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Dendrimers: A Novel Trend of Nanocarriers

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Abstract: Dendrimers are a brand-new type of polymer. They're monodisperse macromolecules with a lot of branches. Dendrimers' structural advantages enable them to play a significant role in nanotechnology, pharmaceuticals, and medicinal chemistry. Dendrimers are ideal for a wide range of biological and industrial applications due to their unique behavior. The bioactive substances can be easily encapsulated into the inside of the dendrimers or chemically conjugated or physically adsorbed onto the dendrimer surface, tailoring the carrier's desirable features to the active material's unique demands and therapeutic applications. The goal of the study is to highlight the production, characterization, drug delivery, and potential applications of dendrimers in diverse research, technological, and therapy fields.

Keywords: Drug delivery, Types, synthesis, characteristics, Application, Patents.

Introduction:

Nanotechnology is a new field of study that looks at materials on a nanoscale size. Researchers in the domains of biomedical engineering, pharmaceutical technology, and medicine have been particularly interested in nanotechnology in recent decades. [1,2] Dendrimers were first found in the early 1980s by Donald Tomalia and colleagues. derives from the word 'dendron,' which means a tree in Latin. Greek Simultaneously, Newkome's group reported the synthesis of comparable molecules. macromolecules. They were dubbed arborols after the tree they came from. 'Arbor' is a Latin term that also means a tree. [3,4] Dendrimers are artificial polymers with branched repeating units that emerge from a focal point with many exposed anionic, neutral, or cationic terminal functionalities on the surface of hydrophilic or hydrophobic substances.[5] Dendrites' synergistic impact is responsible for the increased activity. The field of dendritic polymer formulations evolves as a result of its structured character. Dendrimers are typically utilized to achieve certain goals/targets, such as changing the pharmacokinetic and pharmacodynamic aspects of the active moiety to modify and enhance medication bioavailability.[6] A dendrimer is usually symmetric around the core and has a three-dimensional spherical shape. Dendron is another word that comes up regularly.[7]

Dendrimer In the Delivery of Drugs: Drugs are either non-covalently enclosed in the internal void spaces of the dendrimer or covalently conjugated on the dendrimer's peripheral functionalization groups in dendrimer-based drug delivery.[8] Fig.

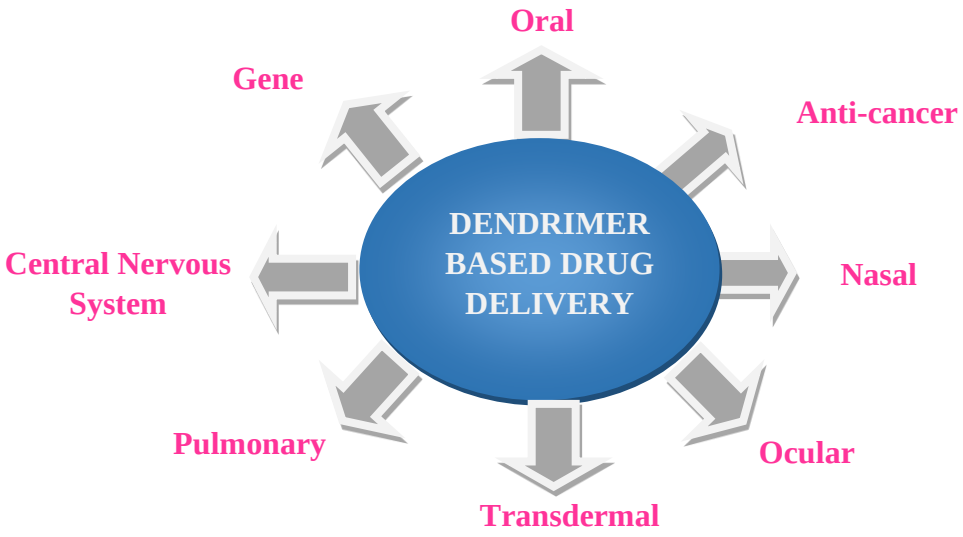

Fig.1 Various Drug Delivery System in Dendrimer.

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Oral Drug Delivery in Dendrimer:

The oral route is often regarded as the preferred method of drug administration.[9] Dendrimers with sizes ranging from 2.5 to 6 nm seem to be the best way to advance to smaller and smaller systems. The flocculation and aggregation of the system in vivo is an issue, and oral uptakes of dendrimers are not as good as previously thought. The use of polyoxyethylene glycol chains or ionic groups can help to alleviate this difficulty, although the hydrophilic nature of the surface dendrimers makes oral uptake difficult.[10,11] The oral absorption of a polylysine dendrimer was investigated, with the highest reported levels of 15% in the small intestine, 5% in the small intestine, and 3% in the blood at 6 hours after administration.[12] Dendrimer-drug size, molecular weight, surface charge, incubation period, and active molecule concentration all influence how well dendrimers are delivered orally.[13]

Anti-Cancer Drug Delivery in Dendrimer:

One of the most common uses for dendrimers is as a vehicle for the delivery of anticancer medicines. Dendrimers' structure and configurable surface activity allow several entities to be encapsulated/conjugated, either in the core or on the surface, making them suitable carriers for anticancer medicines.[14] The ability of dendrimers to deliver controlled and specified drug delivery, which is relevant to nanomedicine, is perhaps their most promising promise. One of the most pressing issues confronting modern medicine is how to improve the pharmacokinetic features of cancer medicines.[15] Passive targeting and, as a result, selective accumulation of macromolecules in tumor tissue is enabled by pathophysiological characteristics of tumors such as excessive angiogenesis leading to hypervascularization, increased permeability of tumor vasculature, and limited lymphatic outflow. The term for this phenomenon is "increased permeation and retention" (EPR).[15,16]

Nasal Drug Delivery in Dendrimer:

Intranasal drug delivery differs from the numerous drug targeting techniques now available. It is non-invasive and lowers API exposure to non-target locations, improving the drug's efficacy and safety. The trigeminal nerve pathway and the olfactory nerve pathway can be used to deliver drug molecules to the brain via the nasal cavity. By creating a combination with pharmaceuticals, dendrimers have been shown to increase their water solubility. The medicine would have a high concentration in the nasal area because of this combination. In terms of nose-to-brain targeting, PAMAM dendrimers, for example, have piqued researchers' interest.[17]

Ocular Drug Delivery in Dendrimer:

Dendrimers offer one-of-a-kind answers to difficult ocular medication delivery challenges. PAMAM dendrimers with carboxylic or hydroxyl surface groups were used in recent research efforts to improve the residence period of pilocarpine in the eye.[18] It was hypothesized that these surface-modified dendrimers would improve pilocarpine bioavailability. This is due to the surplus fluid draining down the nasolacrimal duct and the tears removing the solution. The problems of ocular drug administration can be reduced by adopting specialized delivery systems like dendrimers. Drug delivery methods for the eyes should be sterile, non-irritating, isotonic, biocompatible, biodegradable, and not run out of the eye.[19]

Transdermal Drug Delivery in Dendrimer:

Dendrimers are biocompatible and very water-soluble. Dendrimers have been shown to increase pharmacological qualities including plasma circulation time and skin penetration, allowing for more efficient drug delivery in transdermal formulations.[20] Due to the skin's barrier function, transdermal distribution has a low success rate. Transdermal medication delivery systems have used dendrimers. Nonsteroidal anti-inflammatory medications (NSAIDs), antiviral, antibacterial, anticancer, and antihypertensive treatments have all been demonstrated to work well with dendrimers as transdermal drug delivery methods.[21]As penetration enhancers, PAMAM dendrimer complexes with NSAIDs (e.g. Ketoprofen, Diflunisal) have been observed to promote drug permeation through the skin. When ketoprofen and diflunisal were conjugated with the G5 PAMAM dendrimer, their permeability increased by 3.4 and 3.2 times, respectively.[22] They proved that the PAMAM dendrimer is effective as a drug delivery device by increasing indomethacin flux across the skin in vitro and in vivo.[17]

Pulmonary Drug Delivery in Dendrimer:

Dendrimers have been used to transport Enoxaparin to the lungs.[23] Because of their huge surface area, thin alveolar region, broad vasculature, and avoidance of first-pass metabolism, the lungs are an appealing alternate route and site for drug delivery. As a result of this advantage, the drug's systemic bioavailability is improved, resulting in more effective therapeutic action. Many types of dendrimers have been invented, manufactured,

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and explored for pulmonary administration of various medicines due to their unique structure. These nanosystems have been shown to have great potential as inhaled medication delivery systems for the treatment of pulmonary diseases.[24]

Central Nervous System Drug Delivery in Dendrimers:

The brain is a difficult organ to deliver drugs to since the BBB is the finest gatekeeper, keeping exogenous chemicals out of the CNS. As a result, drug transport to the brain is difficult due to many pharmaceuticals' poor solubility, lipophilicity, bioavailability, and the BBB's ability to block 98 percent of drugs. Because conventional pharmacological therapies are inadequate, developing new ways to safely and effectively deliver therapeutic medications to the CNS is critical.[17] Dendrimers are polymer molecules having branches growing from one or more centers that are regularly branched. They can be synthesized non-covalently with biological agents like DNA or conjugated with pro-drugs or imaging agents, allowing them to be employed as drug delivery or molecular imaging vehicles.[25]

Gene Drug Delivery in Dendrimers:

Dendrimers can be used as vectors, or carriers, in gene therapy. Genes are transferred into the nucleus by vectors that pass through the cell membrane. Liposomes and genetically modified viruses are currently the most used methods.[26] Due to their capacity to transfect genes without causing toxicity, dendrimers are one of the most important gene-delivery systems and have played a key role in the creation of vectors for gene delivery. Furthermore, the nanocarrier's surface has a high charge density, allowing for optimum condensation and nanostructure formation with deoxyribonucleic acid (DNA).[17] Transgene expression was extended following delivery of the DNA–dendrimer complex from the scaffolds when compared to direct delivery to cells.[27]

STRUCTURE AND COMPOSITION:

Dendrimers are monodisperse structures with a central core surrounded by peripheral groups that are three-dimensional, hyper-branched, and monodisperse. For their physicochemical and biological features, these characteristics are essential.[28] Dendrimers have three architectural features: mentioned below(Figure.2)

i. an initiator core,
ii. an internal layer made up of repeating units, and
iii. an external (terminal functionality) attached to the outermost interior layer.[29]

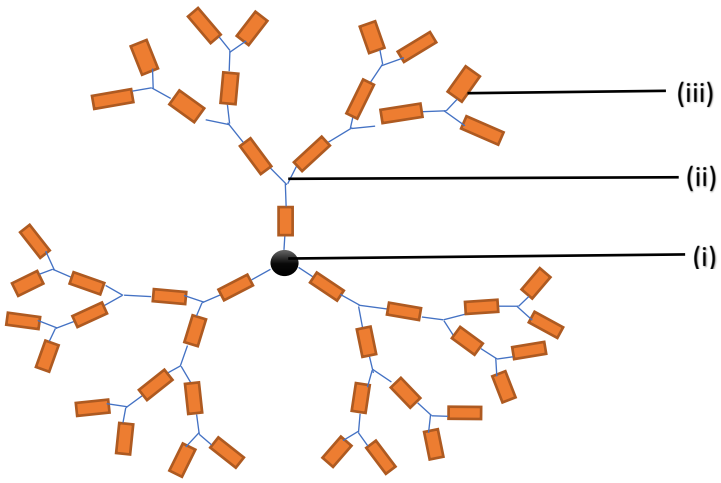

Fig.2. Dendrimer structure in its most basic form

Dendrimer generation occurs when the dendrimer hyperbranched from the center to the periphery, resulting in homo structural layers between the focus sites (branching points). The generation number is the number of focal points from the core to the dendrimer surface, so a dendrimer with five focal points from the center to the periphery is called a 5th generation dendrimer. The dendrimer's core is commonly referred to as "generation zero," or "G0." Because hydrogen substituents are not considered focal points, there are no focal points in the core structure. Half-generations are terms used to describe intermediates in the dendrimer synthesis.[30] Dendrimers are influenced by the surface functional groups as well as the branching unit. The

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extent of branches can be controlled because the physicochemical features of these structures may be controlled during synthesis by changing the core groups.[31]

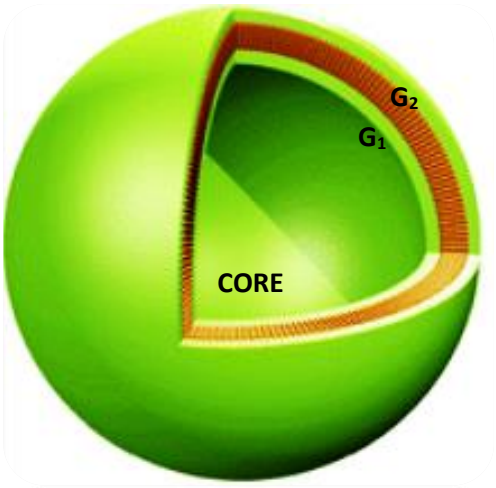

Fig.3 Dendrimer structure in three dimensions

Dendrimer Characteristics:

- Dendrimers are tiny particles with dimensions that are close to those of major bio-building blocks like proteins and DNA. Drugs, signaling groups, targeting moieties, and biocompatibility groups can all be bioconjugated using a large variety of terminal surface groups (Z).
- The medication toxicity is reduced and regulated release is made easier by encapsulating in that vacuum zone. When compared to higher generation neutral polar and cationic surface groups, lower generation anionic or neutral polar terminal surface groups are related to positive biocompatibility patterns.
- The traditional polymerization technique, which yields linear polymers, is frequently random and creates molecules of various sizes, whereas dendrimer size and molecular mass may be precisely controlled during synthesis.[32]
- Linear chains exist in solution as flexible coils; dendrimers, on the other hand, form a tightly packed ball. This has a significant impact on the rheological properties of the materials. Dendrimer solutions are far less viscous than linear polymers. To solve the problem,
- High solubility, miscibility, and reactivity are all due to the existence of numerous chain ends.[33]
- Positive biocompatibility patterns linked to lower generation anionic or neutral polar terminal surface groups, as opposed to higher generation neutral polar and cationic surface groups.
- Most dendrimer surfaces treated with minor functional groups or polyethylene glycol have little or low immunogenicity (PEG).[34]

Dendrimers Are Classified Depending On Their Properties And Structures:

Properties Based Dendrimers:

When compared to standard linear polymers, dendrimers have significantly enhanced physical and chemical properties due to their molecular architecture.[35]This property includes Fig.4.

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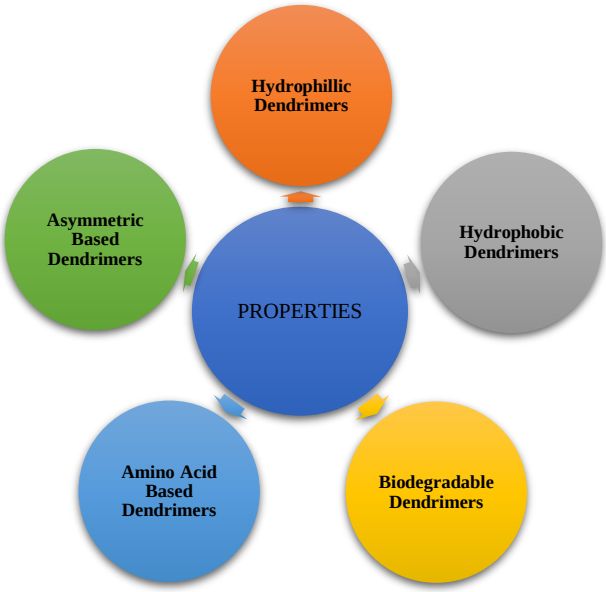

Fig.4. Dendrimers Based On Properties

Hydrophilic Dendrimers:

Following reactions with ethanolamine and excess ethylene-diamine, these newly produced monomers were transformed into tiny generation molecules such as OH and NH surface group moieties. This intermediate liberates the smallest anionic dendrimers with four COOH groups on hydrolysis of methyl ester. Dendrimer growth approaches a critical point, resulting in a drop in synthetic yield. The stearic factor, which is caused by the overpopulation of branching arms, is to blame for this phenomenon. The term "dense packing effect" was coined to describe this strategy.[36]

Amino Acid Based Dendrimers:

The integration of blocks with varied properties such as chirality, hydrophobicity, biorecognition, and the optical property was used to create amino acid (AA) dendrimers. . Because of the unusual structural folding of the branching components, these dendrimers can also be employed as protein mimic, gene, and targeted medication delivery.[37]

Biodegradable Dendrimers:

The goal of developing biodegradable dendrimers was to create large molecular weight polymers with high tissue deposition and quick removal of fragments through urine to prevent nonspecific toxicity. All regulating factors are chemical linkages, monomeric unit lipophilicity, dendrimer size, and dendrimer cleavage susceptibility. Because of their biocompatibility and biodegradability, polyester dendrimers are employed in anticancer and gene therapy.[37]

Hydrophobic Dendrimers:

The solubility of hydrophobic probes, dyes, and fluorescent markers has been successfully explored in dendrimers with hydrophobic interior gaps and hydrophilic surfaces mimicking unimolecular micelles. Dendrimers known as cyclophanes or dendrophanes have been shown to encapsulate aliphatic and aromatic moieties. Drug release has also been found to be controlled by these types of dendritic structures.[37]

Asymmetric Dendrimers:

Dendrons of various generations are usually coupled to a linear core molecule to make these. A nonuniform orthogonal dendritic architecture is formed by the final structure. In this form of a dendrimer, the molecular weight, structure, and amount of functional groups can all be adjusted.[38]

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Structure-Based Dendrimers:

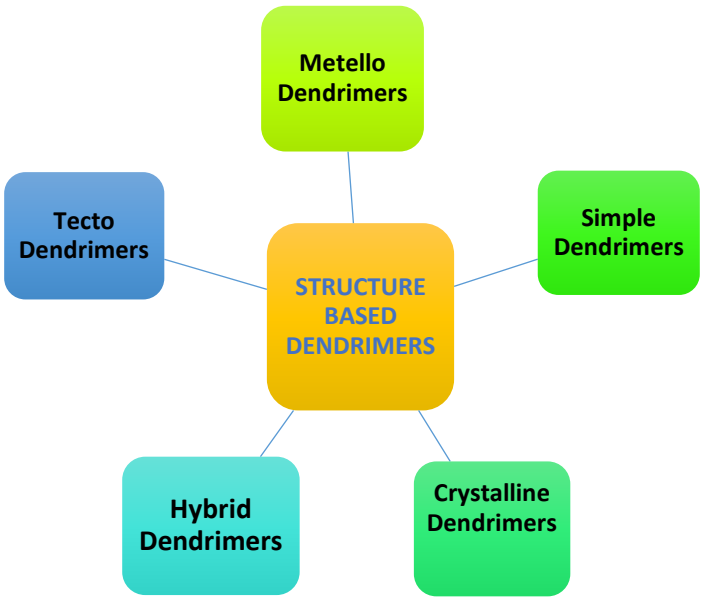

Fig. 5. Dendrimers Based On Structure

Simple Demdrimers:
Simple monomeric units based on symmetrical substitution of benzene tricarboxylic acid ester make up these kinds of dendrimers. They have 45Å molecular diameters and four, ten, twenty-two, and forty-six benzene rings that are connected symmetrically.[35,38]

Crystaline Dendrimers:
Mesogenic monomers, which are created by the functionalization of carboxylate, are responsible for the formation of these dendrimers.**[35]**

Hybrid Dendrimers:
A dendron-like structure is generated by the poylysineskelton in multiple antigen peptide (MAP) dendrimers. Lysine aids in the conjugation of the alkylamine side chain, which serves as a monomer for the branching units. Dendrimers of this sort have been created and discovered to have a wide range of biological uses, including vaccine development and diagnostics.[37]

Tectodendrimers:
Commercially available tectodendrimers are Stratus® CS Acute CareTM and Starburst®. They are dendrimer-based and provide a variety of functions, including identifying sick cells and diagnosing infection.[35]

Metellodendrimers:
Metallodendrimers are generated through a complex formation technique that occurs either at the molecule's peripheral surface or on its inside. The dendrimers created using this approach, such as ruthenium bipyridine, were discovered to have both electrochemical and luminescent characteristics.[35]

Types Of Dendrimers:

PAMAM Dendrimers:
The divergent approach is used to make poly (amidoamine) dendrimers (PAMAM) from ammonia or ethylenediamine initiator core reagents. Commercially accessible PAMAM dendrimers are mainly in the form of methanol solutions. When looking at the structure of high generation dendrimers of this type in detail, the name alludes to the star-like pattern that can be seen.[34]

PPI Dendrimers:
The propylamine spacer moieties of the oldest known dendrimer type produced by Vogtle are referred to as PPI-dendrimers. The dendrimer interior consists of many tertiary tris-propylene amines, and the dendrimers are commonly poly-alkyl amines with primary amines as end groups. PPI dendrimers, which are commercially

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accessible up to G5, have a wide range of applications in material science and biology. PAMAMOS is a term that is occasionally used to refer to this class of dendrimers as an alternative to PPI.[[22]

PAMAMOS Dendrimers:

Inverted unimolecular micelles with hydrophilic, nucleophilic polyamidoamine (PAMAM) interiors and hydrophobic organosilicon (OS) exteriors are known as radially stacked poly (amidoamine-organosilicon) dendrimers (PAMAMOS). These dendrimers are excellent building blocks for honeycomb-like networks containing nanoscopic PAMAM and OS domains. These are the first commercial dendrimers to contain silicone.[22]

DENDRIMER'S SYNTHESIS:

The chemistry of molecular and polymer chemistry is involved in the production of dendrimers. They are linked to the world of molecular chemistry because of their step-by-step regulated synthesis, and they are linked to the world of polymers because of their usage of repeated structure, i.e. monomers. There is a significant distinction between these two construction methods.[39]

Divergent Growth Method of Dendrimer Synthesis:

The divergent growth approach was the first to be proposed, and it is still the most used today. Tomalia and Newkome's seminal work, as well as Vogtle's branching model work, influenced this strategy.[40] A multifunctional core molecule expands outwards to form a dendrimer. The first-generation dendrimer is formed when the core molecule combines with monomer molecules having one reactive and two inactive groups. The molecule's new perimeter is then activated for reactions with more monomers.[41] Fig.6. The divergent growth approach entails repeatedly doing the two previous procedures until the desired dendrimer production is obtained.[42]

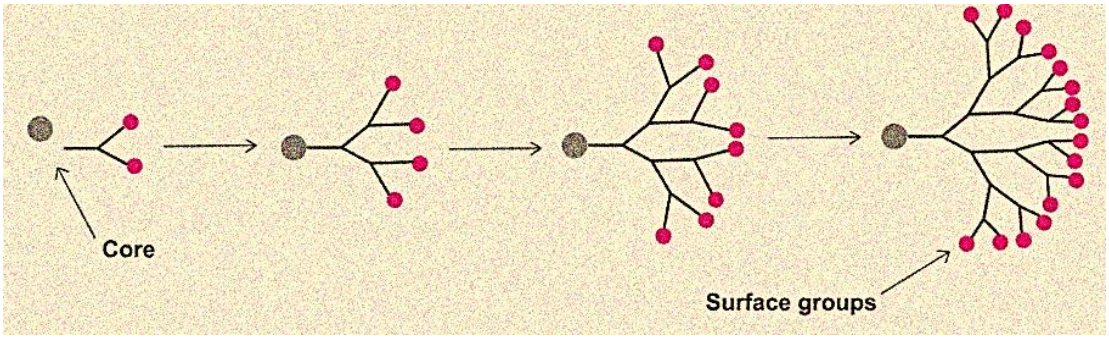

Fig.6. Synthesis of Dendrimers Using Divergent Growth

Convergent Growth Method of Dendrimer Synthesis:

To achieve the appropriate dendritic structure, the convergent growth approach also entails repeating the coupling and activation processes. The dendritic segment is formed by coupling two surface groups to a monomer.[43,44] A dendrimer is built step by step in a convergent manner, starting from the end groups and working inwards. Dendrons, which are forming branched polymeric arms, are connected to a multifunctional core molecule when they reach a certain size.[45] The benefits of convergent growth over divergent growth derive from the fact that for any generation-adding step, only two simultaneous reactions are required. Low yields in the synthesis of big structures plague the convergent methods as well.[46,47]

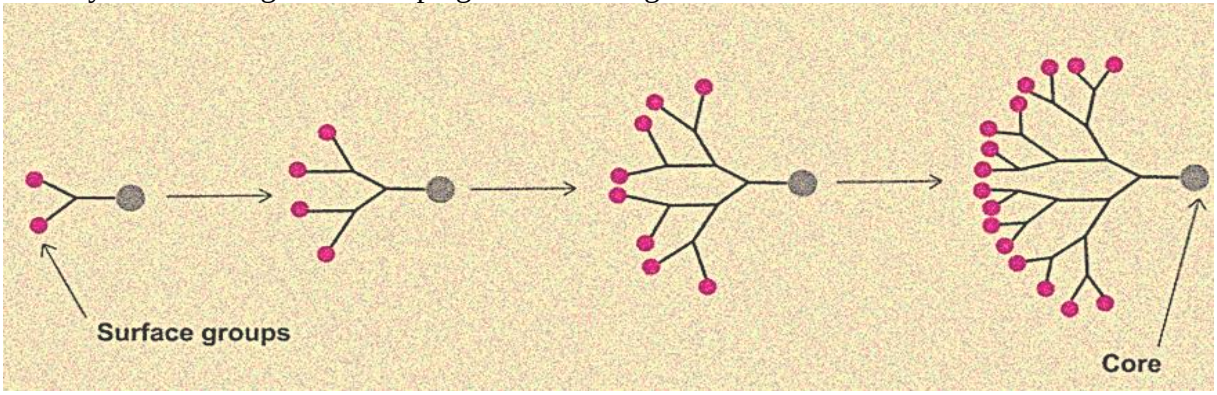

Fig.7. . Synthesis of Dendrimers Using Convergent Growth

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Factors Involved In The Synthesis Of Dendrimers:

Dendrimer synthesis is influenced by several factors. Nonideal dendrimer development can take many forms, including

- incomplete addition reactions,
- intermolecular cyclization,
- fragmentation, and
- terminal functionality solvolysis.

This is especially relevant if fragments have amine functionalities that could interact with propagation sequencing agents to form new but regressed dendrimer entities. They frequently occur as a result of the following factors:

- Polydispersity is caused by the incomplete elimination of a reactant at each generation sequence because the leftover reactant serves as an initiator core for the 0.5 generation and future lower generations.
- Intermolecular interactions lead dendrimers to cyclize when they are exposed to higher temperatures.
- An insufficient amount of sequencing agent may result in dendrimer bridging or nonideal dendrimer formation.[48]

Dendrimer's Application:

- The molecular homogeneity, multifunctional surface, and existence of interior cavities of dendrimers make them ideal for a variety of applications. Dendrimers are ideal for a wide range of high-tech applications, including biological and industrial ones, due to their unique features.
- In-vitro diagnostics using dendrimers have been done. A novel method of cardiac testing has been established by Dade International Inc. in the United States of America. Immunoglobulins bind to proteins in a blood sample, which is then glued to a sheet of glass by dendrimers.
- The time it takes to get the results of a blood test is greatly reduced with this procedure (to about 8 min). The test can last up to 40 minutes when using a randomly arranged immunoglobulin solution. The precision and sensitivity of the test are additionally improved by dendrimer and antibody conjugates.
- In preclinical research, dendrimers have been used as magnetic resonance contrast agents. Anatomical images of organs and blood arteries are created using magnetic resonance imaging (MRI). When a patient is placed in a produced, specified, inhomogeneous magnetic field, the nuclear resonance signal of water is formed, which is then assigned to its source and turned into images.[49]
- Dendrimers are ideal for usage as image contrast media due to their unique features. Dendrimers with gadolinium ions chelated on the surface have been developed by several groups.[50,51]

Patents :

Pharmaceutical Application	Dendrimer	Drug loaded	Summary	Publication Date	Patent	Reference
Drug delivery to the central nervous system	Poly amidoamine	Prion protein	To treat Alzheimer's disease, PrP was conjugated with PAMAM dendrimers. This combination will prevent the production of -amyloid plaques	2019	US20190092837	[52]

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			(which function as neurotoxins in Alzheimer's disease in vitro and in vivo)			
Drug delivery to the cancer	Peptide-dendrimer	Docetaxel	The peptide was conjugated to a dendrimer for prostate cancer targeting, imaging, and treatment.	2018	EP3402484	[53]
Drug delivery to the Gene	Poly -l-lysine	DNA from plasmids	To stabilize plasmid DNA in the extracellular region and facilitate its absorption into the target cell, a PLL system containing a vector with intracellular nuclear protein binding and reducible polymers has been developed.	2012	KR1020120007208	[54]
Drug delivery to the transdermal	Second-generation /oleodendrons	Diclofenac	Dendron, which is based on oleic acid, is employed in transdermal medications as a potential	2013	IN1749/MUM/2010	[54]

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			chemical penetration booster.			

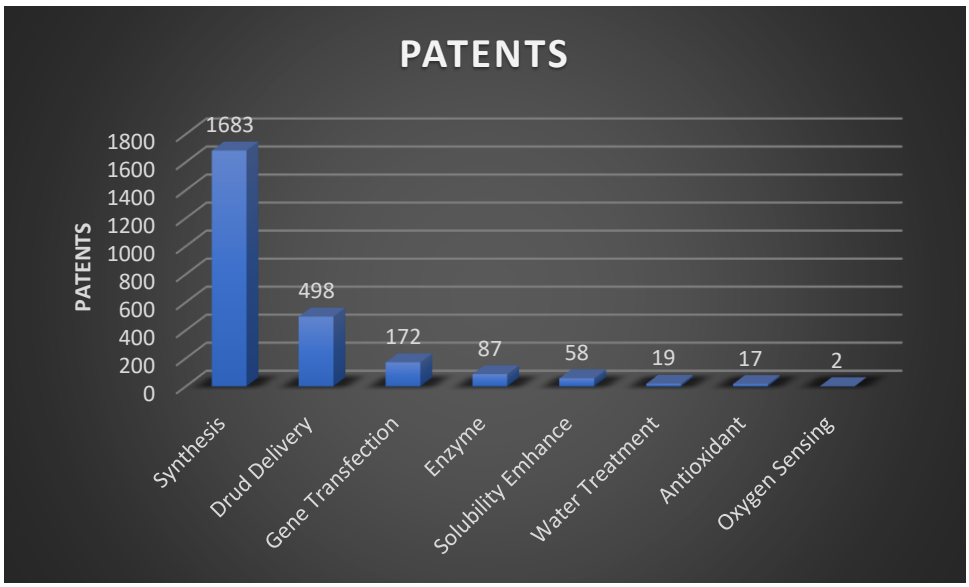

Fig.8. Application Based Patents

Future Opportunities:

Dendrimer uses in medication delivery via numerous channels, such as oral, nasal, transdermal, and parental, has been researched and extensively exploited in recent years. Their structural features have been extensively researched, and they have been discovered to be responsible for their unique qualities such as high payload and tissue accumulation. Dendrimer drug delivery is successful only if specific manufacturing and biological concerns are taken into account. Dendrimer technology's usefulness will be bolstered in the coming years by increasing commercial uses. Dendrimers have a potential future in the pharmaceutical and biological fields, even though they are relatively young structures (about 30 years) and the fact that they are not yet recognized as a pharmaceutical excipient.

Conclusion:

Dendrimers were a novelty two decades ago, and like all other novelties, even in science and technology, they were not instantly understood for what they may become. The entire potential of these branched creations in a wide range of domains can only be realized with time and enormous research in laboratories around the world. Functionalized dendrimer PET is also a viable option. Dendrimers' structural features, including form, structure, size, branching, functioning, space, and density, according to state PET 8 BioMed Research International, make them an ideal candidate for drug delivery via diverse routes. Only a few applications for which the unique dendrimer structure is critical will pass the cost-benefit test unless there is a big breakthrough in this field.

Reference:

1. Huang YW, Cambre M, Lee HJ. The toxicity of nanoparticles depends on multiple molecular and physicochemical mechanisms. International journal of molecular sciences. 2017 Dec;18(12):2702.
2. Oberdörster G, Maynard A, Donaldson K, Castranova V, Fitzpatrick J, Ausman K, Carter J, Karn B, Kreyling W, Lai D, Olin S. Principles for characterizing the potential human health effects from exposure to nanomaterials: elements of a screening strategy. Particle and fiber toxicology. 2005 Dec;2(1):1-35.
3. Tomalia DA, Baker H, Dewald J, Hall M, Kallos G, Martin S, Roeck J, Ryder J, Smith P. A new class of polymers: starburst-dendritic macromolecules. Polymer journal. 1985 Jan;17(1):117-32.

ISSN NO: 2770-2936
Date of Publication:13-04-2022

4. Newkome GR, Yao Z, Baker GR, Gupta VK. Micelles. Part 1. Cascade molecules: a new approach to micelles. A [27]-arborol. The Journal of Organic Chemistry. 1985 May;50(11):2003-4.
5. Lyu Z, Ding L, Huang AT, Kao CL, Peng L. Poly (amidoamine) dendrimers: Covalent and supramolecular synthesis. Materials Today Chemistry. 2019 Sep 1;13:34-48.
6. Noriega-Luna B, Godínez LA, Rodríguez FJ, Rodríguez A, Zaldívar-Lelo de Larrea G, Sosa-Ferreyra CF, Mercado-Curiel RF, Manríquez J, Bustos E. Applications of dendrimers in drug delivery agents, diagnosis, therapy, and detection. Journal of Nanomaterials. 2014 Jan 1;2014.
7. Bauer RE, Enkelmann V, Wiesler UM, Berresheim AJ, Müllen K. Single-Crystal Structures of Polyphenylene Dendrimers. Chemistry–A European Journal. 2002 Sep 2;8(17):3858-64.
8. Ihre H, Hult A, Fréchet JM, Gitsov I. Double-stage convergent approach for the synthesis of functionalized dendritic aliphatic polyesters based on 2, 2-bis (hydroxymethyl) propionic acid. Macromolecules. 1998 Jun 30;31(13):4061-8.
9. Mane PP, Jadhav VS, Humbe VP, Hakke SC, Kale BB. Dendrimer: A novel polymer and tool for drug delivery. Am. J. Pharm Res. 2014;4:3851-62.
10. Bosman DA, Janssen HM, Meijer EW. About dendrimers: structure, physical properties, and applications. Chemical reviews. 1999 Jul 14;99(7):1665-88.
11. Purohit G, Sakthivel T, Florence AT. The interaction of cationic dendrons with albumin and their diffusion through cellulose membranes. International journal of pharmaceutics. 2003 Mar 18;254(1):37-41.
12. Florence AT, Sakthivel T, Toth I. Oral uptake and translocation of a polylysine dendrimer with a lipid surface. Journal of Controlled Release. 2000 Mar 1;65(1-2):253-9.
13. Kim Y, Klutz AM, Jacobson KA. Systematic investigation of polyamidoamine dendrimers surface-modified with poly (ethylene glycol) for drug delivery applications: synthesis, characterization, and evaluation of cytotoxicity. Bioconjugate chemistry. 2008 Aug 20;19(8):1660-72.
14. Padilla De Jesús OL, Ihre HR, Gagne L, Fréchet JM, Szoka FC. Polyester dendritic systems for drug delivery applications: in vitro and in vivo evaluation. Bioconjugate chemistry. 2002 May 15;13(3):453-61.
15. Sampathkumar SG, Yarema KJ. Dendrimers in cancer treatment and diagnosis. Nanotechnologies for the Life Sciences: Online. 2007 Sep 15.
16. Gillies ER, Frechet JM. Dendrimers and dendritic polymers in drug delivery. Drug discovery today. 2005 Jan 1;10(1):35-43.
17. Parajapati SK, Maurya SD, Das MK, Tilak VK, Verma KK, Dhakar RC. Potential application of dendrimers in drug delivery: A concise review and update. Journal of Drug Delivery and Therapeutics. 2016 Mar 14;6(2):71-88.
18. Vandamme TF, Brobeck L. Poly (amidoamine) dendrimers as ophthalmic vehicles for ocular delivery of pilocarpine nitrate and tropicamide. Journal of controlled release. 2005 Jan 20;102(1):23-38.
19. Trivedi V, Patel U, Bhimani B, Daslaniya D, Patel G, Vyas B. Dendrimer: polymer of 21st century. IJPRBS Journal. 2012;1(2):1-21.
20. Chauhan AS, Sridevi S, Chalasani KB, Jain AK, Jain SK, Jain NK, Diwan PV. Dendrimer-mediated transdermal delivery: enhanced bioavailability of indomethacin. Journal of controlled release. 2003 Jul 31;90(3):335-43.
21. Klajnert B, Bryszewska M. Dendrimers: properties and applications. Acta biochimica polonica. 2001 Mar 31;48(1):199-208.
22. Cheng Y, Xu T. The effect of dendrimers on the pharmacodynamic and pharmacokinetic behaviors of non-covalently or covalently attached drugs. European journal of medicinal chemistry. 2008 Nov 1;43(11):2291-7.
23. Bai S, Thomas C, Ahsan F. Dendrimers as a carrier for pulmonary delivery of enoxaparin, low-molecular-weight heparin. Journal of pharmaceutical sciences. 2007 Aug 1;96(8):2090-106.
24. Mehta P, Kadam S, Pawar A, Bothiraja C. Dendrimers for pulmonary delivery: current perspectives and future challenges. New Journal of Chemistry. 2019;43(22):8396-409.

ISSN NO: 2770-2936
Date of Publication:13-04-2022

25. Talanov VS, Regino CA, Kobayashi H, Bernardo M, Choyke PL, Brechbiel MW. Dendrimer-based nanoprobe for dual-modality magnetic resonance and fluorescence imaging. Nano Letters. 2006 Jul 12;6(7):1459-63.
26. Sideratou Z, Tsiourvas D, Paleos CM. Quaternized poly (propylene imine) dendrimers as novel pH-sensitive controlled-release systems. Langmuir. 2000 Feb 22;16(4):1766-9.
27. Pannier AK, Shea LD. Controlled release systems for DNA delivery. Molecular Therapy. 2004 Jul 1;10(1):19-26.
28. Pushkar S, Philip A, Pathak K, Pathak D. Dendrimers: Nanotechnology derived novel polymers in drug delivery. Indian Journal of Pharmaceutical Education and Research. 2006;40(3):153.
29. Klajnert B, Bryszewska M. Dendrimers: properties and applications. Acta biochimica polonica. 2001 Mar 31;48(1):199-208.
30. Zimmerman SC, Lawless LJ. Supramolecular chemistry of dendrimers. InDendrimers Iv 2001 (pp. 95-120). Springer, Berlin, Heidelberg.
31. Wang H, Chang H, Zhang Q, Cheng Y. Fabrication of low-generation dendrimers into nanostructures for efficient and non-toxic gene delivery. Polymeric Gene Delivery Systems. 2017:217-32.
32. Tomalia DA, Reyna LA, Svenson S. Dendrimers as multi-purpose nanodevices for oncology drug delivery and diagnostic imaging.
33. Frechet JM. Functional polymers and dendrimers: reactivity, molecular architecture, and interfacial energy. Science. 1994 Mar 25;263(5154):1710-5.
34. Sakthivel T, Toth I, Florence AT. Synthesis and physicochemical properties of lipophilic polyamide dendrimers. Pharmaceutical research. 1998 May;15(5):776-82.
35. Mittal P, Saharan A, Verma R, Altalbawy F, Alfaidi MA, Batiha GE, Akter W, Gautam RK, Uddin M, Rahman M. Dendrimers: a new race of pharmaceutical nanocarriers. BioMed Research International. 2021 Feb 15;2021.
36. Hawker CJ, Frechet JM. Preparation of polymers with controlled molecular architecture. A new convergent approach to dendritic macromolecules. Journal of the American Chemical Society. 1990 Oct;112(21):7638-47.
37. Tripathy S, Baro L, Das MK. Dendrimer chemistry and host-guest interactions for drug targeting. International Journal of Pharmaceutical Sciences and Research. 2014 Jan 1;5(1):16.
38. Gillies ER, Fréchet JM. Designing macromolecules for therapeutic applications: polyester dendrimer poly (ethylene oxide)“bow-tie” hybrids with tunable molecular weight and architecture. Journal of the American Chemical Society. 2002 Nov 27;124(47):14137-46.
39. Abbasi E, Aval SF, Akbarzadeh A, Milani M, Nasrabadi HT, Joo SW, Hanifehpour Y, Nejati-Koshki K, Pashaei-Asl R. Dendrimers: synthesis, applications, and properties. Nanoscale research letters. 2014 Dec;9(1):1-0.
40. Grayson SM, Frechet JM. Convergent dendrons and dendrimers: from synthesis to applications. Chemical reviews. 2001 Dec 12;101(12):3819-68.
41. Hawker CJ, Frechet JM. Preparation of polymers with controlled molecular architecture. A new convergent approach to dendritic macromolecules. Journal of the American Chemical Society. 1990 Oct;112(21):7638-47.
42. Caminade AM, Turrin CO, Laurent R, Ouali A, Delavaux-Nicot B, editors. Dendrimers: towards catalytic, material, and biomedical uses. John Wiley & Sons; 2011 Aug 31.
43. Parata A, Felder-Flescha D. General introduction on dendrimers, classical versus accelerated syntheses and characterizations. Dendrimers in Nanomedicine; Jenny Stanford Publishing: New York, NY, USA. 2016:1-22.
44. Grayson SM, Frechet JM. Convergent dendrons and dendrimers: from synthesis to applications. Chemical reviews. 2001 Dec 12;101(12):3819-68.
45. Alper J. Rising Chemical" Stars" Could Play Many Roles: Enormous polymers that grow from a tiny core might be used in drug delivery, filtering, catalysis—even artificial cells. Science. 1991 Mar 29;251(5001):1562-4.
46. Klajnert B, Bryszewska M. Dendrimers: properties and applications. Acta biochimica polonica. 2001 Mar 31;48(1):199-208.

ISSN NO: 2770-2936
Date of Publication:13-04-2022

47. Svenson S, Tomalia DA. Dendrimers in biomedical applications—reflections on the field. Advanced drug delivery reviews. 2012 Dec 1;64:102-15.
48. Jain NK, editor. Advances in controlled and novel drug delivery. CBS Publishers & Distributors; 2008.
49. Fischer M, Vögtle F. Dendrimers: from design to application—a progress report. Angewandte Chemie International Edition. 1999 Apr 1;38(7):884-905.
50. Wiener EC, Auteri FP, Chen JW, Brechbiel MW, Gansow OA, Schneider DS, Belford RL, Clarkson RB, Lauterbur PC. Molecular Dynamics of Ion− Chelate Complexes Attached to Dendrimers. Journal of the American Chemical Society. 1996 Aug 21;118(33):7774-82.
51. Bryant Jr LH, Brechbiel MW, Wu C, Bulte JW, Herynek V, Frank JA. Synthesis and relaxometry of high-generation (G= 5, 7, 9, and 10) PAMAM dendrimer-DOTA-gadolinium chelates. Journal of Magnetic Resonance Imaging: An Official Journal of the International Society for Magnetic Resonance in Medicine. 1999 Feb;9(2):348-52.
52. Nieznański K, Nieznańska H, Surewicz WK, Surewicz K, Bandyszewska M, inventors; Instytut Biologii Doswiadczalnej Im Marcelego Nenckiego Polskiej Akadamii Nauk, Case Western Reserve University, assignee. Prion protein-dendrimer conjugates for use in treatment of alzheimer disease. United States patent US 10,815,292. 2020 Oct 27.
53. Wu HC, Chen-Yun YE, inventors; Academia Sinica, assignee. Peptide-conjugated nanoparticles for targeting, imaging, and treatment of prostate cancer. United States patent application US 16/062,274. 2021 Aug 5.
54. Santos A, Veiga F, Figueiras A. Dendrimers as pharmaceutical excipients: Synthesis, properties, toxicity, and biomedical applications. Materials. 2019 Dec 21;13(1):65.