# **Review: Dendrimer – A Novel Drug Delivery Technique**

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# anched, and **A.MERITS**:

Abstract- Dendrimers are monodisperse, hyper-branched, and nanoscale-sized carriers with high functionality. These carriers possess well-defined molecular weights, sizes, and shapes. Hydrophobic drug molecules are either encapsulated in the interior void space or attached to the surface of the dendrimer. They are distinguishable due to their unique characteristics such as poly valency, self-amassing, electrostatic associations, solubility enhancers, and low cytotoxicity. It is utilized in a wide range of applications which include pharmaceutical fields, biomedical fields, drug delivery systems, oncology departments. When compared to conventional macromolecules, it has a denser functional group at the surface. Dendrimers are synthesized by divergent or convergent techniques. It reduces the toxic side effects. This review will cover a number of dendrimer-related topics such as structure, growth, synthesis, and type of polymers.

*Keywords*- Dendrimers, types, drug- interaction, application.

## I. INTRODUCTION

Greek terms "dendron." which means The "tree/branch," and "meros," which means "part," are the source of the word "dendrimer." The analogues of dendrimer include 'arborols' and 'cascade molecules.'[1] Fritz Vogtle and colleagues introduced dendrimer chemistry for the first time in 1978. He synthesized primary cascade molecules, which would eventually be referred to as dendrimers.<sup>[2]</sup> It ranges from 1 to 15 nanometers in size. Dendrimers are most often used to change and improve the bioavailability of drugs by altering the pharmacokinetics and pharmacodynamics characteristics of their active moiety. Unusual physical, chemical, and other characteristics of a dendrimer's form affect its solubility and miscibility. Dendrimers with hydrophilic surface groups are water soluble, while those with hydrophobic surfaces are hydrocarbon soluble. Although they are polymers, they differ from conventional polymers but bear similarity to vesicles such as micelles, liposomes, and globular proteins. The active moiety of a drug molecule has a significant role in targeted and controlled drug delivery to a specific site, achieved by reducing the moiety.<sup>[3]</sup>

# Dendrimer particle range in size from 1-100nm,

- allowing them to easily cross the cell membrane.
- It ensures structural consistency and monodispersity.
- It increases the solubility of drugs that are poorly soluble.
- The unstable drugs are stabilized by incorporating them into the core of dendrimer.
- Outer surface of dendrimer is composed of multiple functional groups that aid in attachment to the target site in the body.
- Dendrimers are biodegradable and have low toxicity and immunogenicity.
- They can either deliver drug inside the cell or improve intracellular trafficking.<sup>[5,6]</sup>
- Better permeability and retention effects which provide them to target tumor cells.
- Dendrimers are being considered as components in numerous routes of administration which include IV, transdermal, pulmonary and ocular.<sup>[7]</sup>

# **B.DEMERITS:**<sup>[8]</sup>

- Oral drug delivery is not suitable as it forms a drugdendrimer complex which does not cross the gut wall.
- The drug-dendrimer construct is considered a new chemical entity, so clinical testing for the new construct is required.

## **II. LITERATURE REVIEW**

Sadhana R Shahi and etal...,In comparison to linear polymers, dendrimers are highly branching molecules with well-defined size, structure, molecular weight, and monodispersity. Dendrimers are shaped like trees, with a core in the middle, branches, and terminal groups. The bioactive substances may be chemically or physically linked to the dendrimer surface, or they may be enclosed within the dendrimers' core. Dendrimers are widely used in the pharmaceutical industry for gene transfection, diagnostic purposes, blood substitutes, and solubility boosters. Dendrimers with changed surfaces may function as nanodrugs for cancer, bacteria, and viruses. This study focuses on the structure, properties, synthesis process, various characterization methods, dendrimer applications, and dendrimer formulation.

Umesh Gupta and etal..., When choosing medication molecules and other bioactives for product development, adequate aqueous solubility was one of the desired features. The pharmacological and therapeutic effectiveness of a medication is frequently influenced by its solubility. Due to poor solubility, majority of newly synthesized therapeutic compounds fail or are rejected in the initial stages of drug research and development. To get an appropriate bioavailability and therapeutic result, the drug must have sufficient permeability, water solubility, and physicochemical stability. To increase the solubility of several poorly aqueoussoluble medications, a variety of alternative strategies have investigated, including been co-solvency, micellarsolubilization, micronization, pН adjustment, chemical modification, and solid dispersion. Due to their special characteristics, dendrimers, a novel class of polymers, have a huge potential to enhance drug solubility. These hyperbranched, mono-dispersed molecules have the unique capacity to bind drug molecules on the periphery as well as to enclose these molecules inside he dendritic structure. Dendrimers have been effectively employed in various studies to improve the solubilization of poorly soluble drugs. The characteristics and function of dendrimers in improving the solubility of poorly soluble drugs will be discussed in this review.

Bhupinder Singh and etal...,Due to their remarkable utilitarian design and macromolecular properties, dendrimers have become one of the most fascinating topics for scientists and have attracted a lot of attention for biological applications. Dendrimers are radially symmetric, nanoscale particles with a highly homogeneous, monodisperse structure. Their three conventional macromolecular design classes are generally thought to produce products that are rather polydisperse and have a range of atomic weights. There are many different types of dendrimers, and they all have inherent qualities such polyvalency, self-amassing, electrostatic relationships. material stability, low cytotoxicity, and dissolvability. Dendrimers are a great option in the field of restoration due to these erratic properties.

AkashSrivastava and etal...,A new class of synthetic macromolecules known as dendrimers has highly branching, three-dimensional nanoscale structures, with very low polydispersity, and excellent functionality. The physical and chemical characteristics of these materials are

significantly influenced by their structure. Due to their distinctive qualities, their use in nanotechnology, pharmaceuticals, and medicinal chemistry is particularly appealing. Dendrimers are excellent for a variety of biological and industrial applications due to their distinct behaviour. The dendrimers are an ideal carrier for drug administration because they have well-defined size, shape, molecular weight, and monodispersity. Due to its uni-molecular micelle structure, dendrimers improve the solubility of drugs that poorly soluble.Due to their capacity to increase drugs' water solubility, bioavailability, and biocompatibility, these polymers have also successfully demonstrated their use as additives in various drug administration methods. Dendrimers can enclose hydrophobic drug molecules because they have open conformations and empty interior holes. In addition, compared to ordinary macromolecules, they have a significantly higher surface functional group density. The review article focuses on the different aspects of dendrimers, including their structure, characteristics, and kinds, as well as their methods of preparation and uses in both pharmaceutical and non-pharmaceutical fields.

**Inder Kumar and etal...**, Dendrimers provide polymeric substances a new level of efficacy. They are monodisperse, moderately branching macromolecules. Dendrimers can contribute significantly to the fields of nanotechnology, pharmaceuticals, and medicinal chemistry due to their structural advantages. Dendrimers are useful for a wide range of biomedical and commercial packaging because of their exact behaviour. The study provides a brief assessment of the physicochemical characteristics of dendrimers and their potential applications in diverse research, production, and therapeutic fields.

**Pooja Mittal and etal...**,Dendrimers are symmetrical, nanosized molecules in which small atoms or groups of atoms are surrounded by symmetrical branches known as dendrons. A dendrimer's structure has the greatest impact on its physical and chemical properties. They grow outward from the coreshell and further react with monomers with one or two dormant molecules. The unique properties of dendrimers, such as hyper branching, well-defined globular structures, and high compatibility with biological systems, are responsible for a wide range of applications, including medical and biomedical fields. In particular, the three-dimensional structure of dendrimers can contain various drugs to form biologically active drug conjugates. This review focuses on the synthesis, the mechanism of drug encapsulation into dendrimers and its wide range of applications in drug delivery.

Vivek Gupta and etal...,This review article is focused on different synthetic strategies used in dendrimer synthesis at

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commercial and laboratory scale. These synthetic strategies includes their own advantages and disadvantages. This review will cover divergent (from core to surface) and convergent (from surface to core) approaches used in dendrimer synthesis and the problems associated with these synthetic strategies. This article also covers the important applications of dendrimers in the field of pharmaceutical sciences. This data of review is collected from various articles, research papers and patents available on dendrimers.

VineetMathur and etal...,Dendrimers are a new class of polymeric materials. They are highly branched, monodisperse macromolecules. Structural advantages allow dendrimers to play important roles in the fields of nanotechnology, pharmaceuticals, and medicinal chemistry. Dendrimers are useful in a variety of biomedical and industrial applications due to their unique behaviour. A bioactive agent can be easily encapsulated or chemically bound within a dendrimer, i.e., conjugated to the dendrimer surface, and has the desired properties of the carrier to meet the specific needs of the active agent and its therapeutic application.

**Tongwen xu and etal...**,Due to its capacity to increase a drug's water solubility, bioavailability, and biocompatibility, dendrimers have successfully demonstrated their value as additives in several routes of drug administration. This review revealed how dendrimers might be used in these specific routes, paying particular attention to delivery methods which include intravenous, oral, transdermal, and ocular. The structures, synthesis, and characteristics of dendrimers were described as a necessary introduction. Additionally, the ways that dendrimers and medicinal compounds interact include simple encapsulation, electrostatic interaction, and covalent conjugation.

MukeshGohel and etal..., They focuses primarily on four areas: dendrimer architecture, synthesis, properties, and applications. Dendrimers' distinctive architecture, which includes their high branching, multivalency, and spherical structure with a distinct molecular weight, these structures are easily distinguished as specialised and ideal nanocarriers for medical uses like medication, transfection of genes, tumour therapy, delivery, diagnostics, etc. Synthetic techniques result in a dendritic architecture with characteristics which alterations to internal structure, polarity, size, shape, and surface structure. The most well-liked medication delivery methods are those utilising nanoparticles since they might improve the stability and selectivity of medicinal medicines. However. drug leakage, immunogenicity, and reticuloendothelial system (RES) absorption. The usage of these is limited by their cytotoxicity, haemolytic toxicity, and hydrophobicity. Surface engineering is used to fix these flaws.

Dendrimer, including polyester, citric acid, and arginine, Glycodendrimers, PEGylateddendrimers, etc. are all types of dendrimers. Bioactive substances can be chemically or readily enclosed inside the dendrimers, on the dendrimer surface, conjugated, or physically adsorbed, matching the carrier's intended attributes to the unique requirements of the medicinal uses of the active ingredient.

**Prabal K Maiti and etal...**,They demonstrate the pHcontrolled sponge activity of PAMAM dendrimer using a completely atomistic molecular dynamics simulation that lasts several hundred nanoseconds. We demonstrate how the PAMAM dendrimer behaves as a wet sponge at different pH levels. At neutral or low pH, the dendrimer noticeably expands and the dendrimer's inside expands to accommodate hundreds to thousands of water molecules. The pH is raised (moves from low pH to high pH for example) causes the dendrimer size to collapse, emptying the inner water that mimics the action of a sponge. The dendrimer size increases at neutral or low pH.The primary and tertiary amines, which are protonated at this pH, are attracted to one another electrostatically.

Vruti Patel and etal...,Dendrimers are hyperbranched nanostructures that have a low polydispersity index with functional surfaces, adaptable qualities, consistency in size, molecular weight, among other distinguishing and characteristics. They can be made using the divergent growth method or the convergent growth approach, and they consist of a central molecule, branches, and periphery groups. However, more contemporary methods, like the double exponential growth approach, click chemistry, and lego chemistry, have also been used for the production of dendrimers. The dendrimer can be categorised as polyamidoamine dendrimer, poly (propylene imine) dendrimer, glycodendrimer, liquid crystalline dendrimer, and peptide dendrimer depending on the various types of core and peripheral groups. Dendrimers are being created by modifying certain aspects of their features, such as PEGylation, liposomes locked inside dendrimers, synthesis of targeted dendritic scaffolds.

# **III. CHARACTERISTIC FEATURES**

# A.PROPERTIES:<sup>[9]</sup>

- 1. Lower generation anionic or neutral polar terminal surface groups have good biocompatibility as compared to higher generation polar neutral and cationic surface groups.
- **2.** It is able to organize bodily excretion according to the diameter of nanoscale particles.

- 3. Small molecules of metals and drugs that minimize the toxicity of the substance and facilitate controlled release can be enclosed in an internal void area.
- 4. Surface groups at the terminal that have potential to bioconjugate drugs, biocompatibility groups, or targeting moieties.
- 5. Functional groups can be introduced to dendrimer surfaces to prevent trans-cellular, epithelial, and vascular bio-permeability.
- 6. It improves surface group surface distribution, receptormediated targeting, and controlled drug release from the internal space.

# **B.STRUCTURE:**

Dendrimers are created from starting atoms like nitrogen, which are then added to repeatedly occurring chemical reactions along with carbon and other components to form a spherical branching structure. A spherical macromolecular structure is produced as the operation is repeated.<sup>[10]</sup>Dendrimers have three distinctive structural elements, which include a central core that can be an atomic group or a single atom. generation in which repeating units form the core, which is positioned radially and contains numerous terminal functional groups that are commonly found on the exterior of the macromolecule.<sup>[11, 12]</sup>

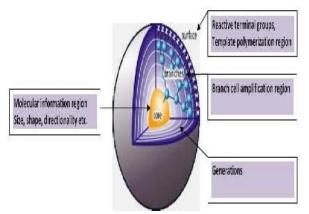


Fig-1: The Dendrimer Structure.

## C.COMPONENTS OF DENDRIMER STRUCTURE:<sup>[13]</sup>

- 1. Pincer
- 2. Shell
- 3. Generation
- 4. End-group

# 1. Pincer:

The dendrimer outer shell contains varying numbers of pincers formed by the final foci in front of the dendrimer

drimer ascular The dendrimer shell is the interfocal generation space (i.e., the spatial segment of the homostructure). Outer shell:

number of surface groups present.

(i.e., the spatial segment of the homostructure). Outer shell: The space between the last outer branch point and the surface is the outer shell.Inner shell: The interior of the dendrimer is inner shell.

surface. Splitting of the dendrimer chains at focal points

reduces the number of pincers in polypropyleneimine (PPI)

and polyamidoamine (PAMAM) dendrimers to half the

## 3. Generation:

2. Shell:

Hyperbranching from the centre to the periphery of the dendrimer results in homostructural layers between foci (branch points). Generation number: The generation number is the number of foci present on the dendrimer, counted from the core to the dendrimer surface. 5th generation Dendrimer: A dendrimer with five foci from the centre to the periphery is called a fifth-generation dendrimer, abbreviated as a G5 dendrimer.

**For example**, 5th generation polypropyleneimine (PPI) is abbreviated as G5-PPI dendrimer. The dendrimer core is sometimes called generation zero (G0). Hydrogen substituents are not considered foci, so the core structure has no foci. Intermediates formed during dendrimer synthesis are sometimes referred to as half-generations.

## 4. End-group:

Terminal groups are commonly referred to as dendrimer surface groups or terminal groups. Dendrimers terminated with amine end groups are called amino-terminated dendrimers. The solubility of dendrimers in solvents depends on the end groups.

# **IV.SYNTHESIS OF DENDRIMER:**<sup>[14]</sup>

Dendrimers, which can have their size and molecular mass precisely controlled during synthesis, the conventional polymerization process that yields linear polymers is typically random in nature and results in molecules of varied sizes.

- Divergent growth method
- Convergent growth method
- Hyper cores and branched monomers growth
- Double exponential growth

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First two are considered as main methods for synthesis of dendrimer.

#### (a)Divergent growth method:

Dendrimer growth starts at a core site using this technique. The first generation dendrimers are created by reacting the core with two or more moles of reagent that has at least two protecting branching sites, then removing the protective groups. Until the dendrimer of the specified size is obtained, this process is repeated. Polyamidoamines (PAMAM), commonly referred to as starbust Dendrimers, was the first Dendrimers to be synthesised using this method.

## Merit

• A large amount of dendrimer is developed with this technique.

#### Demerit

- A significant amount of reagent is needed to prevent problems during synthesis.
- Product purification is a time-consuming process.

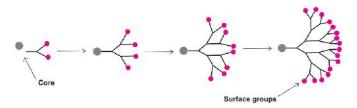


Fig-2: Divergent growth method.

### (b) Convergent growth method:

Convergent dendrimer growth starts at the dendrimer's eventual surface and subsequently grows inside by joining more surface units together. A full dendrimer is created when multiple growing wedges are joined to an appropriate core. The convergent growth method has a number of benefits, including the ability to relatively easily purify the desired product, minimal defects in the final structure, and inability to form high generation dendrimers due to stearic issues that arise in the reactions between the dendron and the core molecule. Convergent growth has the advantage over divergent growth in that purification is carried out after each stage, whereas in dendrimer method it is difficult to carry out chromatographic purification because the reactant and product remain the same.

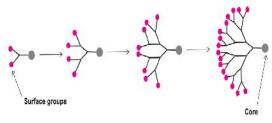


Fig-3: Convergent growth method.

#### (c) Hypercores and Branched monomers growth:

The core is reacted with 2 or more moles of reagents containing at least two protected branch sites, followed by deprotection. The subsequently released reactive sites lead to the first generation dendrimers.

#### Merit

• Higher yield in fewer steps.

#### (d)Double exponential or Mixed growth:

In this approach, two products (both convergent and divergent growing monomers) react to produce an orthogonally protected trimer that can be used to repeat the growth process again. The power of double exponential growth is more subtle than the ability to assemble large dendrimers in relatively few steps.

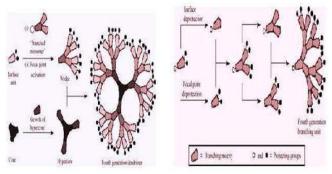


Fig-4 :Hypercores, Branched monomers growth and Double exponential or Mixed growth

## V. TYPES OF DENDRIMERS:<sup>[15-27]</sup>

- PAMAM Dendrimer
- PAMAMOS Dendrimer
- PPI Dendrimer
- POPAM
- Tecto Dendrimer
- Chiral Dendrimers

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- Hybrid Dendrimers
- Liquid Crystalline Polymers
- Amphiphilic Dendrimers
- Micellar Dendrimers
- Multiple Antigen Peptide Dendrimers
- Frechet-Type Dendrimers
- Multilingual Dendrimers

# Pamam Dendrimer:

# Poly(amidoamine) dendrimers / starburst Dendrimer

**Method of synthesis:** Divergent starting from initiator core reagents like ethylenediamine or ammonia. Commercially, PAMAM dendrimers are marketed as methanol solutions. Due to the star-like pattern seen when examining the structure of the high generation dendrimers of this type in two dimensions, PAMAM dendrimer was given the nickname "starburst."

Use:

- Science of Materials
- Computer toners for biomedicine.

Example: Dendritech TM

# Pamamos Dendrimer

# Poly (amido amine organosilicon) Dendrimers with radial layers

This original first commercial silicon-containing dendrimer was found in 1990 by Dr.PetarDvornic and his colleagues at the Michigan Molecular Institute.

# Structure

End group: Hydrophobic organosilicon Interior part: Nucleophilic polyamidoamine Method of synthesis: Divergent and Convergent Use:

- Electronics
- Chemical catalysis
- Nano-lithography
- Photonics

• Precursor for honeycomb (network preparation) **Example:** SARSOX

# > PPI Dendrimer

# **Poly-Propylene Imines**

It was initially created by Vogtle and is the earliest known dendrimer type. Commercially up to G5 it is available. **Structure** 

End group: Poly-alkyl amine, primary amine

Interior part: Tertiary tris-propylene amines.Method of synthesis: DivergentUse: Material science as well as biology.Example: Asramol by DSM

# > Tecto Dendrimer

**Structure:** It has a central dendrimer and many dendrimers around the edges.

Method of synthesis: Divergent

Use:

- Diseased state drug delivery diagnosis
- Diseased cell recognition
- Reporting outcomes of therapy

Example: Mercapto, Stratus CS Acute care TM, Starburst.

# > Chiral Dendrimer

**Structure:**Construction of chemically similar but fundamentally dissimilar branches to a chiral core is the foundation of chilarity.

# Method of synthesis: Convergent

**Use:** Chiral catalysts and chiral hosts for asymmetric synthesis and enantiomeric resolutions respectively.

**Example:** chiral dendrimers obtained from pentaerythritol.

# > Hybrid Dendrimer

**Structure:**These are dendritic and linear polymer hybrids (block or graft polymers) made by completely monofunctionalizing peripheral "zero-generation" amines. Other modified dendritic structures are less likely to offer structurally diversified lamellar, columnar, and cubic self-organized lattices than polyethyleneimine dendrimers.

# Method of synthesis: Divergent

Use: Molecular electronics, bio-medicals, nano-photonics, sensing

**Example:** Polysilsesquioxanes, hybrid dendritic linear polymer

# > Liquid crystalline dendrimer

**Structure:** A mesogenic group-containing highly branched polymer or oligomer with mesophase-behaving mesogenic groups. They are made up of monomers that are mesogenic (liquid crystallised).

Method of synthesis: Divergent

Use: Science and engineering

**Example:** Mesogen functionalized carbosilane dendrimers.

# > Amphiphil dendrimer

**Structure:** Asymmetric globular dendrimers with two separate chain ends. Half are electron donating and the other half are electron withdrawing.

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# Method of synthesis: Divergent

Use:Used as cell and gene transfection

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Structure-directing agent

Example: Bolo-amphiphiles, SuperFect, Hydra amphiphiles.

## Micellar dendrimer:

**Structure:** These are unimolecular micelles made from watersoluble hyperbranched polyphenylenes.

## Method of synthesis: Divergent

Use:

- Imaging agent
- Biological and medical application

Example: Magnevist, Beclomethazone dipropionate, NX-200.

## > Multiple Antigen Peptide Dendrimer:

J. P. Tam introduced this type of dendrimer in 1988 and is mainly used for biological applications. **Structure:** A dendron-like molecular structure based on a polylysine backbone. Lysine with alkylamino side chains serves as an excellent monomer for introducing multiple branch points.

Method of synthesis: Convergent.

- 5. Use: Invaccinesanddiagnosticresearch
  - 6. Example: VivaGel

# > Frechet Type Dendrimer

**Structure**: Dendrimers with a poly-benzyl ether hyperbranched structure and carboxylic acid surface groups **Method of synthesis:** Convergent.

Use:

- Drug carrier
- Organic synthesis
- Purifiers
- Drug delivery
- Detecting agent,

#### Example:

Priostar TM, Dendron azides.

## VI. DRUG-DENDRIMER INTERACTIONS

The ability of dendrimers to increase solubility has stimulated study into potential drug interactions involving dendrimers. Drug-dendrimer interaction can be broadly classified into two categories:

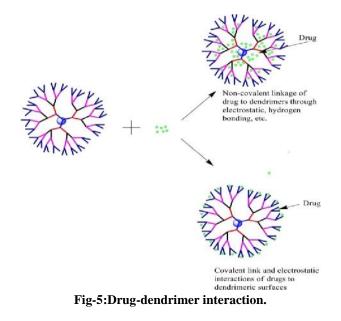
- (a) Drug encapsulation in dendrimeric cavity
- (b) Drug- conjugation.

(a)Drug encapsulation in dendrimeric cavity: A dendrimer's interior structure is often hydrophobic as a result of hydrophobic interactions and hydrogen bond formation and is appropriate for encapsulating hydrophobic drug and bio-actives.<sup>[28]</sup> Dendrimers of higher generation has greater ability

to encapsulate hydrophobic moieties. Although the interior regions of the dendrimer are substantially less exposed to the continuous vehicle phase as the number of branching and surface groups increases because of the de Gennes dense packing and structural folding.<sup>[29]</sup>An important factor in the development of "de Gennes dense packing" is the strength of the interactions between the neighbouring functional groups inside the molecule as well as the characteristics of the bulk solution (such as pH, polarity, temperature, etc.). These characteristics of dendrimer can be used to control the drug molecules' encapsulation and release from the dendritic structures.<sup>[30]</sup> Although non-covalent drug complexation or entrapment in dendrimers is the preferred method for the solubilization of many drugs, this strategy has drawbacks as well. For instance, after exposure to biological fluids, the drug dendrimer structure may be unable to control the drug's release from the dendrimer pockets or cavities due to insufficient intermolecular forces. However, physical drug encapsulation in dendrimeric cavities is a desirable method for solubilizing hydrophobic drug molecules if the dumping of the encapsulated drug can be reduced or eliminated.<sup>[31]</sup>

## (b)Drug-conjugation:

A dendrimer's terminal functional groups serve as sites for the covalent conjugation of biological, medicinal, and diagnostic compounds. A prodrug can be created using such a conjugation. The linker/spacer can be employed to change the macromolecular functioning and release profile of the conjugated entities prior to the drug-dendrimer conjugation. Drugs and dendrimers are conjugated to one another by these linkers, which include ester and amide groups, acid labile acyl hydrazone or cis-aconityl groups, and di-sulfide bridges. Linkers play an essential role in the in vivo stability of dendrimer-drug conjugates, according to studies. There have been numerous attempts to bind drug molecules to dendrimers by disulfide bonds, which glutathione within the cells can modify to control the release of the drug from the complex.<sup>[32]</sup>



# VII. PHARMACEUTICAL APPLICATION:<sup>[35]</sup>

### 1. Dendrimer in Ocular Drug Delivery:

PAMAM dendrimers possess carboxyl or hydroxyl surface groups to increase the residence time of pilocarpine and improve its bioavailability in the eye.

#### 2. Dendrimers in pulmonary drug delivery:

Positively charged PAMAM dendrimers (G2 and G3 technologies) increased the relative bioavailability of pulmonary drug delivery of Enoxaparin.

#### 3. Dendrimers in transdermal drug delivery:

Dendrimers' unique water solubility and its biocompatible properties aid in circulation time and successful drug delivery across the skin. For example, PAMAM dendrimers are complex with NSAIDs such as ketoprofen, diflunisal.

#### 4. Dendrimers in oral drug delivery:

Oral drug delivery investigates the use of human colon adenocarcinoma cell lines. Lower generation PAMAM dendrimers cross the cell membrane through a combination of two processes i.e Paracellular transport and adsorptive endocytosis.

#### 5. Dendrimers in central drug delivery:

Dendrimers have ideal properties that make them useful in targeted drug delivery systems. For example, PAMAM dendrimers conjugated with folic acid and fluorescein isothiocyanate for targeting the tumour cells and imaging respectively.

#### 6. Dendrimers for Controlled Drug Release:

Encapsulation of 5-fluorouracil into PAMAM dendrimers (G=4) designed with carboxymethyl-PEG5000 surface chains resulted in adequate drug loading, decreased release rate, and haemolytic toxicity.

#### 7. Dendrimers in Gene Delivery:

Dendrimers are primarily used as non-viral vectors for gene delivery. Various polyatomic compounds, along with PEI, polylysine, and cations, have been used as non-viral gene sources.

### 8. Dendrimers as solubility enhancers:

Dendrimers have a hydrophilic exterior and a hydrophilic interior and form both covalent and non-covalent complexes with drug molecules and hydrophobic substances to enhance their solubilizing behaviour.

#### 9. Cellular transport Use of dendrimer carriers:

PAMAM dendrimers with lauryl chains which is used to reduce toxicity and improve cellular uptake. For example, dendrimer-ibuprofen conjugate enters cells more rapidly compared to the pure drug. This suggests that dendrimers can successfully deliver drug conjugates to cells.

#### VIII. CONCLUSION

Individual characteristics of dendrimers make them ideal candidates for various applications. Dendrimers are artificial macromolecules with a highly defined structure that combine a large number of functional groups with a small molecular size. Since the first dendrimers were created, the chemistry of dendrimers has become increasingly important. The majority of drugs are class 2 drugs with a solubility problem that is improved by dendrimer drug delivery by encapsulating the molecule in the dendrimer's core. Dendrimer also improves the drug's stability. Drugs are integrated into dendrimers using electrostatic, covalent, and simple encapsulation methods. The structural characteristics of dendrimers, such as their shape, structure, size, branching, functioning, void space, and density, also made them a prime choice for drug delivery via a variety of channels. The multistep synthesis still requires a lot of work, even two decades after dendrimers were discovered.

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