosslinked hyperbranched polymers. J. Membr. Sci., 323(2): 278-287.
48) Xu Y. H. and Zhao D. Y. (2005) Removal of copper from contaminated soil by use of poly (amidoamine) dendrimers. Env Sci &Tech., 39**:** 2369-2375.
49) Cohen S. M., Petoud S. and Raymond K. N. (2001) Synthesis and metal binding properties of salicylate-, catecholate-, and hydroxypyridinonate-functionalized dendrimers. Chem. Eur. J., 7: 272–279.
50) Battah S. H., Chee C. E., Nakanishi H., Gerscher S., MacRobert A. J. and Edwards C. (2001) Synthesis and biological studies of 5-aminolevulinic acid-containing dendrimers for photodynamic therapy. Bioconjugate Chem., 12(6): 980-988. https://doi.org/10.1021/bc010027n

51) Li W. S. and Aida T. (2009) Dendrimer Porphyrins and Phthalocyanines. Chem. Rev., 109(11): 6047-6076. https://doi.org/10.1021/cr900186c
52) Ruth D. and Lorella I. (2005) Dendrimer biocompatibility and toxicity. Adv. Drug Deliv. Rev., 57(15): 2215–2237. https://doi.org/10.1016/j.addr.2005.09.019.
53) Sampathkumar S. G. and Yarema K. J. (2007) Dendrimers in cancer treatment & diagnosis. C. S. S.R. Kumar ed. (John Wiley &Sons, Hoboken, NJ 2007) pp 1-47.
54) Bauer R. E., Grimsdale A. C. and Müllen K. (2005) In Functional molecular nanostructures. topics in current Chemistry, A. D. Schlüter(ed.) (Springer, Berlin, Heidelberg, 2005), 245: pp. 253-286.
55) Fischer M. and Vogtle F. (1999) Dendrimers: From Design to application-A Progress Report. Angewandte Chemie International Edition., 38: 884-905.
56) Lebedev A. Y., Cheprakov A. V., Sakadzic S., Boas D. A., Wilson D. F. and Vinogradov S. A. (2009) Dendritic Phosphorescent probes for oxygen imaging in biological systems. A.C.S. Appl, Mater. Interfaces, 1(6): 1292-1304.
57) Heegaard P. M. H., Boas U. and Sorensen N. S. (2010) Dendrimers for Vaccine and Immunostimulatory Uses. A Review. Bioconjugate Chem. 21(3): 405-418. https://doi.org/10.1021/bc900290d
58) Tam J. P. (1993) "Multiple antigen peptide system," US5229490A.
59) Crespo L., Sanclimens G., Pons M., Giralt E., Royo M. and Albericio F. (2005) Peptide and amide bond-containing dendrimers. Chem. Rev., 105(5): 1663- 1681. https://doi.org/10.1021/cr030449l.
60) Tam J. P. and Lu Y. A. (1989) Vaccine engineering: enhancement of immunogenicity of synthetic peptide vaccines related to hepatitis in chemically defined models consisting of T- and B-cell epitopes. Proc. Natl. Acad. Sci. USA, 86(23): 9084-9088. https://doi.org/10.1073/pnas.86.23.9084
61) Wang C. Y., Looney D.J., Walfield J.Y., Hosein B., Tam J. P., A.M. and Wong-staal D.F.(1991) Long-Term High-Titer Neutralizing Activity Induced by Octameric Synthetic HIV-1 Antigen. Science, 254(5029): 285-288. https://doi.org/10.1126/science.192558
62) Tam J.P. (1988) Synthetic peptide vaccine design: synthesis and properties of a high-density multiple antigenic peptide system. Proc. Natl. Acad. Sci. USA,85(15): 5409-5413. https://doi.org/10.1073/pnas.85.15.5409
63) Baigude H., Katsuraya K., Okuyama K. and Uryu T. (2004) Synthesis of structurally-controlled AIDS Vaccine model with Glyco-peptide dendrimer Scaffolds. Macromol. Chem. Phys., 205(5): 684-691 https://doi.org/10.1002/macp.200300097
64) Schlüter A. D. and Rabe J. P. (2000) Dendronized Polymers: synthesis, characterization, assembly at interfaces, and manipulation. Angew. Chem., Int. Ed. Engl.,39(5): 864-883.
65) Wang R., Charoenvit Y., Corradin G., Porrozzi R. R., Hunter R. L., Glenn G., Alving C. R., Church P. and Hoffman S. L.. (1995) Induction of protective polyclonal antibodies by immunization with *Plasmodium yoeliicircumsporozoite* protein multiple antigen peptide vaccine. J. Immunol.,155: 1637-1641.
66) Zhang G. D., Harada A., Nishiyama N., Jiang D.-L., Koyama H., Aida T. and Kataoka K. (2003) Polyion complex micelles entrapping cationic dendrimer porphyrin: effective photosensitizer for photodynamic therapy of Cancer. J. Control. Rel., 93(2-5): 141-150. https://doi.org/10.1016/j.jconrel.2003.05.002
67) Vandamme T. F. and Brobeck L. (2005) Poly (amidoamine) dendrimers as ophthalmic vehicles for ocular delivery of pilocarpine nitrate and tropicamide. J. Control. Release, 102(1): 23-38.
68) Bai S., Thomas C. and Ahsan F. (2007) Dendrimers as a carrier for pulmonary delivery of enoxaparin, a low molecular weight heparin. J. Pharm. Sci, 96(8): 2090-2106.
69) Tomalia D. A., Baker H., Dewald J. R., Hall M., Kallos G., Martin S., Roeck J., Ryder J. and Smith P. (1986) Dendrimers II: Architecture, nanostructure and supramolecular chemistry. Macromolecules, 19: 2466-2468.
70) Froehling P. E. (2001) Dendrimers and dyes- a review. Dyes and Pigments, 48(3): 187-195.
71) Jain N. K. and Gupta U. (2008) Application of dendrimer-drug complexation in the enhancement of drug solubility and bioavailability. Expert Opin Drug Metab Toxicol., 8(14): 1035-1045.
72) Raetz C. R. and Whitfield C. (2002) Lipopolysaccharide endotoxins. Annu Rev Biochem., 71: 635-700.
73) Koten Gv., Albrecht M., Gossage R., Lutz M. and Spek A. (2000) Diagnostic organometallic and metallodendritic materials for SO_2 gas detection: reversible binding of sulfur dioxide to arylplatinum (II) complexes. Chemistry: A European Journal., 6(8):1431-45.
74) Dass C. R. (2002) Vehicles for oligonucleotide delivery to tumors. Journal of Pharmacy and Pharmacology, 54:3-27.
75) Richardson S. C.W., Pattrick N. G., Man Y. K. S., Ferruti P. and Duncan R. (2001) Poly(amidoamine)s as potential nonviral vectors: ability to form inter poly electrolyte complexes and to mediate transfection in *vitro*. Biomacromolecules, 2:1023-1028.

76) Gérard H. C., Mishra M. K., Mao G., Wang S., Hali M., Whittum-Hudson J. A., Kannan R. M. and Hudson A. P. (2013) Dendrimer-enabled DNA delivery and transformation of *Chlamydia pneumoniae*. Nanomedicine, http://dx.doi.org/10.1016/j.nano.2013.04.004.
77) Tekade R. K., Kumar P. V. and Jain N. K. (2009) Dendrimers in oncology: an expanding horizon. Chemical Reviews, 109:49-87.
78) Oliveira J. M., Salgado A. J., Sousa N., Mano J. F. and Reis R. L. (2010) Dendrimers and derivatives as a potential therapeutic tool in regenerative medicine strategies-A review. Progress in Polymer Science, 35:1163-1194.
79) Jang W. D., Selim K. M. K., Lee C. H. and Kang I. K. (2009) Bioinspired application of dendrimers: from bio-mimicry to biomedical applications. Progress in Polymer Science, 34:1-23.
80) Wu C., Brechbiel M. W., Kozak R. W. and Gansow O. A. (1994) Metal-chelate-dendrimer-antibody constructs for use in radio immunotherapy and imaging. Bioorg & Med Chem Lett., 4:449-454.
81) Kolhe P., Khandare J., Pillai O., Kannan S., Lieh-Lai M. and Kannan R.M. (2006) Preparation, cellular transport, and activity of polyamidoamine-based dendritic nanodevices with a high drug payload. Biomaterials, 27:660-669.
82) Pasut G. and Veronese F. M. (2007) Polymer-drug conjugation, recent achievements and general strategies. Prog Polym Sci., 32:933.
83) Maciejewski M. (1982) Concepts of trapping topologically by shell molecules. J Macromol Sci Chem A., 17:689.
84) Herrmann A., Mihov G., Vandermeulen G. W. M., Klok H-A. and Mullen K. (2003) Peptide functionalized polyphenylene dendrimers. Tetrahedron, 59:3925
85) Cheng Y., Man N., Xu T., Fu R., Wang X., Wang X. and Wen L. (2007) Transdermal delivery of nonsteroidal anti-inflammatory drugs mediated by polyamidoamine (PAMAM) dendrimers. J Pharm Sci., 96:595-602.
86) Rupp R., Rosenthal S. L. and Stanberry L. R. (2007) VivaGel (SPL7013 Gel): a candidate dendrimer-microbicide for the prevention of HIV and HSV infection. Int. J. Nanomedicine, 2:561-566.
87) Tyssen D., Henderson S. A., Johnson A., Sterjovski J., Moore K., La J., Zanin M., Sonza S., Karellas P., Giannis M. P., Krippner G., Wesselingh S., McCarthy T., Gorry P. R., Ramsland P. A., Cone R., Paull J. R., Lewis G. R. and Tachedjian G. (2010) Structure activity relationship of dendrimer microbicides with dual action antiviral activity. PLoS ONE;5:e12309.
88) Wang B., Navath R. S., Menjoge A. R., Balakrishnan B., Bellair R., Daia H., Romero R., Kannan S. and Kannan R. M. (2010) Inhibition of bacterial growth and intramniotic infection in a guinea pig model of chorioamnionitis using PAMAM dendrimers. Int J Pharma., 395:298-308.
89) Barata T., Teo I., Lalwani S., Simanek E., Zloh M. and Shaunak S. (2011) Computational design principles for bioactive dendrimer based constructs as antagonists of the TLR4-MD-2-LPS complex. Biomaterials, 32:8702-8711.
90) Grayson S. M. and Fréchet J. M. J. (2001) Convergent dendrons and dendrimers: from synthesis to applications. Chem. Rev.,101(12): 3819-3868. https://doi.org/10.1021/cr990116h
91) Denkewalter R. G., Kolc J. and Lukasavage W. J..US Patant. 1981; 4: 289- 872.
92) Hawker J. C. and Frechet J. M. J. (1990) Preparation of Polymers with controlled molecular architecture: A new convergent approach to gendritic macromolecules. J Am Chem Soc., 112(21): 7638-7647. https://doi.org/10.1021/ja00177a027.
93) Newkome G. R. M., Baker G. R., Saunders M. J. and Grossman S. H. (1991) Uni-Molecular Micelles. Angew ChemInt Ed Engl., 30(9):1178-1180. https://doi.org/10.1002/anie.199111781
94) Newkome G. R., Moorefield C. N., Keith J. M., Baker G. R., Escamilla G. H. and Angew (1998) Chemistry Within a Unimolecular Micelle Precursor: Boron Super clusters by Site-specific and Depth-specific transformations of dendrimers. Chem., Int. Ed. Engl., 33(12): 666-668.
95) Wang R., Charoenvit Y., Corradin G., Porrozzi R. R., Hunter R. L., Glenn G., Alving C. R., Church P. and Hoffman S. L. (1995) Induction of protective polyclonal antibodies by immunization with *Plasmodium yoeliicircumsporozoite* protein multiple antigen peptide Vaccine. J. Immunol.,155: 1637-1641.
96) Tomalia D. A., Hedstrand D. M. and Ferritto M. S. (1991) Comb-burst Dendrimer Topology: New macromolecular architecture derived from dendritic grafting. Macromolecules, 24(6):1435-1438. https://doi.org/10.1021/ma00006a039
97) Vogtle F., Richardt G. and Werner N. (2009) Introduction. In: Vogtle F, Richardt G, Werner N, editors. Dendrimer Chemistry: Concepts, Syntheses, Properties, Applications. Wiley: Academic; 1-24.
98) Vogtle F., Richardt G., Werner N. and Rackstraw A. J. (2009) Dendrimer Chemistry: Concept, Synthesis, Properties, Applications. Weinheim: Wiley-VCH.
99) Seiler M. (2002) Dendritic Polymers-Interdisciplinary Research and Emerging Applications from Unique Structural Properties. Chem Eng Technol., 25:237-253.