IJBPAS, July, 2022, 11(7): 3447-3462

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

DENDRIMERS - AN OVERVIEW ON TYPES AND APPLICATIONS

HAARIKA B[*1], R. PRASANTHI[2] AND SREENIVAS N[2]

1, 2: Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, 12-5-31/32, Vijayapuri colony, Tarnaka, Secunderabad, 500017, Telangana, India

***Corresponding Author: Dr. Balusu Haarika: E Mail:** haarikabalusu09@gmail.com

Received 15th June 2020; Revised 20th July 2020; Accepted 10th Nov. 2021; Available online 1st July 2022

https://doi.org/10.31032/IJBPAS/2022/11.7.6252

ABSTRACT

Dendrimers are nanosized, symmetrical molecules having a small atom which is surrounded by many symmetric branches known as dendrons. Dendrimers structure possesses the greatest impact on drug release. They grow outwards from core-shell that further reacts with monomers. These are having high compatibility with the biological systems. The presence of hyper branching, the well-defined spherical structure are the unique characteristics. These dendrimers are having a wide range of applications including medical and biomedical areas. Nano formulations based on dendrimers enhances solubility of low soluble drugs, arrives to the target tissue, enhanced bioavailability and havecontrolled drug release. In this review, we mainly focussed on the types of nanosystems, synthesis, classification and applications of dendrimers in drug delivery. Dendrimer structures which are synthesized by two different methods that are divergent and convergent growth methods.

Keywords: Dendrimers, Nano systems, Nano devices, Divergent and Convergent growth methods

INTRODUCTION

Nanotechnology is an emerging field of science that includes nanomaterials synthesis and development. Nanoparticles are defined as an objects ranging in size from 1 to100 nm. Nowadays different metallic nanomaterials are produced using copper, magnesium, gold, zinc, titanium, alginate and silver. Nanoparticles can be synthesized both chemically or biologically. With chemical synthesis methods many adverse effects have been observed due to the presence of some toxic

chemicals absorbed on the surface. Eco-friendly alternatives for chemical and physical methods are biological ways of synthesis using plant extracts, microorganisms, enzymes and fungus **[1]**.

They are prepared from materials such as proteins, polysaccharides and synthetic polymers. The large secretory parts in fungi are responsible for their extracellular synthesis of nanoparticles in them. The matrix material selection depends on the size of nanoparticles and also depends on drug's inherent properties, charge, permeability, aqueous solubility, stability, biodegradability, biocompatibility, toxicity, drug release and antigenicity of the final product **[2]**.

The nanoparticles are of different shapes, sizes and structures. It may be spherical, cylindrical, conical, flat, hollow, tubular, spiral or irregular **[3]**.

TYPES OF NANOSYSTEMS

I. Nano-structured

Polymeric nanoparticles:the size is between 10 to 1000nm. These are biodegradable, biocompatible, they offer complete drug protection. Used as an excellent carrier for controlled and sustained delivery of drugs, stealth and surface-modified nanoparticles can be used for active and passive delivery of bioactive.

Dendrimer: Size is less than 10nm, highly branched, three main parts core, surface and branches. These are monodispersing polymer systems produced by controlled polymerization. They may be long circulating and having controlled and targeted deliveries to liver as well as bioactive macrophages.

Polymeric micelles: Size varies from 10 to 100 nm. They may block amphiphilic copolymer micelles, with high drug entrapment, payload and biostability. Help in long circulating, target-specific active and passive drug delivery.

Polymer-Drug Conjugates: Drug is chemically linked to a polymer instead of being encapsulated into it. This conjugation changes drug behaviour greatly such as increasing water solubility to lipophilic drugs, improving stability, bioavailability and prolonging plasma half-life, bio distribution altering, drug targeting, and controlled release of drugs under specific pH or presence of certain enzymes.

Carbon nanotubes: Size varies from 0.5 to 3 (diameter) and 20 to1000 (length). These are third allotropic crystalline forms of carbon sheets of single layer also called single walled nanotube (SWNT) and multiple layer also called multi walled nanotube (MWNT). These crystals have unique electrical properties (conducting, semiconducting, or insulating) and have remarkable strength. Applications includes enhanced solubility, carrier for gene delivery, peptide delivery, penetration to cell cytoplasm and to the nucleus **[3]**.

Metallic nanoparticles: Size is less than 100nm. These are stable, gold and silver colloids. The very small size of these results in the high surface area available for functionalization. These help in highly sensitive diagnostic assays, drug and gene delivery, radiotherapy enhancementthermal ablation.

Silica Nanoparticles: Size varies from 20 to 1000nm.White powder, absorptive, abrasive colloidal silica or silicon dioxide nanoparticles. They are generally spherical in shape and amorphous in nature. They have very important applications in the drug deliveries and in the preparation of nanomedicines.

Quantum dots: Size varies from 2 to 9.5nm. These are Semiconducting materials synthesized with II-VI and III-V column elements. These are having bright fluorescence, narrow emission, high photo stability and broad Ultra Violet excitation. Applications involve longterm multiple colour imaging of liver cells, DNA hybridization, and immunoassay, labelling of breast cancer marker HeR_2 surface of cancer cells, receptor mediated endocytosis **[4]**.

II Nano Devices

Respirocytes: Which provides metabolic support and prevents tissue damage due to hypoxia, of reduced blood flow by the use of an artificial red blood cell. Respirocytes are blood borne 1micro meter size diamondoid storage tanks. These are spherical nanodevices, reversibly pressurized up to 1000 atmp. The respirocyte when fully loaded it consists of 18 billion precisely arranged structural atoms and 9 billion temporarily resident molecules. Endogenous serum glucose powers twelve pumping stations are spaced evenly on an equatorial circle. Each station has its glucose tank, independent glucose metabolizing power plant, environmental glucose sensors, and an array of 3-stage molecular sorting rotors assembled for reversibly pumping O_2, CO_2, and H_2O between the ambient medium and an interior chamber.

NEMS: Nanoelectromechanical systems are devices on the nanoscale that integrates electrical and mechanical functionality. These are the latest logical miniaturization techniques of microelectromechanical systems (MEMS devices). These typically integrate transistor like nano electronics with mechanical actuators, motors, pumps and form physico-chemical and biological sensors. Low mass and high mechanical resonance frequencies having potentially large quantum mechanical effects such as zero-point motion. They have a high surface-to-volume ratio that is useful for surface based sensing mechanisms. Applications include accelerometers and sensors to detect chemical substances in the air. NEMS has many uses in industry and

science. These are used to measure vibration on cars, machines, process control systems, safety installations and inbuildings **[5]**.

DENDRIMERS

Dendrimers are nano-sized particles with the hyper branch, radially symmetric having definite molecular weight, size, shape, homogeneous and monodisperse structures. They consist of tree-like branches and highly ordered 3D structures. In that, all the bonds are converging to a focal point. Synthesis of Dendrimers involve an iterative model of reaction steps, in that each additional repetition giving to a higher generation dendrimer.

Dendrimers are also called cascade molecules. Polyionic dendrimers have no determined shape. They may change in size, shape and flexibility as increasing generations. The end-groups reaching the outward can be functionalized by modifying their physicochemical or biological properties **[6]**.

Dendrimers have a broad range of applications in supramolecular chemistry particularly in self-assembled processes and host guest reactions. The great role of anticancer therapies and diagnostic imaging, the newest class of macromolecular nanoscale delivery devices. Dendrimers are more ideal delivery vehicle candidates for the study of the effects of polymer size and charge, composition on biologically relevant properties such as lipid bilayer interactions, cytotoxicity, blood plasma retention time, bio distribution, internalization and in filtration.The tremendous rise in dendrimer basedpatents attracts the attention of researchers to keep interest in this important area. Donald Tomalia and Dow are recognized as first persons for getting patent in Dendrimers **[7]**.

Uniqueness of Dendrimers

Enhanced permeability and retention effect, high permeability, Dendrimers cross bio-barriers like blood-brain and cell membrane barrier. Uniform and Nanosize range of dendrimers enhance the ability to cross cell membranes, reduce the risk of undesired clearance from the body through the liver or spleen. They have sustained/extended effect, higher solubilisation potential, high uniformity, purity, stability, loading capacity, multifunctional platform, low immunogenicity and toxicity **[8]**.

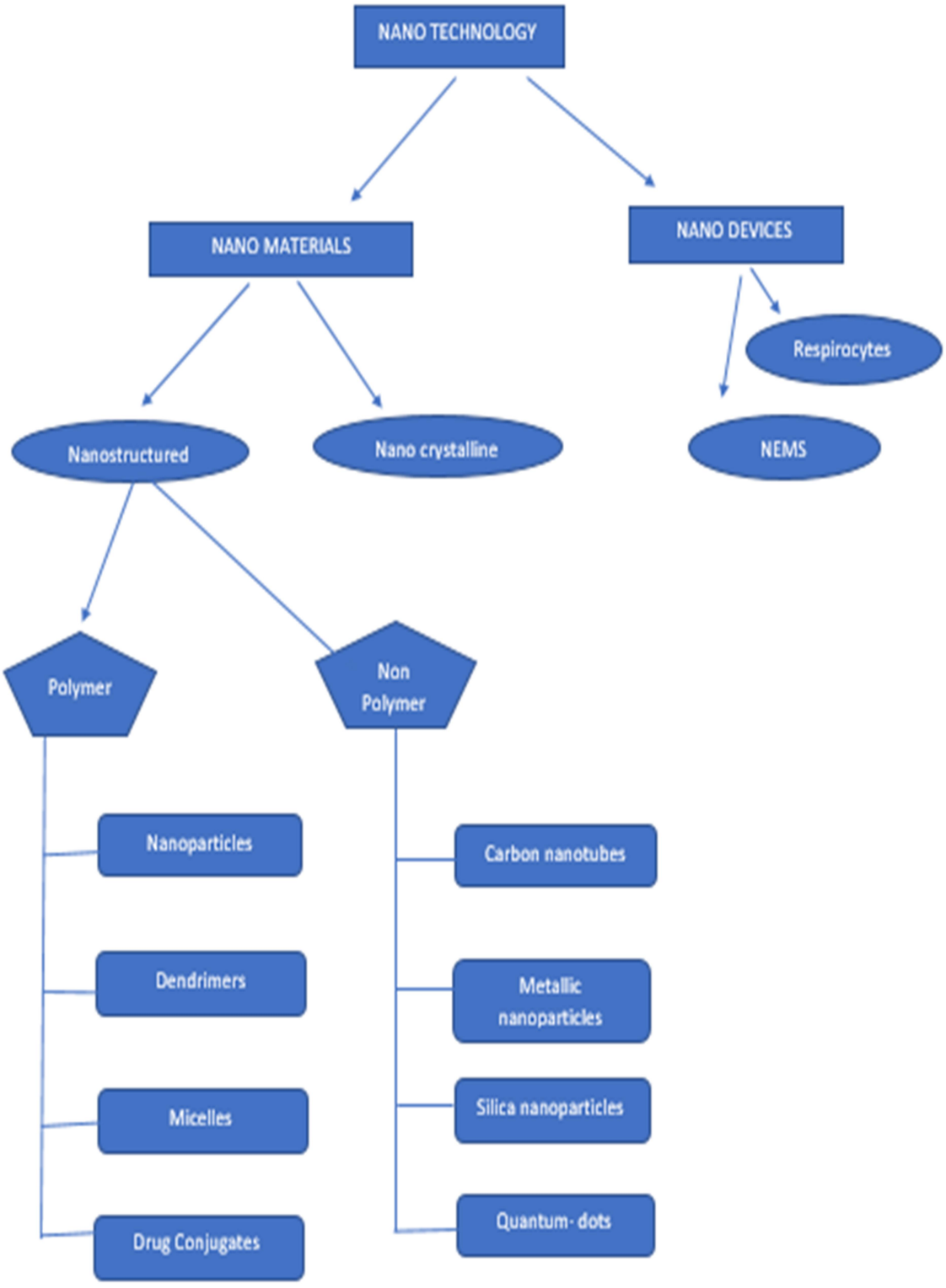

Figure 1: Types of Nanosystems

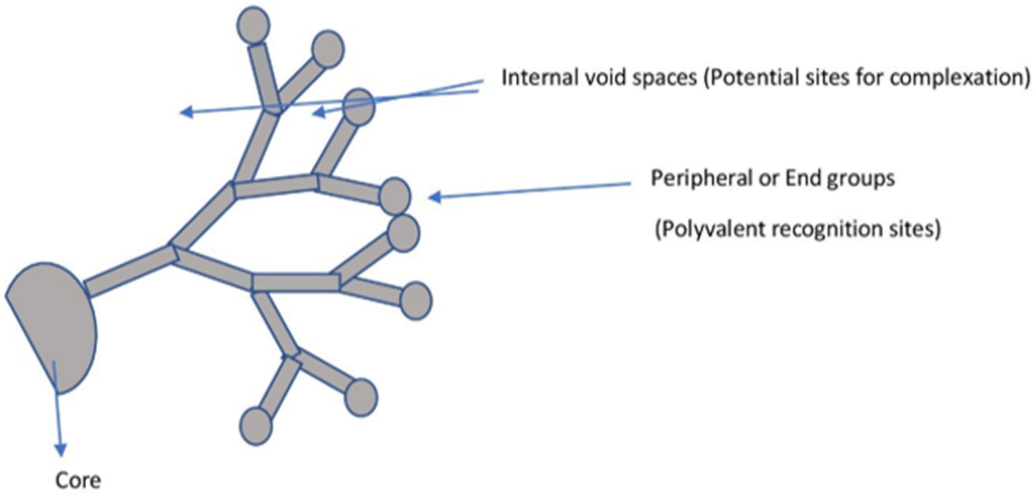

Figure 2: Structure of Dendrimer

CLASSICAL SYNTHESIS PATHWAYS

Dendrimer structures are synthesized by two different methods. They are divergent and convergent growth methods.

Divergent growth method

The divergent growth method is widely used. In this process, the construction of the dendrimer starts from the core to the outwards. It consists oftwo steps: (I) coupling of monomers, (II) activation of the monomer end-group to promote the reaction with the new monomer. The divergent growth synthesis pathway consists of the repetition of the two above steps.

The divergent processing starts with activation of the core and coupling of the first monomer to create the first generation of the dendrimer. In next step the activation of this first generation (G_1) to react with other branched monomers takes place to get the second generation (G_2) and so on. The number of the generations corresponds to the number of branches from the core. In this, each step of the reaction must be fully completed before adding a new generation to avoid deficiently formed branches. The surface of the dendrimers may be modified in each step, to obtain the desired pharmaceutical excipient at the end. This method leads to the synthesis of highly symmetric dendrimer molecule **[9]**.

Convergent growth method

In contrast to the divergent method, the convergent method synthesizes dendrimers start from the surface and not from the

core. It includes the reiteration of the coupling and activation steps to get the desired dendrimer structure. Initially, two surface groups are coupled to a monomer to give the dendritic segment, i.e., Dendron generation zero. In the second step, the activation of this fragment reacts with other monomers, thus creating the first generation dendron, which is called a dendritic wedge. It ends at the core, where more dendrons are joined together, to form the dendrimer.

In this type of synthesis, structural control achieved is greater than the divergent approach. In the divergent approach the relatively lower number of coupling reactions at each growth stepallow the product of unmatched purity **[10]**.

CLASSIFICATION OF DENDRIMERS [11]

I. Chemical classification

1. Poly amidoamine (PAMAM) Dendrimers.
2. Polypropyleneimine (PPI) Dendrimers
3. Polyether(PE) Dendrimers
4. L-lysine-based Dendrimers
5. Phenyl acetylene Dendrimers.
6. Glyco or Carbohydrate Dendrimers

II. Physical classification

1. Simple Dendrimers
2. Liquid crystalline Dendrimers
3. Chiral Dendrimers
4. Micellar Dendrimers
5. Hybrid Dendrimers

III. Miscellaneous

1. Dendrophanes
2. Metallodendrimers
3. Polyamino phosphine
4. Dendritic box
5. Carbohydrate vaccine Dendrimers

I. Chemical classification

1. Poly Amido Amine (PAMAM) Dendrimer: These are spheroidal or ellipsoidal in shape. These are available with different functionalities like amine, hydroxyl and carboxylic groups. Available as mixed functional groups up to generation-10 either in methanolic or aqueous solutions. It is having high solubility, high stability and reactivity due to the incidence of several functional end groups and unfilled internal cavities. Synthesized by divergent growth method. They have several pharmaceutical and biological applications. For e.g., in drug delivery and in gene delivery, phototherapy, transdermal drug delivery and as a diagnostic tool. Commercially supplied as Dendritech TM (USA) **[12]**.

2. Poly Propylene Imine (PPI) Dendrimer: Closely resembles PAMAM dendrimers but having repeated units and less polarity. In PPI dendrimers alkyl chain make the internal microenvironment. These are less polar compared to their core structure is based on di amino butane with primary amines as end groups and tertiary

propylene amines as the centre. These are available commercially up to G-5 and are extensively used in material science and in biology and synthesized by divergent growth method. Commercially supplied as, Astramol TM by DSM (Netherlands, up to generation-5) **[13]**.

3.Polyether(PE) Dendrimers: Also called Frechet-type Dendrimers. These were based on hyperbranched skeleton of polybenzyl ether. The carboxylic acid group is attached to the surface of dendrimers that provides a site for further functionalization and also improves the solubility of dendrimers, synthesized by convergent growth method. For e.g., Frechet type dendron azides, TM Priostar **[14]**.

4. L-lysine-based Dendrimers: These are dendron-like molecular assemblies based on a polylysine frame. Lysine with its alkyl amino side chain performs as an excellent monomer for the overture of frequent branching points. It is useful in vaccine and as well as in diagnostic research, synthesised by both convergent and divergent growth methods **[15]**.

5. Phenyl acetylene dendrimers: Phenyl acetylene dendrimers are synthesized by divergent, convergent and double stage convergent methods. It involves the catenation of repeated units around a core which increases the number of reactive functional groups on the dendrimer periphery **[16]**.

II. Physical classification

1. Simple dendrimer: They have simple monomer units. The convergent synthesis of a sequence of monodisperse is Lester dendrimer, based upon symmetrically substituted benzene tricarboxylic acid ester is described. These materials consist of 4, 10, 22 and 46 benzene rings symmetrically linked **[17]**.

2. Liquid crystalline dendrimer: These are made of mesogenic monomers e.g. mesogen functionalized carbosilane dendrimer. Functionalization to the end group of carbosilane dendrimers with 36 mesogenic units which can be attached through a C-5 spacer and leads to liquid crystalline dendrimers that form broad smectic phase in the temperature range of 17°C to 130°C**[18]**.

3. Chiral dendrimer: In these, the chirality is based on the building of four constitutionally assorted but chemically alike branches to an achiral core e.g. chiral dendrimers obtained from pentaerythritol **[19]**.

4. Micellar dendrimer: These are arranged as unimolecular micelle dendrimers. Fully aromatic and water soluble dendrimers forming a collection of aromatic polymeric chains that are able to generate an environment that resembles some micellar

structures, which form a complex with small organic molecules in water **[20]**.

5. Hybrid dendrimers: These are the preparation of dendritic and linear polymer in hybrid block or graft copolymer form. Which provide an opening to use them as surface-active agents, compatibilizers or adhesives, for e.g., Hybrid dendritic linear polymer, Polysilsesquioxanes.These are synthesised by divergent method**[21]**.

III. Miscellaneous

1. Dendrophanes: Dendrophanes are water-soluble dendritic cyclophanes of first, second and third generation dendrimers, with polyether amide branch 12, 36 and 108 terminal carboxylate groups, which are prepared by divergent synthesis. Dendrophanes incorporated as the initiator core of a tetraoxide [6.1.6.1] paracyclophane with a suitably sized cavity for inclusion complexation of benzene/naphthalene derivatives. The third-generation ester is also independently prepared by a semi-convergent synthetic strategy **[22]**.

2. Metallo dendrimer: Theseare dendrimers that are attached with the metal ion to form the complex either in the interior or on the peripheral. The ruthenium bipyridine complex-based dendrimer has attribute electrochemical and luminescence properties **[23]**.

3. Polyamino phosphine: Prepared by divergent synthetic approach. These are categorized by their mode of connectivity. Their host cavities, maintained by the dendritic branches and allowed for the incorporation of nanoparticles, metal particles, which make these products attractive in catalysis and imaging studies. These are highly water-soluble, neutral dendrimers appended with, grown from or acting as hosts to specific molecules that give rise to a wide variety of biomedical applications such as drug delivery systems and MRI imaging agents **[24]**.

4. Dendritic box: The flexible core is based on poly (propylene imine) dendrimers which are synthesized by the divergent approach. A repetitive reaction sequence is used with the double Michael addition of a primary amine to acrylonitrile then by the heterogeneously catalyzed hydrogenation of the nitriles to primary amines, yields di-amino-butane-based poly (propylene imine) dendrimers [DAB-dendrimer]. These are very flexible and possess glass transition temperatures of -40 °C and -65°C for the CN- and NHz-terminated dendrimers respectively. More recently a variety of end-group modifications have been reported, a critical end-group modification of cascade polyaniline with an appropriate bulky group is performed for the construction of the rigid shell of the dendritic box. For e.g., the N-hydroxy succinimide ester of a test-butyloxycarbonyl (t-BOC), L-

phenylalanine is brought into reaction with the fifth generation poly (propylene imine) dendrimer in a CH_2Cl_x-triethylamine mixture **[25]**.

5. Carbohydrate vaccine dendrimers: Glyco or carbohydrate dendrimers are composed of surface engineered with carbohydrates. These are either carbohydrate-coated, carbohydrate-centred or fully carbohydrate-based. These are used to study the protein-carbohydrate interactions, incorporation into analytical devices, targeting MRI contrast agents, formulation of gels, drugs and gene delivery systems **[26]**.

6. Amphiphilic dendrimers: They are the class of globular dendrimers that have asymmetrical structures but highly controlled division of chain-end chemistry. They oriented at the interface by forming an interfacial liquid membrane for neutralizing aqueous organic emulsion **[27]**.

Table 1: Marketed products of dendrimers

Dendrimers products	Therapeutic Application	Company Name
Stratus CS®	Cardiac Marker diagnostic	Dade Behring
Starburst®	Dendrimers Commercial	Sigma Aldrich
Priofect®	SiRNA & DNA transfction reagents	MERCK
SPL7013	Arthritis and cosmetic treatment	STARPHARMA
Targeted MRI	Imaging Contrast agent	Baker
NanoJuiceTM	DNA transfection agent kit	EMD Chemicals
SuperFect®	Gene Transfection technology	Qiagen

APPLICATIONS OF DENDRIMERS:

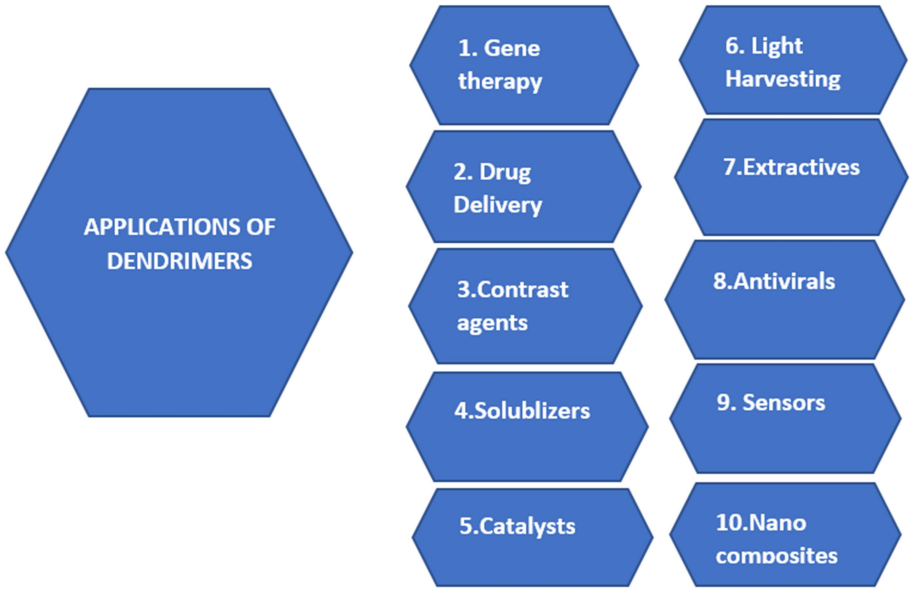

Figure 3: Applications of Dendrimers

1. Gene therapy

Dendrimers act as carriers and are also called vectors in gene therapy. These vectors transfer genes through the cell membrane into the nucleus. Presently liposomes and genetically engineered viruses are mainly used for this. PAMAM dendrimers also have been tested as genetic material carriers. Activated dendrimers are commercially available as transfection reagent called SuperFectTM **[28]**.

2. Drug delivery

Gadomer-17 dendrimers are highly branched macromolecules complexed with gadolinium (III) ions which are promising candidates for magnetic resonance angiography and in clinical trials. Its molecular weight is 17 kilo daltons. These surface-modified dendrimers are used to carry the drug molecules to a specific site and release them in a controlled manner. These dendrimers are used as coating agents to protect drugs or deliver drugs to a specific location in the body. Also used as time-released vehicles for biologically active agents. PAMAM dendrimers on acetylation can form dendrimer-5FU conjugates **[29]**.

3. Contrast agents

Dendrimers act as contrast agents for magnetic resonance imaging (MRI). MRI is a diagnostic method for producing anatomical images of organs. Gadolinium salt of diethylene triamine penta acetic acid (Gd (III)/DTPA) is used as a contrast agent but it diffuses into the extra venous part due to its low molecular weight. Advantages of dendrimer as contrast agents on Gd (III)/DTPA complexes are having enhanced relaxivity, prevent diffusion into the interstitial space and target-specific site release **[30]**.

4. Solubilizers

Good solubility increases the therapeutic effectiveness of any drug in the body. Dendrimers improve the solvency and disintegration of numerous medications. The upgrade of these depends upon pH and temperature of the medium. Dendrimers can improve the dissolvability of hydrophobic drugs, utilizing real epitomes or with the help of covalent conjugation **[31]**.

5. Catalyst

Catalytic functionalities are incorporated in the core or surface of the dendrimer to get catalytic dendrimers. These are attached directly and covalently to solid supports via siloxy bonds. These supportive dendrimers are easily separated from the reaction mixture and they are stable. To use as shape-selective oxidation catalysts, sterically hindered dendrimer-metalloporphyrins are synthesized. In Intra and intermolecular cases these are examined as regioselective oxidation

catalysts. In the hydrogenation of organic compounds, palladium complexes are employed as catalysts. The formation of the coordinative unsaturated palladium is responsible for high activity. Reymond and co-workers synthesized catalytic peptide dendrimers first with series of serine, aspartate and histidine **[32]**.

6. Light-harvesting

Frechet and co-workers at Berkeley investigated the use of dendrimers to harvest broadband light and convert the energy into monochromatic light with amplification and into electricity through charge separation. These systems consist of light-harvesting dendrimers with numerous laser dye chromophores, at the periphery such as coumarins. For example, a single chromophore oligothiophene lies at the core of the dendrimer. Dendrimer containing six ruthenium (II), polypyridine type units undergo as many as 26 reversible ligand centered reduction processes. As it is capable of exchanging 32 electrons altogether since that compound also exhibits six reversible metal-centered oxidation processes **[33]**.

7. Extractives

Fluorinated dendrimers are used to extract strong hydrophilic compounds from water into liquid CO_2,as they show good solubility in supercritical CO_2. This helps to develop technologies in hazardous organic solvents to replace liquid CO_2.

8. Antivirals

Sialylated dendrimers called sialodendrimers, that are potent inhibitors of the haemagglutination of human erythrocytes by influenza viruses. Sialodendrimers bind to hemagglutinin and prevent the attachment of the virus to cells in the body **[34]**.

9. Sensors

As they have an organized structure, ease of modification, and strong adsorption behaviour to a variety of substrates, they are used to produce monolayers/stacked film layers, can be used as sensors for detecting hazardous chemical materials **[35]**.

10. Nanocomposites

PAMAM dendrimer forms stable interior molecular nanocomposite with zero-valent metal, metal cation, electrophilic ligand and semiconductor particle. These materials are actively investigated in catalysis, electronics and optoelectronics **[36]**.

CONCLUSION

Dendrimers have the high level of control over the structure, size, shape, branching length, density and surface functionality. Thus makes these dendrimers as an ideal carrier in biomedical applications. They can also use in different fields such as drug delivery, gene transfection, photodynamic therapy, bio pharmacy, pharmacy, extractives, sensors, immunology and imaging. Dendrimers are one of the

promising structures for solvency improvement.

CONFLICT OF INTEREST

The authors declaredthat they have no conflict of interest.

REFERENCES

[1] Saba Hasan *et al*., A Review on Nanoparticles: Their Synthesis and Types, Res. J. Recent. Sci. 4, (2015), 1-3.

[2] R.Nivesh Krishna *et al*., Nanoparticles and Their Applications – A Review, J. Pharm. Sci. & Res. 9(1) 2017, 24-27.

[3] Nahar M, Dutta T, Murugesan S, Asthana A, et. al., Functional polymeric nanoparticles: an efficient and promising tool for active delivery of bioactive. Crit Rev Ther Drug Carrier Syst, 23(4) 2006, 259–318.

[4] Rong tong *et al*., Current status of Nanoencapsulates and Polymer-drug conjugates, Pharmaceutical Sciences Encyclopedia: Drug Discovery, Development, and Manufacturing, John Wiley & Sons, Inc, 2, 2016,1-31,

[5] Ye Hu, Daniel H. Fine, Ennio Tasciotti, Ali Bouamrani and Mauro Ferrari Nanodevices in diagnostics John Wiley & Sons, 3, 2011, 11-32.

[6] Ardhendu Kumar Mandal, Dendrimers in targeted drug delivery applications: a review of diseases and cancer, International Journal of Polymeric Materials and Polymeric Biomaterials, 70(4), 2021, 287-297.

[7] Drug delivery approaches and nanosystems, Novel Drug Carriers. Edited by Raj K. Keservani, Anil K. Sharma, 1, 2018

[8] Ankita Gupta, Shaifali Dubey, Mayuri Mishra, *et al*., Unique Structures, Properties and Applications of Dendrimers, Journal of Drug Delivery and Therapeutics, 8(6-s), 2018328-339.

[9] Abbasi *et al*. Dendrimers: synthesis, applications, and properties, Nanoscale Research Letters, 9, 2014, 247.

[10] Saranya Sasi, Sharon Kunnath Joseph, Arya mangalath Arian. An Updated review on the application of Dendrimers as successful nanocarriers for brain delivery of therapeutic moieties, Int J App Pharm, 13(1), 2021, 1-9.

[11] Tariq Baig, Jyoti Nayak, Vandana Dwivedi, *et al*., A Review about Dendrimers: Synthesis, Types, Characterization and Applications. IJAPBC – 4(1), 2015, 44-59.

[12] S. Mahmood Fatemi, SeyedJamilaldin Fatemi & Zeynab Abbasi, PAMAM dendrimer-

based macromolecules and their potential applications: recent advances in theoretical studies, Polymer Bulletin, 77, 2020, 6671–669.

[13] Neeharika Gogulapati, Balasubramanian Valli Manalan, Rama Rao Nadendla, Poly (propylene imine) Dendrimer: Synthesis, characterization and applications in various drug delivery, Asian Journal of Pharmacy and Pharmacology 6(3), 2020, 190-203.

[14] Ana Santos, Francisco Veiga , Ana Figueiras *et al*., Dendrimers as Pharmaceutical Excipients: Synthesis, Properties, Toxicity and Biomedical Applications, Materials, 13, 2020, 65

[15] Sijin Chen, Shuting Huang, Yan Li, Chuncai Zhou Recent Advances in Epsilon-Poly-L-Lysine and L-Lysine-Based Dendrimer Synthesis, Modification, and Biomedical Application, Frontiers in Chemistry, 9, 2021.

[16] Claudia Sandoval-Yañez 1, and Cristian Castro Rodriguez, Dendrimers: Amazing Platforms for Bioactive Molecule Delivery Systems, Materials, 13, 2020, 570.

[17] Pooja Mittal, Anjali Saharan, Ravinder Verma, Dendrimers: A New Race of Pharmaceutical Nanocarriers, BioMed research international, 2021.

[18] Robert Deschenaux, Bertrand Donnio, Daniel Guillon Liquid—Crystalline Fullerodendrimers. New Journal of Chemistry, 31(7), 2007, 1064-1073.

[19] Malinga-Drozd, M.; Uram, Ł.; Wróbel, K.; Wołowiec, S. Chiral Recognition of Homochiral Poly (amidoamine) Dendrimers Substituted with R- and S-Glycidol by Keratinocyte (HaCaT) and Squamous Carcinoma (SCC-15) Cells in Vitro. Polymers, 13, 2021, 1049.

[20] Sibusiso Alven, Blessing Atim Aderibigbe, The Therapeutic Efficacy of Dendrimer and Micelle Formulations for Breast Cancer Treatment Pharmaceutics, 12, 2021, 1212.

[21] Rohini Kharwadea, SachinMorea, AmolWarokara *et al*., Starburst pamam dendrimers: Synthetic approaches, surface modifications, and biomedical applications, 13(7), 2020, 6009-6039.

[22] Helvestica Sebastiano Mattei, Peter Wallimann, Benoit Kenda, Walter Amrein, Fraçois Diederich

Dendrophanes: Water-soluble dendritic receptors as models for buried recognition sites in globular proteins,80(8), 2004, 2391 – 2417.

[23] Natalia Sanz del Olmo, Riccardo Carlonid, Paula Ortega, *et al*., Metallodendrimers as a promising tool in the biomedical field: An overview, Advances in organometallic chemistry, 74, 2020, 1-468.

[24] R. Newkome, C.D. Shreiner, *et al*., Poly(amidoamine), polypropylenimine, and related dendrimers and dendrons possessing different 1/2 branching motifs: Anoverview of the divergent procedure. Polymers, sciencedirect, 49(1), 2008, 1-173.

[25] Alycia Gardner, varo de Mingo Pulido, Brian Ruffell. Dendritic Cells and Their Role in Immunotherapy, Front. Immunol., 2020.

[26] Peter M. H. Heegaard, Ulrik Boas, Nanna Skall Sorensen. Dendrimers for Vaccine and Immuno-stimulatory Uses. A Review, Bioconjugate Chem., 21, 2010, 405–418.

[27] Calvin Andeve, Rahul Kalhapure, Dhiraj Radheshyam Sikwal, Thirumala Govender. Amphiphilic Dendrimers for Drug Delivery: Handbook of Materials for Nanomedicine: Polymeric Nanomaterials, 2020, 159-212.

[28] Shiva kheiriabad, Jafer Ezzati, Michael Hamblin, *et al*., Dendrimers for gene therapy, Dendrimer-Based Nanotherapeutics, 2021, 285-309.

[29] Rouhollahkhodadust, Gozde unsay, Serap Yalcin, *et al*., PAMAM dendrimer-coated iron oxide nanoparticles: Synthesis and characterization of different generations, Journal of Nanoparticle Research, 15(3), 2013.

[30] Adriana Aurelia Chis, Carmen Dobrea, Claudiu Morgovan, *et al*., Applications and Limitations of Dendrimers in Biomedicine, Molecules, 25, 2020, 3982.

[31] Mohammed Abrar Hafijmiya Malek and Dr. Pravinkumar M. Patel. Dendrimers for drug solubility enhancement– A Review, International Journal of Pharmaceutical Sciences and Research, 11(2), 2020, 507-523.

[32] Cristiana Cesari, Riccardo Conti , Andrea Cingolani. Synthesis and Reactivity of Poly(propylene imine) Dendrimers Functionalized with Cyclopentadienone N-Heterocyclic-Carbene Ruthenium

(0) Complexes Catalysts, 10, 2020, 264.

[33] Wei-JianLia, Xu-Qing Wanga, WeiWang *et al*., Dynamic artificial light-harvesting systems based on rotaxane dendrimers, Giant, 2, 2020, 100020.

[34] Valentina Del Genio 2 and Stefania Galdiero, Peptides and Dendrimers: How to Combat Viral and Bacterial Infections AnnaritaFalanga, Pharmaceutics, 13, 2021, 101.

[35] B. Noriega-Luna, Luis A. Godínez, F. J. Rodríguez Corrigendum to "Applications of Dendrimers in Drug Delivery Agents, Diagnosis, Therapy, and Detection". Corrigendum, 2020.

[36] Nobel Tomar, Dendrimers as Nanocarriers in Cancer Chemotherapy, International Journal of Chemical and Molecular Engineering. 5(2), 2019, 14–32.