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Review Article

DENDRIMERS AND ITS APPLICATION

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ABSTRACT
A dendrimer can described as a macromolecule characterized by its highly branched 3D structure which provides a high degree of surface functionality and versatility Dendrimers also referred to as the "Polymers of the 21st century." Dendrimers components, namely (1) an initiator core (2) Interior layers (generations) composed of repeating units, radically attached to the interior core. (3) Exterior (terminal functionality) attached to the outermost interior generations. The properties of dendrimers are dominated by the functional groups on the molecular surface for example a dendrimer can be water soluble when its end group likes a carboxyl group. The major application of dendrimers are: Gene and oligonucleotide delivery, Targeting of anticancer chemotherapy, As anti-infective agent, In vivo diagnostics, Targeted and Controlled release drug delivery, In photodynamic therapy, In industrial processes etc. Recent successes in simplifying and optimizing the synthesis of dendrimers provide a large variety of structures with reduced cost of their production. Also as research progresses, newer applications of dendrimers will emerge and the future should witness an increasing numbers of commercialized dendrimer based drug delivery systems.

Key Words: Dendrimers, Interpenetrate, Initiator core, Arborols, Cascade molecule, Divergent methods, Convergent methods, PAMAMs, Poly(propylene imine) dendrimers, Segment-block dendrimers, Layer-block dendrimers, Contrast agents, Delivery of drugs, Industrial processes.

INTRODUCTION

Dendrimers are repeatedly branched roughly spherical large molecules and posses well defined chemical Structures[1]. The word Dendrimer comes from a Greek word which means to "tree". The other synonyms for dendrimer include arborols and cascade molecules. A dendrimer is typically symmetric around the core (Fig.1), and often adopts a spherical three-dimensional morphology. In the view of polymer chemistry dendrimers are nearly perfect monodisperse macro molecules with a regular highly branched three dimensional structures (Fig.3) and consists of three architectural components like core, branches, and end groups[2,3]. They are built from a starting atom, such as nitrogen, to which carbon and other elements are added by a repeating series of chemical reactions (Fig.2) that produce a spherical branching structure[4].

The three distinguished architectural components [4,5] of a dendrimers are namely

(i) An initiator core.

(ii) Interior layers (generations) composed of repeating units, radically attached to the interior core.

(iii) Exterior (terminal functionality) attached to the outermost interior generations.

TYPES OF DENDRIMERS

1. PAMAM Dendrimer

Poly (amidoamine) dendrimers (PAMAM) are synthesized by the divergent method starting from ammonia or ethylenediamine initiator core reagents. They are constructed using a reiterative sequence consisting of (a) a double Michael addition of methyl acrylate to a primary amino group followed by (Fig.4) (b) amidation of the resulting carbomethoxy intermediate with a large excess of ethylenediamine.

2. PAMAMOS Dendrimer

Radically layered poly (amidoamine-organosilicon) dendrimers (PAMAMOS) are inverted unimolecular micelles that consist of hydrophilic, nucleophilic polyamidoamine (PAMAM) interiors and hydrophobic organosilicon (OS) exteriors[8]. These dendrimers are exceptionally useful precursors for the preparation of honeycomb-like networks with nanoscopic PAMAM and OS domains[9].

3. PPI Dendrimer

Poly (propylene imine) dendrimers (PPI) are synthesized by the divergent method starting from 1, 4-diaminobutane. They are grown by a reiterative sequence consisting of (a) a double Michael addition of acrylonitrile to the primary amino groups followed by (b) hydrogenation under pressure in the presence of Raney cobalt. Products are made up to generation[10].

4. Tecto Dendrimer

These are composed of a core dendrimer, surrounded by dendrimers of several steps (each type design) to perform a function necessary for a smart therapeutic nanodevice. Different compounds perform varied functions ranging from diseased cell recognition, diagnosis of disease state drug delivery, reporting location to reporting outcomes of therapy. Tecto-dendrimers are composed of a core dendrimer (Fig.5), which may or may not contain the therapeutic agent, surrounded by dendrimers. The surrounding dendrimers are of several types, each type designed to perform a function necessary to a smart therapeutic nanodevice[10].

5. Multilingual Dendrimer

In these dendrimers, the surface contains multiple copies (Fig.6) of a particular functional group[11].

6. Chiral Dendrimer

The chirality in these dendrimers are based upon the construction of a constitutionally different but chemically similar branches (Fig.7) to chiral core[12].

7. Hybrid Dendrimers linear polymer

These are hybrids (block or graft polymers) of dendritic and linear polymers[12].

8. Ampiphilic Dendrimer

They are built with two segregated sites of chain end (Fig.8), one half is electron donating and the other half is electron withdrawing[13].

9. Micellar Dendrimer

These are unimolecular micelles (Fig.9) of water soluble hyper branched polyphenylenes[13].

SYNTHESIS OF DENDRIMERS

Dendrimers can contain three major portions, The core, inner shell and outer shell generally dendrimers can synthesized to exhibit different functionality in each of these portions, to control physical properties such as solubility, thermal stability, and attachment of compounds for particular applications. With the help of Synthetic methods (Fig.10)of dendrimers synthesis can precisely control the size and number of branches on the dendrimer[13].

There are two defined methods of dendrimer synthesis

1. Divergent synthesis
2. Convergent synthesis

Divergent Method

This is mechanical reaction. The dendrimer is assembled from multifunctional core, which is extends outward by a series of reactions (Fig.11), Each step of the reaction must be driven to full completion to prevent mistakes in the dendrimer, which can cause trailing generations (some branches are shorter than the others). Such impurities can impact the functionality and symmetry of the dendrimer, but are extremely difficult to purify out because the relative size difference between perfect and imperfect dendrimers is very small[14].

Convergent Method

Dendrimers generally made of small molecules that end up at the surface of the sphere and reactions proceed inward and are evenly attached to the core this method (Fig.12) makes it much easier to remove impurities and shorter branches along the way, so that the final dendrimer is more monodisperse[14].

APPLICATION OF DENDRIMERS IN DRUG DELIVERY

A successful drug must perform the demanding tasks of selectively recognizing and binding to a molecular target, then triggering an appropriate biological response, all the while possessing pharmacological properties that render it ''drug-like''[14]. In some cases, nature has supplied compounds – such as aspirin or penicillin – that can be used directly as drugs but the more common situation is that many otherwise promising therapeutic agents are not successful in the clinic because of their poor pharmacological properties[15]. The properties of dendrimers, in particular the synthetic ability to provide them with many different biological properties, along with their capacity to carry conjugated surface molecules or encapsulated guest molecules, make them immediately attractive as potential vehicles (Fig.13) for drug delivery[16,17]. Dendrimers have emerged as promising nanoscale delivery vehicles for targeted delivery of drugs and imaging agents[18]. Dendrimer-drug conjugates have been investigated for oral, parenteral ocular transdermal colon and topical routes of administration[19]. The Dendrimer-drug conjugates are designed to carry therapeutic agents to specific tissues to reduce systemic effects and increase efficacy at the targeted sites[20].

Researchers are working to convert dendrimers like these into useful drug-delivery tools. But dendrimers are already widely used in the lab. Qiagen's Superfect DNA transfect ion reagent is a dendrimer whose positively charged surface binds the nucleic acids negatively charged phosphate backbone.

If Dendrimer-drug conjugates can be designed to be confined to either maternal or fetal compartments, there will be significant therapeutic benefits[21.] The success of this strategy depends on the stability and specificity of the conjugate in the body as it reaches the target site (or, target tissue) with subsequent release of drugs before the conjugate is eventually cleared from the body[22]. The release drugs from the dendrimer conjugate is often slow and is largely governed by the nature of linking chemistry and the release of drugs from dendrimers conjugates can be modulated by choice of appropriate spacer or linker to avoid release in physiological conditions such as blood or plasma and to trigger release at the target site[23]. Interestingly, this criterion is not essential in all instances, and some dendrimer conjugates exhibit efficacy in their conjugated forms. The dendrimer biodistribute rapidly and are localized in major organs within minutes of administration[24]. The inability to control passage of small drug molecules across human placenta has been accepted[25.]

However progress towards achieving safe and selective drug therapy during pregnancy by proper drug design and development has not been undertaken. The ability to design biocompatible. Dendrimer-drug conjugates that rapidly biodistribute, are stable during retention in circulation, and release the drug only at a targeted site suggests a possible mechanism to avoid the undesirable transfer of certain small drug molecules to fetus, which could be toxic to the concepts. The benefits and safety of drugs conjugated to the dendrimers and administered to the pregnant woman and unborn fetuses are yet to be studied[26]. The present study describes the *ex-vivo* transport and biodistribution of dendrimer conjugates in the dually perfused human placental lobule[27]. This study also develops the potential for use of polymer–drug conjugates as delivery vectors to selectively treat the mother without affecting the fetus [28].

Drug delivery efforts are complicated by the diversity of molecules that hold potential therapeutic or diagnostic value briery reviewing three classes of drug candidates based on size demonstrates the wide applicability to drug delivery[29]. First, regarding ''small molecules'', many low molecular weight drug candidates are limited by poor solubility in aqueous environments or, if they are soluble, face rapid elimination from the bloodstream through filtration in the kidney[30]. In the past, efforts have been made to modify the molecule itself, often following the ''rule-of-five'' guidelines developed by Lipinski to raise awareness of the properties and structural features that render molecules more or less ''drug-like. Dendrimers present an attractive alternative strategy to the redesign of the drug because they allow unfavorable properties of a small molecule, such as insolubility, to be overcome by the larger characteristics of the macromolecule[31]. An approach for improving the pharmacological properties of higher molecular weight drug candidates, analogous to Lipinski's guidelines for the modification of small molecule drugs, has been applied for protein therapeutics such as recombinant antibodies and protein toxins used in cancer treatment[32]. In these cases, the amino acid sequences of recombinant proteins have been ''humanized'' by genetic engineering to avoid immunogenicity and their glycosylation patterns have been modi- fied to increase serum half-life[33].

These efforts, undertaken with actual proteins, illuminate design features that can benefit the development of protein mimics, dendrimers[34]. In particular, the ''humanizing'' experiments show that small changes, such as the substitution of a single amino acid for another, can avoid significant problems like undesired systemic immune responses. In the same manner, small changes in the surface properties of dendrimers, such as the addition of poly(ethylene glycol) (PEG), can avoid unwanted immunogenicity[35]. Finally, even extremely large therapeutic candidates, notably plasmids or naked viral DNAs used for non-viral gene delivery that are well beyond the size of traditional drugs, are also benefiting from dendrimer-assisted delivery[36]. Dendrimers have ideal properties which are useful targeted drug delivery system. One of the most effective cell specific targeting agents delivered by dendrimers is folic acid PAMAM dendrimers modified with carboxymethyl PEG5000 surface chains revealed reasonable drug loading a reduced release and reduced hemolytic toxicity compared with the non-PEGylated dendrimer A third-generation dendritic unimolecular micelle with indomethacin entrapped as model drug gives slow and sustained in vitro release, as compared to cellulose membrane control[37,38,39] .

Controlled release of the Flurbiprofen could be achieved by formation of complex with amine terminated generation 4 (G4) PAMAM Dendrimers. The results found that PEG-dendrimers conjugated with encapsulated drug and sustained release of methotrexate as compare to unencapsulated drug[39,40]. In control drug release dendrimers act as the anticancer drugs adriamycin and methotrexate were encapsulated into PAMAM dendrimers (i.e. G=3 and 4) which had been modified with PEG monomethyl ether chains (i.e. 550 and 2000 respectively) attached to their surfaces[41]. A similar construct involving PEG chains and PAMAM dendrimers was used to deliver the anticancer drug 5-fluorouracil. Encapsulation

of 5- fluorouracil into G=4 Dendrimers in gene delivery increase in the cytotoxicity and permeation of dendrimers Dendrimer-based transfixion agents have become routine tools for many molecular and cell biologist's dendrimers are extensively used as non-viral vector for gene delivery[42]. The use of dendrimers as gene transfixion agents and drug-delivery devices have been extensively reviewed part[43]. Various polyatomic compound such as a PEI, polylysine, and cationic have been utilized as non-viral gene carrier[44].

Nanoparticle uptake from the gut is important as an additional route of entry into systemic circulation (Fig.$_{14}$) and the translocation of particular substance across gastro intestinal track is now well documented phenomena offering new potential for the delivery of drugs even with the very poor dissolution profiles and label chemistries via encapsulation in bio degradable nano particles [46-51]. Researchers stated that in the last few years have seen acceleration in the number of publications describing the varying facets of this approach and the multidisciplinary nature of this field[53]. This review delineates data from this rather fragmented area and from cognate fields to provide a physicochemical viewpoint of the importance of surface chemistries of oral drug delivery vehicles and their interactions in and with gut contents prior to uptake[56]. Evolving vistas include a better understanding of the plasticity of the intestinal epithelium and M-cell induction as well as the influence of disease states on particulate uptake. In this review we address a number issues deemed vital to an understanding of the subject including (i) some background knowledge on particulate uptake (the subject of several reviews), (ii) factors affecting uptake such as diameter and surface charge and character, (iii) the dynamic nature of particle interactions in the gut, (iv) the dynamic nature of the processes of capture, adhesion, uptake, transcytosis and translocation, and (v) the influence of surface Ligands[61-62].

There is now a growing importance using dendrimers in drug, gene and vaccine delivery and according modern studies dendrimers are also using as therapeutic agents[63]. The oral absorption and organ distribution of some dendrimers has been studied and the structure and size-related toxicity and biocompatibility of many types of dendrimers is being actively researched[64]. Interaction of dendrimers with other drugs and dyes providing potential applications in areas such as the solubilisation of hydrophobic molecules and molecular inclusion formation[65]. Dendrimers have been designed to act as nanoscopic containers or dendrite boxes and unimolecular micelles and reverse molecular micelles have been described. Dendrimers have been variously proposed as pH-sensitive controlled drug release systems, catalysts and as chromatographic materials[66]. Dendrimers posses unique characteristics including monodispersity and modifiable surface functionality including highly defined size and structure, these ideal characteristics of dendrimers makes polymers attractive candidates as carrier in drug delivery applications. Drug delivery can be achieved by coupling a drug to polymer through one of two approaches[67].

Dendrimer attached to the cell membrane, dendrimer conjugation to DNA Standard Hydrophobic drugs can be complexed within the hydrophobic dendrimer interior to make them water-soluble or drugs can be covalently coupled onto the surface of the dendrimer. Using both methods in this study the experiment conducting team compared the efficacy of generation 5.

PAMAM dendrimers in the targeted drug delivery of methotrexate coupled to the polymer [68]. The amine-terminated dendrimers bind to negatively charged membranes of cells in a non-specific manner and can cause toxicity in vitro and in vivo. To reduce toxicity and to increase aqueous solubility, modifications were made to the surface hydroxyl groups of the dendrimers. For targeted drug delivery, the dendrimer was modified to have a neutral terminal functionality for use with surface-conjugated folic acid as the targeting agent. The complexation of methotrexate within a dendrimer changes the water insoluble drug into a stable and readily water-soluble compound. When this dendrimer complexed drug, however, was placed in a solution of phosphate buffered saline, the methotrexate was immediately released and displayed diffusion characteristics identical to free methotrexate. Covalently coupled methotrexate dendrimer conjugates were stable under identical conditions in water and buffered saline. Cytotoxicity tests showed that methotrexate as the dendrimer inclusion complex had an activity identical to the free drug in vitro. In contrast, folic acid targeted dendrimer with covalently conjugated methotrexate specifically killed receptor-expressing cells by intracellular delivery of the drug through receptor-mediated endocytosis. This study demonstrates that while drug as a dendrimer inclusion complex is readily released and active in vitro, covalently conjugated drug to dendrimer is better suited for specifically targeted drug delivery [69-72].

Example

Dendrimer would be limited in their transfer across the human placenta when compared to smaller drug molecules alone, suggesting novel methods for selectively delivering therapeutics to the pregnant woman (Fig.$_{15}$) without significant transfer to the fetus, especially since the half life of the dendrimers in blood is relatively short[71].

APPLICATION OF DENDRIMERS FOR GENE DELIVERY

Delivery vectors for intracellular delivery of nucleic acids. Apart from viruses, synthetic cationic vectors (Fig.$_{16}$) such as cationic polymers, branched dendrimers, cell-penetrating (CP) peptides and cationic liposomes can be used to deliver genes into cells. Properties of an engineered synthetic vector for gene therapy in the future. In addition to exhibiting good biocompatibility, loading capacity and transfection efficiency, a future synthetic vector may also be designed to have a desired intrinsic biological activity that would enhance the effects of gene therapy.

The delivery of small molecules complexed as guest molecules in internal void spaces of dendrimers is, at least in retrospect, intuitively obvious. By contrast, the delivery of extremely large macromolecules, such as MDa-sized plasmid DNA for non-viral gene therapy, is counter-intuitive because the encapsulation of a ''guest'' molecule many times the molecular weight of the dendrimer itself appears impos-Dendrimers in Cancer Treatment and Diagnosable. Nonetheless, experimental evidence had demonstrated that gene delivery (Fig.$_{17}$) strategies also benefit from the participation of dendrimers. For example, from its original discovery of efficacy for gene delivery, the fractured form of PAMAM, known as Superfect TM is now a commercially-available transfection agent for in vitro applications. Typical approaches to optimize dendritic gene delivery for in vivo use have involved the surface modification of a PAMAM backbone, either with arginine or hydroxyl groups. Alternatively, the results reported by Kim and coworkers, who demonstrated improved gene delivery with a novel PAMAM-PEG-PAMAM triblock copolymer, show that construction of dendrimers composed of new building blocks is warranted . Although still in their infancy, there are efforts afoot to exploit dendrimers for the delivery of smaller nucleic acids such as antisense oligonucleotides and short interfering RNAs (siRNA); the success of these applications is likely to depend on the continuing development of novel materials for dendrimer synthesis [75].

APPLICATION OF DENDRIMERS AS ''PRO-DRUGS''

Once a dendrimer carrying an encapsulated drug reaches the intended site of action, the guest molecule generally must be released to gain bioactivity. Indeed, a concern is that the active drug would ''leak'' out prematurely, thereby reducing the amount available for the intended therapeutic intervention, or more ominously, result in systemic toxicity. Reassuringly, early

experiments showed that the close packing of dendritic branches on the surface of the macromolecule effectively formed a ''membrane'' that reduced diffusion to immeasurably slow rates. In other cases, the release of encapsulated guest molecules was relatively faster, occurring over a few hours, apparently through hydrolytic degradation of the dendrimer in aqueous conditions. The observation that guest molecules could be liberated at different rates demonstrated that viable opportunities exist to tailor the release for either slow or rapid delivery.

At present, additional control of delivery rates is being sought; for instance, the ability of a dendrimer to instantaneously release its entire drug payload upon reaching its cellular target would be valuable. Promising steps in this direction are being taken by the development of pH-sensitive materials, the fine tuning of hydrolytic release conditions, and the selective liberation of guest molecules on the basis of their size or shape.

PHARMACEUTICAL APPLICATIONS

Dendrimer as Solubility Enhancers

Solubility is very important factor in drug delivery, on the other hand there are many drugs with very strong therapeutic activity these are not able use due to poor solubility properties. Water soluble dendrimers (Fig.19)are capable of binding and solubilizing small acidic hydrophobic molecules with antifungal or antibacterial properties, because dendrimers posses hydrophobic core and hydrophilic surface layer. This characteristic offers the opportunity to soluble poorly soluble drugs by encapsulating them within the dendritic structure at all concentrations of dendrimer.

Example

A hydrophilic–hydrophobic core-shell dendrimer with PAMAM interior and long alkane chain exterior was shown to bind 5-flurouracil, a water-soluble anti-tumor drug .After phospholipid coating of the dendrimer–fatty- acid macromolecule, oral bioavailability in rats of 5-flurouracil was nearly twice the level of free 5-flurouracil . Dendrimer-based carriers could offer the opportunity to enhance the oral bioavailability of problematic drugs[74].

Cellular Delivery Using Dendrimer Carriers

According to Kannan et al. the dynamics of cellular entry into A549 human lung epithelial carcinoma cells of a range of PAMAM dendrimers (G4-NH_2, G3-NH_2, G4-OH, PEGlayted G3 [G3-PEG]) and a hyper branched polymer (polyol). G4-$NH_2$and G4-OH entered cells more rapidly than did G3-NH_2, polyol or G3-PEG. It was suggested that the rapid entry of G4-NH_2 might be a result of the cationic nature of the amine surface groups, which may interact electro statically with negatively charged epithelial cells and enter via fluid phase pinocytosis. The lower rate of cellular entry of G3-NH_2com-pared with G4-NH_2may be a result of fewer surface charges on the G3-NH_2dendrimer.Because polyol and G3-PEG do not have cationic surface groups, their cellular entry may result from non-specific adsorption to the cell membrane and subsequent endocytosis. Dendrimer–ibuprofen complexes entered the cells rapidly compared with pure drug (1 hr versus>3 hr), suggesting that dendrimers can efficiently carry (Fig.20) the complexed drug inside cells. PAMAM dendrimers were surface-engineered with lauryl chains to reduce toxicity and enhance cellular uptake[75].

Dendrimers as Nano-Drugs

By modifying Poly(lysine) dendrimers with sulfonated naphthyl have been found to be useful as antiviral drugs against the herpes simplex virus can potentially prevent/reduce transmission of HIV and other sexually transmitted diseases (STDs). The early studies suggest that PAMAM dendrimers covalently modified with naphthyl sulfonate residues on the surface also exhibited antiviral activity against HIV. This dendrimer-based nano-drug inhibited early stage virus/cell adsorption and later stage viral replication by interfering with reverse transcriptase and/or integrate enzyme activities. On the other hand PPI dendrimers with tertiary alkyl ammonium groups attached to the surface have been shown to be potent antibacterial biocides against Gram positive and Gram negative bacteria[76].

Dendrimers In Photodynamic Therapy

The photosensitizer 5-aminolevulinic acid has been attached to the surface of dendrimers and studied as an agent for PDT of tumorigenic keratinocytes .Photos ensitive dyes have been incorporated into dendrimers and utilized in PDT devices. This cancer treatment involves the administration of a light- activated photosensitizing drug that selectively concentrates in diseased tissue. The possibility of improving the properties of dendrimers through appropriate unfunctionalization of their periphery makes dendrimers promising carriers for photosensitizers[82].

NON-PHARMACEUTICAL APPLICATIONS

Diagnostics

Paramagnetic metal chelates such as Gd(III)- N,N',N'',N'''-tetracarboxymethyl-1,4,7,10-tetraazacy-clododecane (Gd(III)-DOTA), Gd(III)-diethylenetri- amine pent acetic acid (Gd(III)-DTPA), and their derivatives used as contrast agents for magnetic resonance imaging (MRI).

The (Gd(III)-DTPA) conjugate (MagnevistR) (Schering AG) and is a widely used MRI contrast agent. In another approach, the conjugation of (Gd(III)-DOTA) to poly(l-glutamic acid) (molecular weight 50 kDa) via the biodegradable disulfide spacer cystamine was studied to find a safe and effective macromolecular MRI contrast agent. Consequently, dendrimer-based Gd(III) chelates consisting of generations 2 and 6 PAMAM dendrimers with 12 and 192 terminal surface amines conjugated to the chelating ligand 2-(4-isothiocyanatobenzyl)-6- ethyldiethylenetriamine- pent acetic acid through a thio urea linkage were synthesized .These contrast agents exhibited excellent MRI images of blood vessels upon intravenous injection. These dendrimer polychelates were exploited for high-quality MR angiography (MRA) images up to 60 min post injection. DNA-dendrimers, which are constructed for routine use in high-throughput functional genomic analysis, and as biosensors for the rapid diagnosis have genetic, and pathogenesis diseases [77].

Dendritic Catalysts / Enzymes/

Dendrimers have a multifunctional surface and all catalytic sites are always exposed towards the reaction mixture. They can be recovered from the reaction mixture by easy ultra filtration methods[39]. Dendritic shells can be used to create a microenvironment favorable for catalysis or provide shielding for functional groups at the dendritic core. Because of their 'pseudo'-spherical nature and their resultant conformations the metal sites in these well-defined polymeric catalysts should be easily accessible for substrate molecules and reagents, and therefore exhibit characteristics- fast kinetics, specificity and solubility [40].

1. Metallodendritic catalysts
2. Catalysis with phosphine-based dendrimers
3. Catalysis with (metallo) dendrimers containing chiral ligands
4. Non-metal containing dendrimers

Industrial Processes

Dendrimers can encapsulate insoluble materials, such as metals, and transport them into a solvent within their interior. Cooper and co-workers synthesized fluorinated dendrimers, which are soluble in supercritical CO_2 and can be used to extract strongly hydrophilic compounds from water into liquid CO_2. This may help develop Technologies in which hazardous organic solvents are replaced by liquid CO_2[80].

CONCLUSION

Although the application of dendrimers in the field of drug, gene, and vaccine delivery is in its infancy, dendrimers offer several attractive features, including the control one has over the primary

nature of the system. They provide a platform for the attachment of drugs or genes and their release through several mechanisms. Dendrimers can be endowed with many favorable properties for drug delivery, an ultimate challenge – ergo, a 'real-world'' test – of these versatile nano-devices will be whether they can successfully meet the formidable tasks of diagnosing and treating of malignant disease. Although significant work remains in several areas, prospects now appear bright for dendrimer-based approaches to cancer treatment[84-88].

We have not discussed here the toxicity of the systems simply because the range of materials is so great, and one cannot generalize. Obviously, the toxicity, biodegradability, and biocompatibility of dendrimers and dendrons have to be explored for each system and each application, but this should not inhibit research in the area. The most interesting and valuable systems are yet to come.

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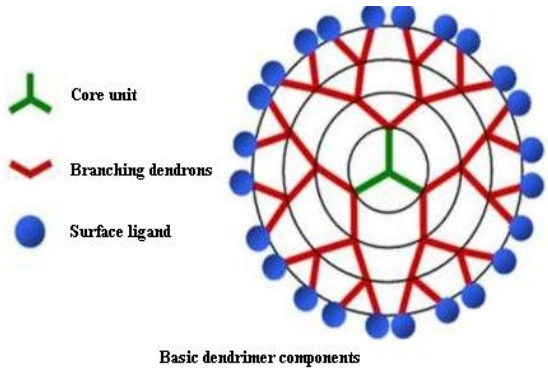


Fig.1. Basic components of Dendrimer

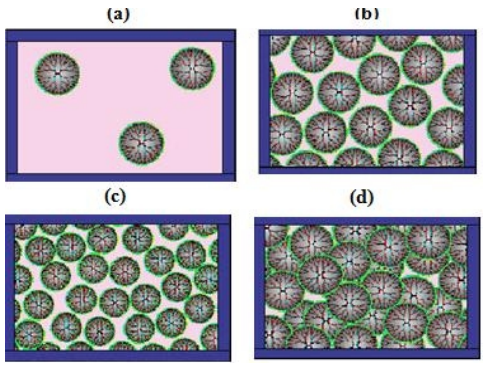


Fig.2. Dendrimer at different concentrations (a) Dilute (b) Contact (c) Collapse (d) Interpenetrate

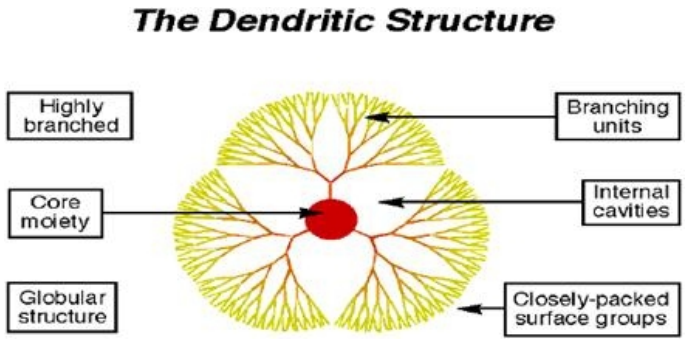
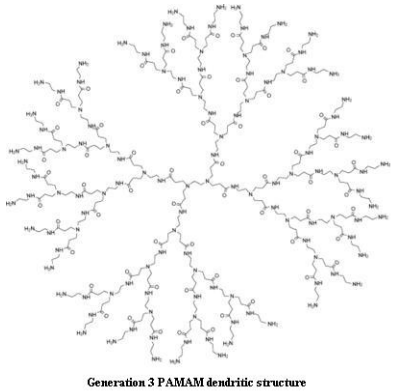
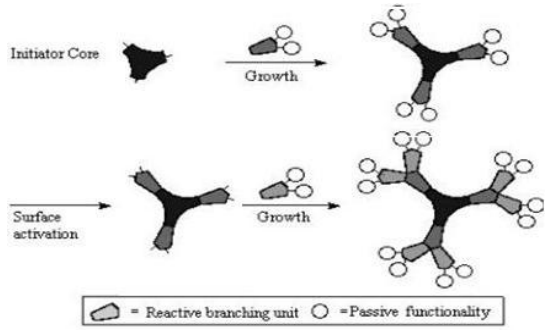


Fig.3. Structure of Dendrimer


Generation 3 PAMAM dendritic structure



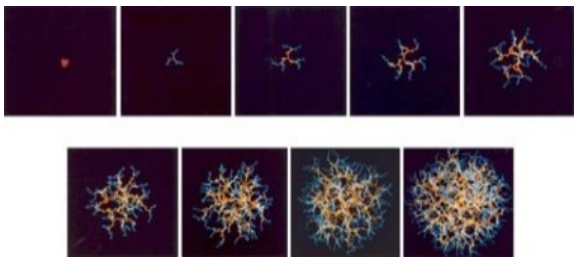


Fig.4. Synthesis of commercially available PAMAM dendrimer

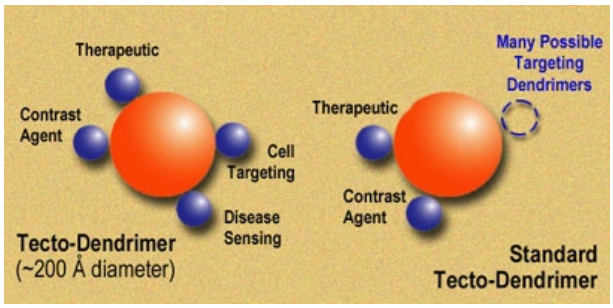


Fig.5. Structure of Tecto-Dendrimer and Standard Tecto-Dendrimer

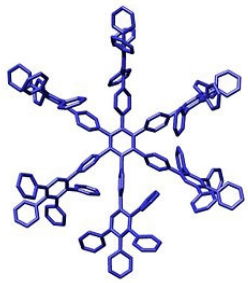


Fig.6. Structure of Multilingual dendrimer

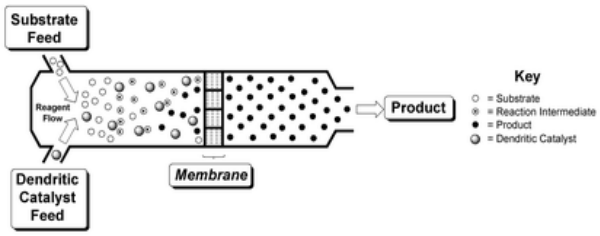


Fig.7. Separate dendritic catalysts from reaction mixtures at the end of the reaction by simple physical processes such as ultrafiltration as a consequence of the nanosize dimensions of dendrimers.

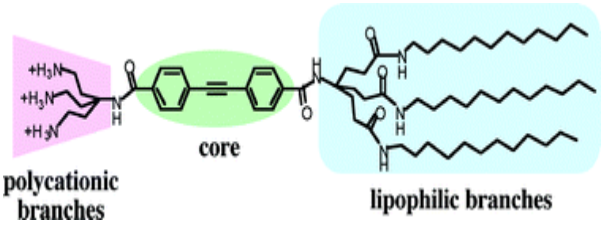


Fig.8. Structure of Ampiphilic Dendrimer

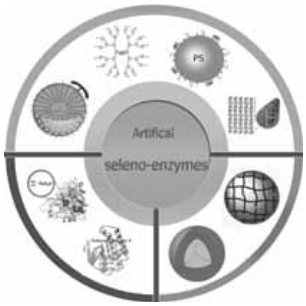


Fig.9. Structure of Micellar Dendrimer

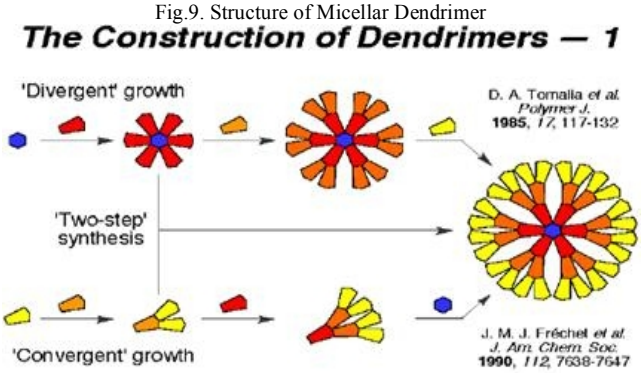


Fig.10. Construction of Dendrimers

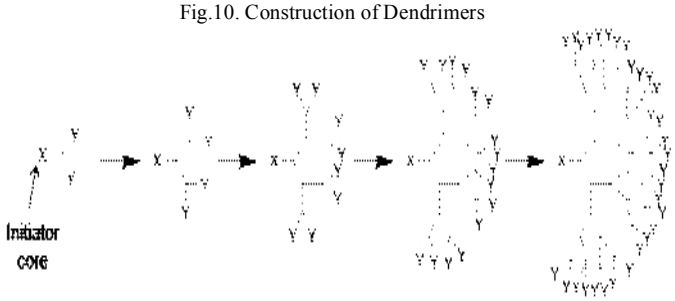


Fig.11. Divergent Dendrimer growth

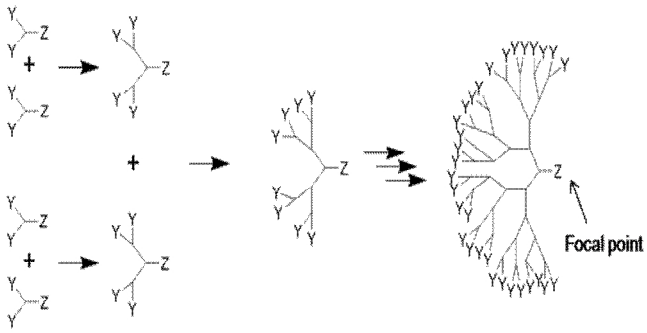


Fig.12. Convergent Dendrimer growth

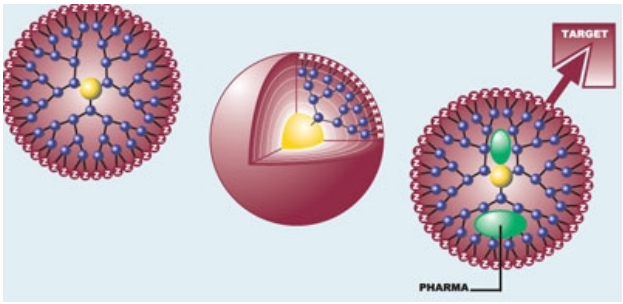


Fig.13. Dendrimers as drug delivery tools

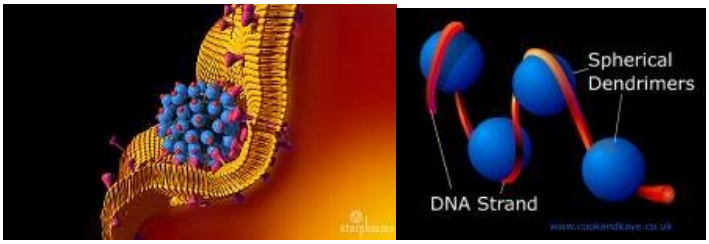


Fig.14. Dendrimers as drug carriers in nanotechnology

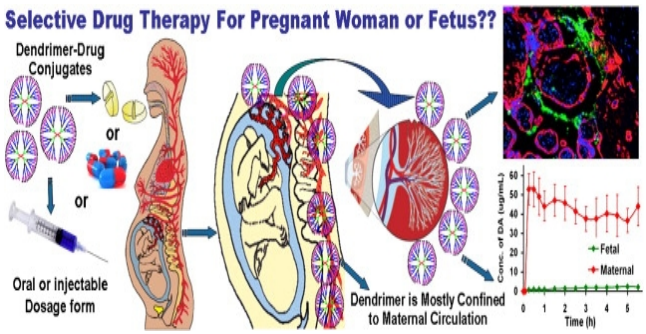


Fig.15. Drug therapy for pregnant woman

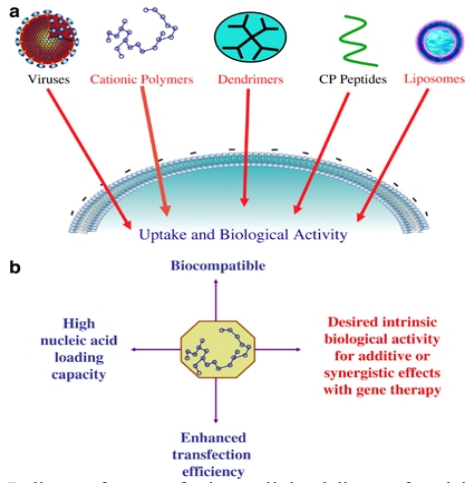


Fig.16. Delivery of vectors for intracellular delivery of nucleic acids.

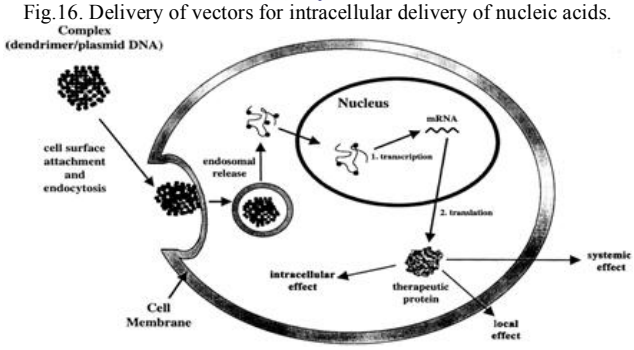


Fig.17. Dendrimer involved in gene transfection

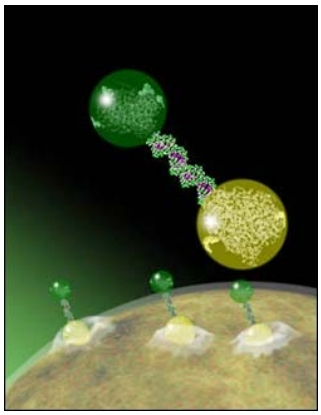


Fig.18. **DNA molecules used to assemble nanoparticles in dendrimers**

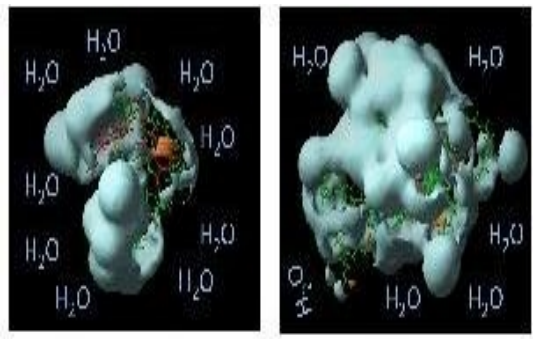


Fig.19. Dendrimers as Potential Solubility Enhancers for Drugs

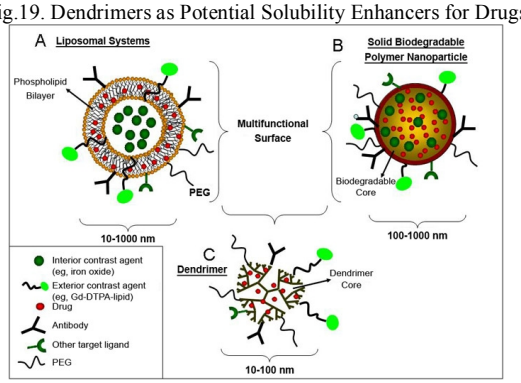


Fig.20. Schematic of nanosystems that may function as combined drug delivery and imaging agents for targeting T cells: (A) liposomal systems, (B) solid biodegradable nanoparticulates, and (C) macromolecular dendrimer complexes. PEG indicates polyethylene glycol; Gd-DTPA, gadolininum-diethylene triamine pentaacetic acid.