JOURNAL OF BIOMEDICINE AND BIOCHEMISTRY
Volume 1 Issue 3 (2022), pp. 57–69

Journal JBB
ISSN:2958-0528

REVIEW ARTICLE

Dendrimer as a Recent Drug Delivery System: An Overview

Ghada Hamid Naji[1,*], Noor Yousif Fareed[2], and Worood Hameed Al-Zheery[3]

[1]College of Pharmacy, University of Babylon, Iraq.
[2]Department of Pharmaceutics, College of Pharmacy, University of Basrah, Iraq.
[3]Department of Pharmacy, Al-Esraa University College, Iraq

Corresponding author:

ghadahamid1988@gmail.com

[1]College of Pharmacy,
University of Babylon,
Iraq.

Received:September 23, 2022,
Revised:October 19, 2022,
Accepted:October 26, 2022,

DOI: 10.57238/jbb.2022.20109

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Abstract

Dendrimers, their production, characterization, and use in drug delivery are briefly covered in this article. Dendrimers are classically symmetric nanoscale molecules with an inner core and an outer shell that have well defined, homogeneous, and monodisperse structures. Dendrimers have a unique potential for encasing or entrapping bioactive substances because of their tree-like structure. As a result, they could win a prestigious statue in the fields of pharmaceutical, medical, and nutraceutical sciences. Numerous advantageous biological characteristics exist in them, including polyvalency, self-assembly, electrostatic interactions, best chemical stability, and minimal cell toxicity. While problems with solubility, stability, and bioavailability are limiting concerns for their implementation.

Keywords: Nanoparticles, Convergent, Divergent, Diagnostic Agent, Polymers

1 Introduction

Dendrimers are defined as homogenous, monodisperse molecules with nanoscale dimensions and radial symmetry that have arms or branches that resemble trees [1]. The Greek word dendron, that means "branching of a tree," is the source of the English word "dendrimer." Dendrimers are composed from polymeric globular branching and regular configurations that have specified forms and sizes ranging from 1 to 15 nanometers (nm), and they are utilized to enhance certain properties of a substance [2]. Physicochemical or biological properties of dendrimers can be changed through the functionalization of the end-groups (i.e., the groups reaching the outer periphery) [60, 61]. Divergent synthesis was founded by Fritz Vogtle in 1978, R.G. Denkewalter at Allied Corporation in 1981 [3], Donald Tomalia at Dow Chemical in 1983 and 1985, and George Newkome in 1985 [4]. Jean Fréchet introduced a convergent synthetic approach in 1990 [5]. Dendrimers are easily taken up by cells due to their nano size range [6]. Because of their unique characteristics dendrimers consider as promising candidates for a variety of applications [7]. Dendrimers can be functionalized through introduction of special functional groups on to their outer surface, such as COOH, COONa, NH2, or OH [8]. Dendrimers have many desired properties unlike traditional polymers that make them applicable in biological field, these properties include good water solubility [9], compatibility with biological systems [10], polyvalency and defined molecular weight [11]. Three different components make up a typical dendrimer: (a) a central core that is either a single atom or an atomic group with at least two identical chemical functions; (b) building blocks with multiple

interior layers made of repeating units; and (c) numerous peripheral functional groups, typically found on the exterior of the macromolecule, that play a significant role in its properties [12]. Figure 1 shows a fourth generation dendrimer, which has four focal points as you move from the center to the edge [1]. The term "generation number" describes how many focal points are present when the dendrimer surface moves away from the core [13].

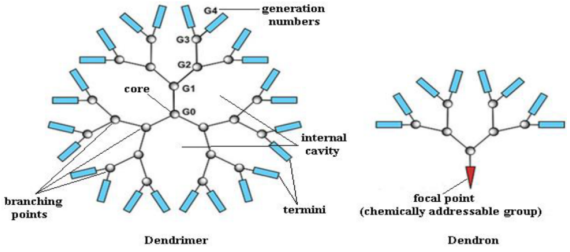

Figure 1: Demonstration of fourth generation dendrimer [14].

Dendrimers have a promising application in anticancer therapies and diagnostic procedures due to their well define , nanosized and desirable biological properties [15]. Additionally, they have a wide range of uses in supramolecular chemistry, especially in host-guest interactions and self-assembly procedures [7].

2 Advantages of dendrimers

There are many features of dendrimers that make them an appropriate choice in case of drug delivery, diagnostic and therapy vehicle.

1. Low polydispersity index (PDI) : Dendrimers often show a lower PDI this is because of careful control through production. The outermost divisions form spheres around a core of lesser density as branch density increases, and the outer surface density also increases. However, much of the space remains hollow as it gets closer to the core. This space can be designed to contain a variety of drugs [16].

2. High permeability Nanometer size range and uniformity in size of the dendrimers improve their ability to cross cell membrane (e.g blood brain barrier andccell membrane) and reduces the possibility of their removal from the body viaaliver or spleen [17, 18].

3. High regularity and purity The employed production method yields dendrimers showing homogeneous size distribution, clearly distinct surface functionality, and insignificant impurity. We could distribute drugs specifically using monodispersed dendrimers [19, 20].

4. High loading capacity By encapsulation and absorption on the surface, dendrimers configurations often used tooload and stock an extensive spectrum of organic and inorganic compounds. Drugs can become entrapped inside interior cavities as well as electrostatically adhere to dendrimer surfaces. [21].

5. Low immunogenicity When dendrimers are injected or administered topically, they have a modest or minor immunogenic response [22]. Chemical instability,ddrug leakage, aggregation andffusion during sstorage, solubilityiiin physiological environments, phospholipid lysis, and natural phospholipid purityaare all difficulties innthe vesicular system.

6. Improved permeability and retention outcome Dendrimers have a strong permeability and retention effect (depending on molecular weight) because to their small nano size range, which enables them reach directly to tumor cells more efficiently than small compounds due to tumor cells' leaky vasculature. One approach is through the lymphatic system, where drug-loaded dendrimers may be maintained. [23].

3 Synthesis of dendrimers

Dendrimers can be synthesized by two main processes:

3.1 Divergent method

Dendrimers are generated using this procedure, which is known as a bottom-up approach, starting with the core molecule and working outward. The first stage in the evolution of dendrimers is the production of a multifunctional core, Bn (n 2). To ensure accurate development, monomer type ABn (n 2) is used, where A is the active group and B is the deactivated/protected group. The primary layer of the dendritic structure is created by the interaction of the core active B functions with an excess of the A functionalities. The B functions of this layer are deprotected/activated to continue the extension, resulting in the formation of a first-generation dendrimer. Through the adding of a different monomer layer to the macromolecule, two dendrimer were produced. The number of dendrimers produced and the number of end groups produced increases when these procedures are repeated [24]. High rate of polymerization, synthesis of high molecular in addition to modification and change in surface groups of dendrimers

considered as the main advantages of this method. [25,26]. The best significant disadvantage of this technique, particularly in poly(amidoamine) dendrimers, is the occurrence of side reactions during synthesis. Incomplete reactions also occur in the end groups, resulting in structural flaws [27]. Other limitations for this method of dendrimer synthesis include a lack of diversity in the outer layers of the group, the creation of some low molecular weight compounds, and high reaction temperature sensitivity, which can produce reversible Michael addition reactions [28].

3.2 Convergent method

Dendrimer manufacturing starts at the end groups and moves inward to the core using a top-down approach. This technique mainly comprises tying branches to the central core and attaching peripheries to branches. Peripheries are joined to branches to produce the "wedge" shape. Typically, a core is connected to three to four wedges with varying peripheries [29]. The main advantages of this strategy are the ease with which the product may be purified and the great reduction in structural defects. The convergent technique has a large number of stages, difficulty synthesising dendrimersgwith higherkgenerations, and lower returns due to the central dendrons' decreasedd reactivity [30]. Owing to the presence of spatial inhibition in the reactionhbetween dendrons and molecularrnucleus in the convergent method, the synthesis of higher generations is extremely difficult. Figure 2 displays theksynthetic path for divergent and convergent methodologies.

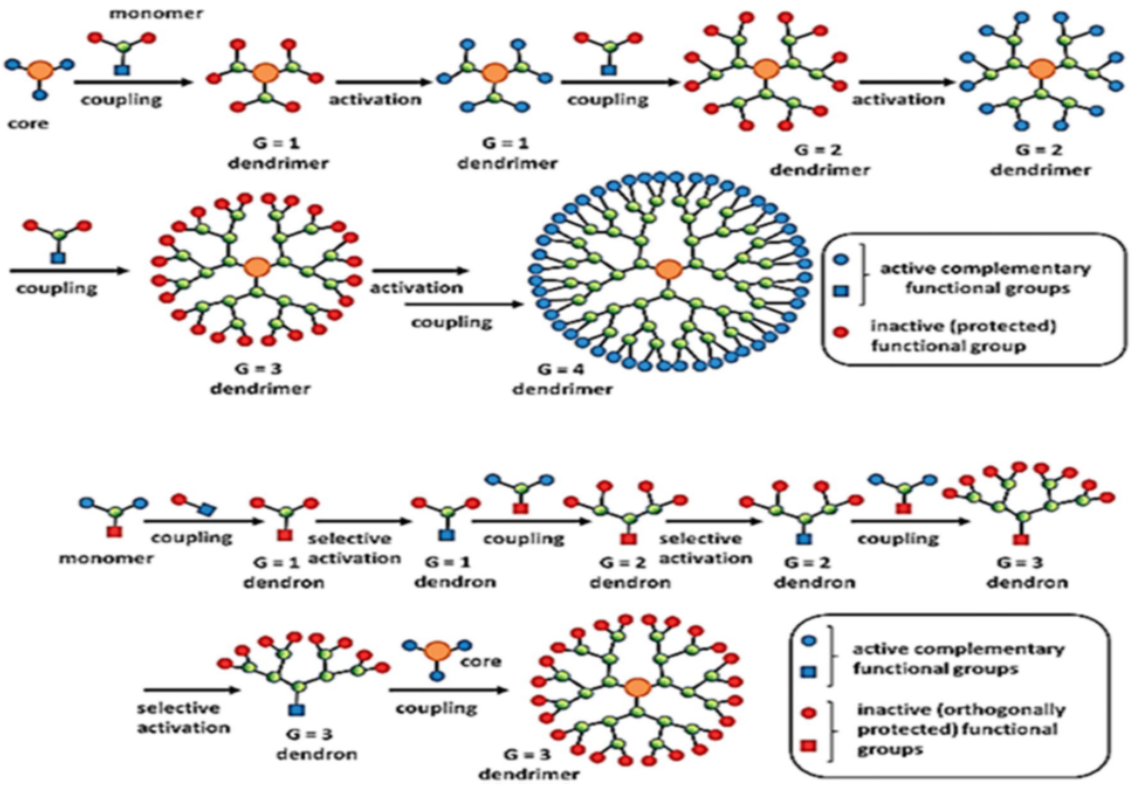

Figure 2: The two pathways for divergent and convergent approaches [27]

4 Other approaches for synthesis

4.1 Hypercores andkBranched Monomers growth

They required the pre-assembly of oligomeric species that will be combined to make dendrimers in fewer number of steps and with good yields, Figure 3.

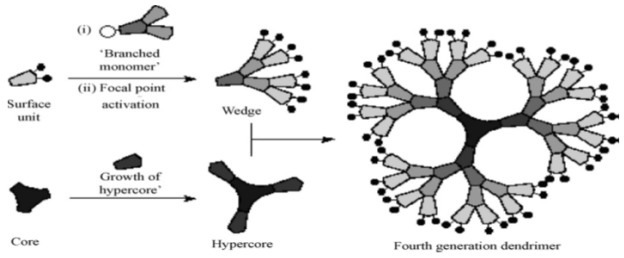

Figure 3: Hypercoresuand Branched Monomers growth [31].

4.2 DoublegExponential growth

It's similar to a linear polymer rapidegrowth process. From a single starting material, this process allows for the synthesis of monomers for both divergentkand convergent growth, Figure 4. The two products that result are then reacted to produce an orthogonally protected trimer that can be utilized to repeat the growth process. Fast synthesis is a strength of the double exponential growth strategy, which may readily be extendedfwith either divergent or convergent growth [31].

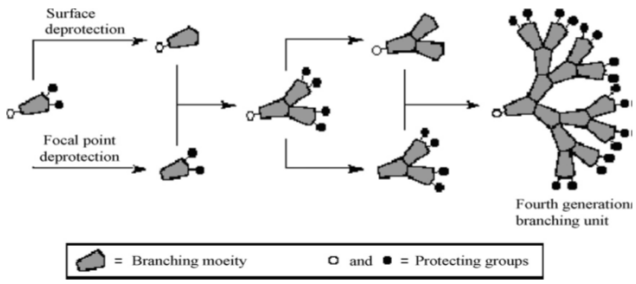

Figure 4: Double exponential growth method [31].

4.3 Lego chemistry

To synthesize phosphorus dendrimers, highly functionalized cores and branching monomers were used. The new technique allows for multiplications of the number of terminal surface groups from 48 to 250 in a single step after significant changes to the overall synthetic scheme. Small amounts of solvent are required for this synthesis, which also yields byproducts like water and nitrogen that are good for the environment.

4.4 Click chemistry

This method can produce dendrimers with a variety of surface groups in high purity and yield. Only sodium chloride was used as a byproduct in the isolation of allggeneration 2 and certain generationy3 Cu(I)-catalyzedfdendrimers [31].

5 Classification of Dendrimers

5.1 Simple dendrimer

They have monomer units that are easy to understand. Lester dendrimer is defined as a convergent synthesis of monodisperse dendrimers, the benzene tricarboxylic acid ester is defined mostly on the basis of symmetricallyjjsubstituted benzene tricarboxylic acid ester. Thesekmaterials have 46 A molecular diameters and are made up of 4, 10, 22, and 46 benzene rings linked symmetrically. [32].

5.2 Liquidkcrystalline dendrimer

These are created from mesogenic monomers, such as mesogenic polymers. Carbosilane dendrimer with mesogen functionalization. Functionalization of carbosilane dendrimers' end groups with mesogenic devices connected via a C-5 spacer results in liquid crystalline dendrimers forming an extensive smecticfphase at temperatures ranging from k17°C to 130°C [32].

5.3 Chiralgdendrimer

The chirality of chiral dendrimers is primarily relied on the formation of constitutionally different but chemically similar branches to an achiral middle, example. Pentaerythritol-derived chiral dendrimers [32].

5.4 Micellar dendrimer

Dendrimers with a unimolecular micelle configuration. Fullyfaromatic, water-soluble dendrimers that form a group of aromatic polymeric chains provided establishing an environment similar to gmicellar structures, that produce a complex with smallkknatural molecules in water [32].

5.5 Hybridkdendrimers

They are dendritic and linear polymer preparations of hybrid mass or graft copolymers. This creates room for their application as, for instance, surface-active agents, compatibilizers, or adhesives. Dendritic hybrid linear polymers [32].

5.6 Amphiphilic dendrimer

They are the wonders of globular dendrimers, which have an irregular but extremely well-controlled chain-end chemical division. These can be directed at the interface to generate liquid membranes that neutralize aqueous organic emulsions [32].

5.7 Metallodendrimer

Dendrimers interact with the steel ion to produce a complexation, which can be seen as Metallodendrimers, either within or on the periphery. The dendrimer based on the ruthenium bipyridine complex possesses desirable electrochemical and luminescent properties [32].

Table 1: Types, characteristics and methods of synthesis of Dendrimers

Number	Dendrimer type	Method of Synthesis	Examples	Characterization
1	PAMAM (Poly Amido Amine) Dendrimer	Divergent	Dendritech TM (USA)	It has an elliptical or spherical form. This type characterized by a high solubility and reactivity because of the richness of functional end groups and unfilled internal voids [33,34].
2	PPI(Poly Propylene Imine) Dendrimer	Divergent	Asramol by DSM (Netherlands)	It has a Di aminogbutane core structure and primary amines serve as end groups and tertiary propylene amines represent the center. This type is extensively utilized in material science and biology, and is commercially accessible up to G-5 [35]
3	Chiral Dendrimer	Convergent	They derived from pentaerythritol	Dendrimer chirality was determined using upon the chiral core's construction of constitutionally different but chemically similar branches [36].
4	Multilingualf Dendrimers	Convergent	VivaGelk	Dendrimers that have several prints of a functional group on their external surface are called this [37].
5	Tecto Dendrimers	Divergent	Stratus® CS Acuteg Care ™, Starburst®, Mercapto	These include of core surrounded by other dendrimers that each of them had a specific role, giving to a smart therapeutic system that could diagnose damaged cells and administer medicaments to them [38].
6	Hybrid Dendrimers	Divergent	Hybrid dendriticg linear polymer, Polysilsesquioxanes	They have characteristic of both dendritic and linear polymer [38].
7	Amphiphilicm Dendrimers	Divergent	SuperFect, Hydraamphiphiles and k bola-amphiphiles	These composed from two halves is electron donating and another is electron retreating.
8	Peptide Dendrimers	Convergent	Beta Casomorphinv (human)	Dendrimers that take amino acids as diverging or internal elements be known as peptide dendrimers [37]. These dendrimers best for both diagnosing and delivering vaccines.
9	Frechet-Typex Dendrimers	Convergent	Frechet typeq dendron azides,TM Priostar	Composed from a hyperbranched polybenzyl ether structure. The functional group COOH found at the surface of dendrimers which serves as a site for further functionalization and enhances dendrimer solubility [37].
10	PAMAMOSH (Poly Amidoamine Organosilicon) Dendrimers	Convergent and Divergent	SARSOX	Take into account inverted unimolecular micelles with outside hydrophobic organosilicon (OS) and inside hydrophilic, nucleophilic polyamidoamine as commercially viable dendrimers that incorporate silicon [37].
11	Multiple Antigen Peptide Dendrimers	Convergent and Divergent	vaccine and diagnostic research	These are polylysine-based molecular assemblies that resemble dendrons. The alkyl amino side-chain of lysine made it a suitable monomer for the addition of several branching pointsi [39].

6 Modes of Drug Encapsulation in Dendrimers

Different mechanisms for drug loading inside dendrimers can be exist such as through physical encapsulation, gelectrostatic interaction, and covalentkkconjugation. While drug release depends on core moiety and type of polymer used

6.1 Physical Encapsulation

By altering their shapes, cavities, and structural layouts, the other particles were trapped in the internal moiety of the macromoleculehusing this technique. The lipophilic and hydrophobicjinteractions, which result in interactions with drug moleculeskcontaining nitrogen or oxygentatoms and the release of the hydrogen bond, cause the interior cavities to remain empty, Figure 5. The loading of drugs by many in-

teractions, including hydrogen bonds and physical interactions. Several medications, includingkkanticancer medications like doxorubicin hydrochloride and methotrexate, can be dissolved with this method [40].

6.2 Electrostatic interaction

The interaction in this form of encapsulation occurs on the surface of dendrimers, which include a significant amount of NH2 and COOH groups that were employed to increase the solubility of lipid soluble active ingredients, Figure 6. Naproxenj, ibuprofeng, ketoprofen, diflunisal, and indomethacing are all easily ionizable drugs that formhhcomplexes with the multifunctionalhsurfaces of dendrimers bearing terminalggroups [40].

6.3 Covalent conjugation

This approach is employed for compounds with active groups on their exterior surface, as shown ing Figure 6. In this method, the hydrophilic labile links are broken down chemically and enzymatically to produce the conjugation. Examples of drugs that are conjugately bonded through spacers like polyethylene glycol paminobenzoic hacid, p-aminohippuric acid, and lauryl chainsg include ypenicillin V, venlafaxine, 5- aminosalicylic acid, naproxen, and propranololkconjugated with PAMAM dendrimers. By using a spacer, the drug's stability and kinetics are improved. This will leads to enhancing the drug solubility and achieved controlled release of medicaments [41].

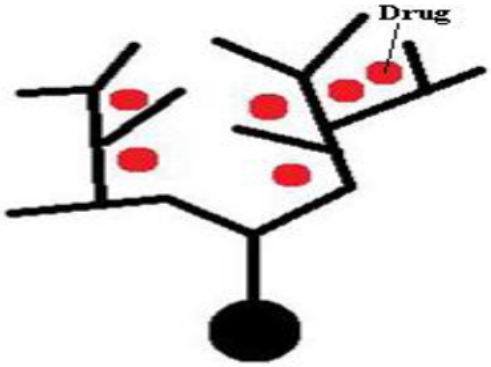

Figure 5: A dendrimer particle along with drug molecules loaded with in the branches [42].

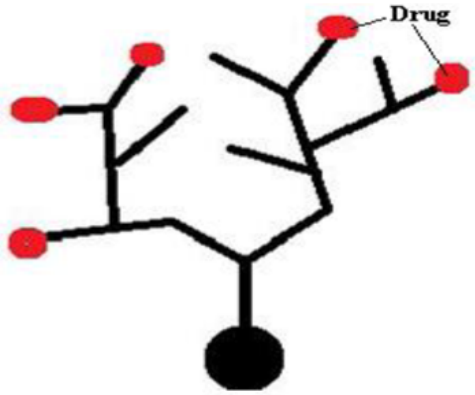

Figure 6: Drug molecule attached at the terminal surface of dendrimer branches [42].

7 Mechanism of Drug Delivery through Dendrimers

Drug delivery from dendrimers to the body can be occurred through two main mechanisms which are:

- First mechanism is through in vivo break down of drug dendrimer covalent bonding that occur in the presence of suitable enzymes or an environment able to splitting the bonds.
- Second mechanism is by changing the physical environment for example pH and temperature this will cause release of drug from dendrimers. This method, which happens in the core (endo-receptor) or outer shell (exo-receptor) cavities, is unaffected by external forces [43].

8 Influences changing Dendrimers characteristics

8.1 Effect of pH

The use of molecular dynamics to examine the structural behavior of PAMAM dendrimers as a function of pH reveals that the dendrimer has a prolonged conformation based on a substantially ordered structure at low pH (pH 4). Because of resistance between the positively charged amines at the dendrimer surface and the tertiary amines in the interior at this pH, the interior becomes increasingly hollow as the generation number grows. At pH 7, back-folding occurs, possibly as a result of hydrogen bonding between the positively charged surface amines and the interior uncharged tertiary amines. At higher pH (pH>10), the dendrimer agreement as the molecule's price equalizes, resulting in a more round (globular) form in which the non attractive interactions among

the dendrimer hands with the floor clusters are at their lowest. The structure backfolds more severely at this pH because of the fragile inter-dendron repulsive forces. [44, 45].

8.2 Effect of solvent

Dendrimers of all generations show more returned-folding when the solvent best is reduced, i.e. when the solvation is reduced. In comparison to higher generation dendrimers, low generation dendrimers have the strongest inclination toward back-folding due to poor solvation. NMR experiments on poly propylene imine dendrimers revealed that a non-polarffsolvent, such as benzene, dissolve the dendrimers weakly, encouraging intramolecular contacts between andtback-folding. Nevertheless, primary dendrimer such as PPI, can extend its conformation due to general hydrogen bonding that occur between the solvent and the dendrimer amines, when a weak acidic solvent for example chloroform acts as a hydrogen donor for the interior amines. According to both experimental and hypothetical revisions on amino-terminated PPI and PAMAM dendrimers, nonpolar aprotic (deprived) diluters produce better molecular densities in the middle because of back-folding, polar liquids, on the other hand, solvate the dendrimer fingers and increase the molecular density of the dendrimer surface (polar dendrimers). The extra hydrophobic dendrimer sections may be exposed when the polar surface groups are back-folded, which reduces the surface polarity of the back-folded dendrimer [46].

8.3 Effecthof salt

Increase ionic strength (increase salt amount) show a tough effect on charged PPI dendrimers, favoring concentrated conformation and a high degree of back-folding, comparable to what is seen when pH is raised when solvation is inadequate. The repulsive forces among the charged dendrimer segments result in a prolonged confirmation under low salt conditions, which reduces rate repulsion inside the structure [44].

8.4 Effect of concentration

Small particles like solvents, salts, oroprotons don't always affect the conformation of dendrimers with flexible structures; nevertheless, the molecular mass and shape of dendrimer can be significantly impacted by larger substances, such as other dendrimers or surfaces.. A growing number of smaller dendrimers are produced as dendrimers become more conscious, according to research using small-angle X-ray scattering (SAXS) on PPI dendrimers (G4, G5) in a polar solvent like methanol. Additionally, the repulsive interactions can be lessened through molecular shrinkage that exist among the molecules of dendrimers, enabling dendrimers to display more closely packed intermolecular packing [47].

9 Applications of Dendrimers

Dendrimers have special structural features such as nanoscopic size, spherical surface, good branching, and exciting properties such as low viscosity, hight-solubility, and good reactivity, which, in combination of great functionalities of dendritic polymers, make them suitable for a wide range of potential applications in various fields [48].
Integrated medical and diagnostic applications include gene therapy, chemical sensors, drug delivery systems, adhesives and coatings, light harvesting materials, catalysts, electrical applications, separating agents, and many more [49, 50].

9.1 Dendrimer in transdermal drug delivery

Dendrimers are capable of increasing medication qualities like solubilityjjand plasma circulation time through transdermal formulations and successfully delivering pharmaceuticals due to their desired properties such as water solubility and biocompatibility. For example, increasing drug penetration through the skin by combining PAMAM dendrimers with NSAIDs such as Ketoprofen and Diflunisal, and increasing PAMAMndendrimer bioavailability via employing indomethacink as a typical drug in transdermalhhdrug application [51, 52].

9.2 Dendrimers in oral drugjdelivery

Because to its progressiveness in production, small cost, simplicity of administration, and elasticity in dosage form preparation, oral medication delivery is the most favorable and has received greater importance in the therapeutic area. Solids make up the majority of the controlled release method for oral use, which relies on dissolving, diffusion, or a combination of the two to regulate the drug's release rate [53]. One notable advantage of oral drug administration is that the medication is slowly liberated from the dose and keeps a constant blood level using regulated drug delivery systems, resulting in less fluctuating plasma drug levels. Along with the benefits, oral administration has significant drawbacks, such as limited solubility in aqueous vehicles along with poor diffusion through intestinal tissues [54].

D'Emanuelegand his colleagues looked at the impact of dendrimer production and conjugationhon PAMAM dendrimer cytotoxicity, penetration, and transfer mechanisms. The cytotoxicity and penetration of dendrimers increased as the concentration and production of dendrimers increased. Conjugation with lauryl chloride resulted in a reduction in cytotoxicity.

9.3 Dendrimer application in Nasal DrugfDelivery

Nasal administration is an interesting alternative to parenteral administration, which can be bulky, and oralggadministration, which suffer from unacceptably and poorh bioavailabilities [55]. The dendrimer polyamidoamine (PAMAM)tthas gotten a lot of attentionkfor nose-to-brain directing. Dendrimers are a type of dendrimer that grows from a central core. On their surface, a variety of molecules can be connected. An arginine was attached to the surface of a PAMAM dendrimer by Kim et al [56]. Nanoparticles having a particle size equal to 188.7 1.9 nm and a charge of +22.3 mVn were created as a result. The nanoparticles were electrostatically linked using smallhinterference RNA (siRNA)ktargeting the high mobility group box 1 proteiny(HMGB1). HMGB1 is a danger signal emitted by dying cells that exacerbates the damage caused by a stroke or other neurotoxic shocks. They showed a wide distribution in the brain after intranasal delivery, with the hypothalamus,yamygdala, cerebral cortex, andgstriatum.

Additionally, a successful knockdown of the target protein, HMGB1, was associated with the localization of the PAMAM dendrimer and siRNA. The group that received the construct intranasally had a considerably smaller infarction volume when a stroke was induced in rats.

Perez et al. demonstrated the possibility of mucoadhesive dendrimer gel compositions for nose to brain administration [57]. They created dendriplexes by coupling radioactivejjsiRNA to PAMAM dendrimers and incorporating these particles intojjjmucoadhesive gels having either 1% (w/w) chitosan or 0.25 % (w/w)lcarbopol 974P NFTM.

In order to achieve in-situ gelation, the chitosangor carbopol was blended by 23 % (w/w) of thermosensible poloxamer. Transition of the phase exists between the temperature of nasal region (32 °C to 35 °C) and roomktemperature in such a thermosetting gel. As a result, it can be given as a liquid.

No toxicity was found when varied concentrations of the different gels werektested. Intranasal injection of two doses was required to achieve higher radioactivity concentrations in the brain than IV giving dendriplexes or by nasal therapy of bare siRNA.

9.4 Dendrimers in CNS Drug Therapy

Because the great bulk of prospective central nervous system drugs have poor brain absorption, improved delivery techniques may be beneficial in allowing them to penetrate the BBB. The medication is encapsulated in the particle or linked with it, obscuring its physiochemical properties [58].

Nanoparticles have been produced and have shown promise in the delivery of CNS drugs [59]. Dendrimers have received a lot of attention due to their benefits, that include [1] drug levels will be maintained in a medicinally needed level, [2] improved half-life, [60] improved solubility, drug stability, and penetrability of medicaments, and [61] capacity to distribute a range of medications, [3] reducedkmacrophage absorption, [4] quick cellular entrance, [5] increased delivery efficiency, and [6] minimized adverse oeffects through targetedkdelivery [62,63].

9.5 Dendrimers in protein and peptide delivery

As a result of its quick clearance from serum jand relatively low penetrability to the brain, the administration of helpful protein and peptide particles for the management of several neurodegenerative illnesses highly difficult. The dendrimer method is being used in the development of effective delivery systems. Pierpaoloh Moscariello et al. (2018) created a dendronized streptavidin (DSA) that resembled natural proteins structurally. Figure 7 demonstrates how biotin click chemistry was used to connect PAMAModendrimers of two generations (G2 and G3) along with distinct positivek charges to the streptavidinjcore [64].

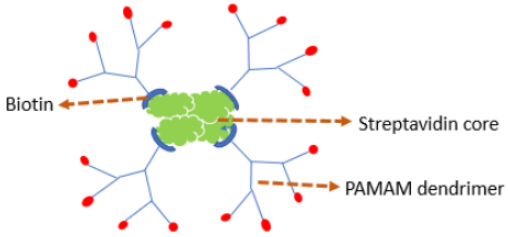

Figure 7: The PAMAMmdendrimers linked to the streptavidin core through biotin [65].

The work effectively showed that a protein molecule can traverse the BBB via transcytosis via the endosomal path with great biological compatibility, indicating that novel flexible nano platforms for biopharmaceutical administration can be advanced in the future [66].

9.6 Dendrimers in antitumor therapy

Dendrimers molecules have been used as a diagnostic reagent for tumor identification by magnetic resonance imaging and as a contrast agent; these compounds can be employed for specific imaging purposes by altering their size and hydrophilicity and combining them with tumor targeting antibodies [67]. The drug should be harmless in the absence of irradiation, acting as a prodrug when not treated.
Dendrimers have photosensitizers called 5- aminolevulinic acid, which was linked at the outward of dendrimers and explored as a treatment of tumorigenic keratinocytes using photodynamic therapy (PDT) [68]. The beneficial uses of dendrimers in the realm of cancer, where various models of tumor targeting for diagnostic purposes were documented and where a cancer-specific cell surface element that canf be implanted has been disclosed.

9.7 Dendrimers in foetal neurotherapy

During pregnancy, some infections such as bacterial vaginosis, chlamydia, cytomegalovirus, syphilis, and others can cause life-threatening illnesses in neonates. It is preferable to treat prenatally to manage such infections as early as feasible in the foetal period. Zhang F et al. published a study using PAMAM dendrimers in a maternal intrauterine inflammation-induced rabbit model with Cerebral Palsy. It is a chronic childhood disease in which an intrauterine infection is a significant risk factor. They employed hydroxyli (D-OH)+and carboxyl (D-COOH) end groups to modify the surface of PAMAM dendrimers and injected the dendrimer solutions intra-amniotically to examine placental barrier crossing and microglial targeting to minimize neuroinflammation.
Both D-OH and D-COOH penetrate fetaliicirculation, however D-OHjhas betterHbrain accumulation because of surface charge density that is neutral, whereas D-COOH is limited to blood vessels, according to distribution studies. This research suggests that delivering dendrimers intra amniotically could be an useful way to treat fetal infection and associated neurological problems. These results provide a ray of courage for a dendrimer-based translational therapy to treat pediatric brain damages [69].

10 Conclusion

Dendrimers are attractive prospects for a number of applications due to their distinctive characteristics. Dendrimers are synthetic macromolecules having many functional groups, a precise molecular structure, and a small molecular size.
The chemistry of dendrimers has gained a lot of attention since the first dendrimers were created. The purpose of this research was to devise a method for creating and examining a novel class of macro- and micromolecules. Dendrimers have been known for more than 20 years, but the multi-step preparation remain needs more time and work.
Dendrimer drug delivery has a variety of intriguing qualities while being in its early stages. Dendrimers are anticipated to be a practical polymer in the biomedical, pharmaceutical, and biopharmaceutical industries in the twenty-first century. Dendrimers are useful carriers in a range of applications due to their readily modifiable characteristics, including as size, shape, branching length, and surface functionality.Toxicity issues may still exist, but they will be remedied by altering the dendrimer structure. For this technology to be commercialized, more research is needed to determine cost-effectiveuusynthesis methodologies and the interaction between dendrimer and therapeutic compounds.

Conflict of Interest: No conflicts of interest exist between the authors and the publication of this work.
Ethical consideration: The ethical committee approved the study at the University of Babylon.

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How to cite

Naji G. H.; Fareed N. Y.; Al-Zheery W. H.; Dendrimer as a Recent Drug Delivery System: An Overview. Journal of Biomedicine and Biochemistry. 2022;1(3):57-69. doi: 10.57238/jbb.2022.20109