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Review Article……!!!

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DENDRIMER: A REVIEW

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ABSTRACT

Dendrimers are an interesting class of synthetic macromolecules having highly branched, threedimensional, nanoscale architecture with very low polydispersity and high functionality. Thesefeatures have made their application in nanotechnology, pharmaceutical and medicinal chemistry particularly attractive. This review article is focused on different synthetic strategies used in dendrimer synthesis at commercial and laboratory scale. These synthetic strategies includes their own advantages and disadvantages. This review willcover 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 importantapplications of dendrimers in the field of pharmaceutical sciences. This data of review is collected from various articles, research papers and patents available on dendrimers.

INTRODUCTION:[1-4]

Theterm dendrimer is originated from the Greekword 'Dendron'which means tree like and'meros' which means parts or unit. Dendrimersare tree like in structure and appearance. Ithas a three dimensional structural symmetry.A large number of branches during polymersynthesis lead to formation of macromoleculewith many end groups. Out of highly branchedpolymers, dendrimers are perfectly branched uniform structure and hyper branchedpolymers are randomly branched . Agenerally accepted definition of dendrimeris amonodisperse macromolecule with perfectlybranched regular structure and having at leastone branched junction at each repeat unit.However it is difficult to place, dendriticpolymers, especially Dendron's anddendrimers, definitely in any branch ofchemistry. They are sometimes described interms of supramolecular chemistry or polymerchemistry, although in some cases they areneithersupramolecule nor polymer in reality.However they are treated as macromolecules.A structurally perfect dendrimer hasmonodispersity, defined molecular size, anddefined number of end groups.Nanoarchitecture with shell structure,structural precision, hydrophilic or lypophilicbalance by design, accessible molecularsurface and good flexibility; which offersresearchers possibility to work in thatparticular area. Using distinct properties of thedendrimer in architecture; photo physical,photochemical, electrochemical or catalyticfunctions at the core of dendrimers haveplaced active sites for researchers. Presentreview will have more focus on recent studiesand many important applications ofdendrimers in various fields of science.

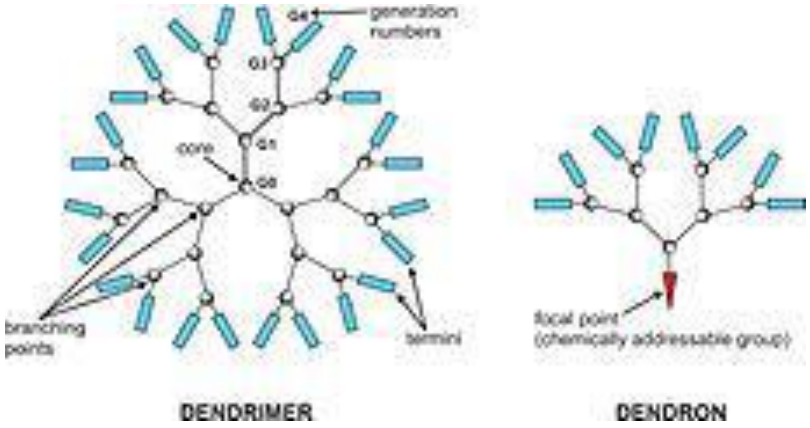

Fig 1: 'Dendrimer', 'Dendron'

PROPERTIES:[5,6]

(1) Dendritic polymers that can be constructed with a well-defined molecular structure, i.e. being mono-disperse, unlike to linear polymers.

(2) Nanoscale sizes that have similar dimensions to important bio-building blocks, e.g., proteins, DNA.

(3) When dendrimer surfaces modified with small functional groups or polyethylene glycol (PEG) show non or low-immunogenicity.

(4) Ability to arrange excretion mode from body, as a function of nanoscale diameter.

(5) An interior void space may be used to encapsulate small molecule drugs, metals, or imaging moieties, reduces the drug toxicity and facilitatescontrolled release.

(6) Numbers of terminal surface groups suitable for bioconjugation of drugs, signalling groups, targeting moieties or biocompatibility groups.

(7) Surfaces that may be designed with functional groups to resist trans-cellular, epithelial or vascular bio permeability.

(8) Dendrimers are monodisperse macromolecules. Size and molecular mass of dendrimers can be specifically controlled during classicalpolymerization process.

(9) When the molecular mass of dendrimers increases, their intrinsic viscosity goes through a maximum at the fourth generation and then begins to decline.

(10) The presence of many chain-ends is responsible for high solubility and miscibility and for high reactivity.

(11) Dendrimer solubility is strongly influenced by the nature of surface groups.

(12) The dendrimer should be: nontoxic, on-immunogenic, able to cross bio barriers (biopermeable), able to stay in circulation for the time needed to have a clinical effect and able to target to specific structures.

HISTORY OF DENDRIMER:[7-11]

Dendrimers are an attractive exclusive class ofpolymers with controlled structure. A dendrimer isboth a covalently assemble molecule and also adistinct nanoparticle. The first dendrimers becompleted by divergent synthesis advanced by FritzVogtle in 1978, R.G. Denkewalter at AlliedCorporation in 1981, Donald Tomalia at DowChemical in 1983 and in 1985, and by GeorgeNewkome in 1985. In 1990 a convergent syntheticapproach was introduce by Jean

Fréchet. A lot ofresearch has already been completed by studying thedifferent properties and application of dendrimers buta lot of researchers still believe it to be in its initialstages.

TYPES OF DENDRIMERS:[12-17]

(1) Radially layered poly (amidoamineorganosilicon)dendrimers(PAMAMOS)

In 1990, Dr. PetarDvornic and hiscolleagues at Michigan Molecular Institutediscovered this unique first commercialsilicon containing dendrimers. Consist ofhydrophilic, nucleophilicpolyamidoamine(PAMAM) interiors and hydrophobicorganosilicon (OS) exteriors. Excellent itsnetworks regularity and ability to complexand encapsulate various guest species offerunprecedented potentials for new applications in nanolithography, lectronics, photonics, chemical catalysis etc. and useful precursors for the preparation of honeycomblike networks with nanoscopicPAMAM and OS domains.

(2) Poly (amidoamine) dendrimers (PAMAM)

Synthesized by the divergent method, starting from initiator core reagents like ammonia or ethylenediamine. When looking at the structure of the highgeneration in two-dimensions, star like pattern observed. They are commercially available as methanol solutions and ingeneration G 0-10 with 5 different core type and 10 functional surface groups.

(3) Poly (Propylene Imine) dendrimers (PPI)

Poly (Propylene Imine) dendrimers (PPI) generally having poly-alkyl amines as end groups, and numerous tertiary trispropylene amines present in interior portion. It commercially available up to G5, and wide applications in material science as well as in biology.PPI dendrimers are available as AstramolTM.

(4) Chiral dendrimers

The chirality in these dendrimers is basedupon the construction of constitutionallydifferent but chemically similar branches to chiral core. Their potential use as chiral hosts for enantiomeric resolutions and as chiral catalysts for asymmetric synthesis.

(5) Liquid crystalline dendrimers

A highly-branched oligomer or polymer of dendritic structure containing mesogenic groups that can display mesophasebehaviour. They consist of mesogenic (liq. crystalline) monomers e.g. mesogen functionalized carbosilanedendrimers.

(6) Tectodendrimer

TectoDendrimer are composed of a core dendrimer, perform varied functions ranging from diseased cell recognition, diagnosis of disease state drug delivery, reporting location to reporting outcomes oftherapy.

(7) Hybrid dendrimers

Hybrid dendrimers are hybrids (block or graft polymers) of dendritic and linear polymers. Obtained by complete monofunctionalization of the peripheral amines of a "zero-generation "polyethyleneiminedendrimer, provide structurally diverse lamellar, columnar, and cubic selforganized lattices that are less readily available from other modified dendritic structures.

(8) Multilingual Dendrimers

Multilingual Dendrimers contains multiple copies of a particular functional group on the surface.

(9) MicellarDendrimers

Micellardendrimers are unimolecular water soluble hyper branched polyphenylenes micelles.

SYNTHESIS OF DENDRIMER:[18-24]

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

First two are the Main two methods for synthesis of dendrimers.

a) Divergent growth method:

This method was introduced by Tomalia. In this method growth of Dendrimers originates from a core site. The core is reacted with two or more moles of reagent containing at least two protecting branching sites, followed by removal of the protecting groups, lead to the first generation dendrimers. This process is repeated until the dendrimer of the described size is obtained. By this approach the first synthesized Dendrimers were polyamidoamines (PAMAM), also known as starbustDendrimers**.**

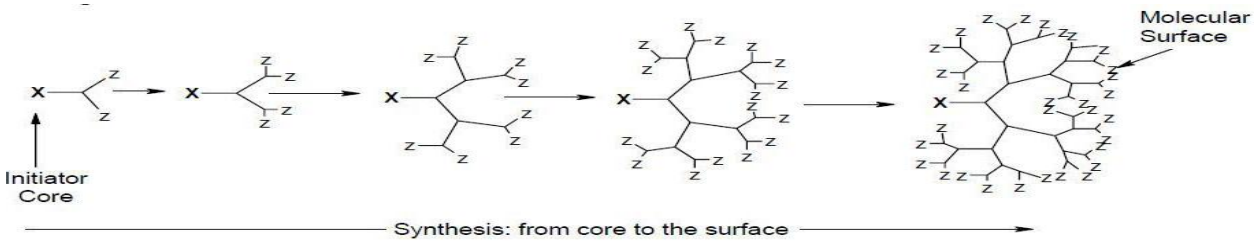

Fig 2: Divergent synthesis of dendrimer

(b) Convergent Dendrimer Growth

Convergent dendrimer growth begins at what will end up being the surface of the dendrimer, and works inwards by gradually linking surface units together with more. When the growing wedges are large enough, several are attached to a suitable core to give a complete dendrimer. convergent growth method has An advantage of convergent growth over divergent growth is that purification Is done after each step whereas in divergent method since the reactant and product remains same it is difficult to purify by chromatographic technique. several advantages like relatively easy to purify the desired product, occurrence of defects in the final structure is minimised, does not allow the formation of high generation dendrimer because stearic problems occur in the reactions of the dendrons and the core molecule.

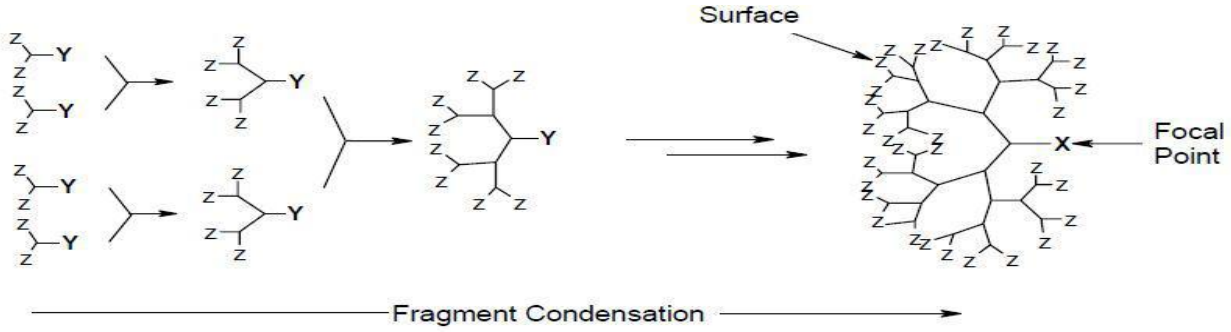

Fig 3: Hypercores' and 'Branched Monomers' growth

Linkage of the oligomeric species in a radial, branch-upon-branch. Core is reacted with two or more moles of reagent containing at least two protecting branching sites, followed by removal of the protecting groups. The subsequent liberated reactive sites lead to the first generation Dendrimers.

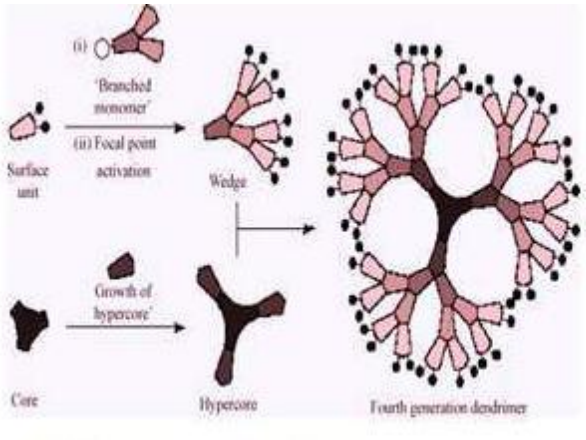

Fig 4: 'Hypercores' & 'Branched' monomer growth

(d) Double Exponential' or mixed growth

In this approach two products (monomers for both convergent and divergent growth) are reacted together to give an orthogonally protected trimer, which may be used to repeat the growth process again. Strength of double exponential growth is more subtle than the ability to build large dendrimers in relatively few steps.

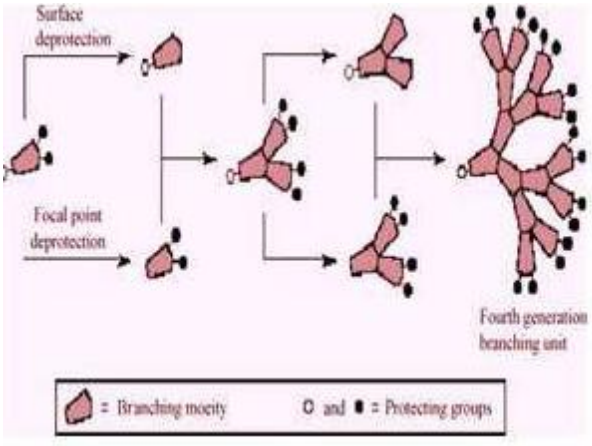

Fig 5: Double exponential growth

APPLICATION OF DENDRIMERS:[25-32]

Therapeutic Application:

Dendrimer in photodynamic therapy

Dendrimers for Boron Neutron capture therapy

Diagnostic Application

Dendrimers as MRI contrast agent

Dendrimers as X-Ray contrast

Dendrimer as molecular probe agent

Pharmaceutical Application

Dendrimers in pulmonary drug delivery

Dendrimers in Transdermal drug delivery

Dendrimers in ocular drug delivery

Dendrimers in oral drug delivery

Dendrimers for controlled release drug delivery

Dendrimers in targeted drug delivery

Dendrimers in gene delivery

Dendrimers as solubility enhancer

Cellular delivery using dendrimers carrier

Dendrimers based product in cosmetics

Dendrimers based commercial products

Dendrimers in Gene Delivery:

Dendrimers can be use as a carrier in gene therapy. Example- PAMAM dendrimers have terminal amino groups which interact with phosphate group of nucleic acid. So PAMAM have been tested as a genetic material vector [15 Super Fect TM is a transfection reagent, it consist of activated dendrimers. Activated dendrimers carry a large amount of genetic material than viruses.

Dendrimers as solubility enhancer:

Dendrimers are unimolecularmicellar in nature because these have both hydrophobic and hydrophilic layer. Hydrophylic layer forms the outer surface. Dendrimers do not have a critical micelle concentration. Due to these properties dendrimers enhance the solubility of poorly soluble drug by forming covalent. Non-covalent complexes with drug molecules and hydrophobes.

Dendrimers as cellular drug delivery carrier:

Pure drug entered into the cell in 3 hours but the dendrimers ibuprofen complexes entered into the cell in 1 hour. So these results show that dendrimers can carry the complex drug efficiently inside the cell.

Dendrimers in targeted and controlled release drug delivery:

The dendrimers facilitate the passive targeting of drug to solid tumours. This is due to their enhanced solubility and plasma circulation time. EPR (Enhanced Permiation and Retention) in tumour tissues leads to reduce cytotoxicity of anticancer drug and increased uptake by cancer cell lines.

Dendrimers in cosmetics:

Dendrimers have a great contribution on cosmetics. Various cosmetic industry used dendrimers in the formulation. L'Oreal has a patent for using dendrimers in the production of cosmetics like mascara or nail polish.

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