

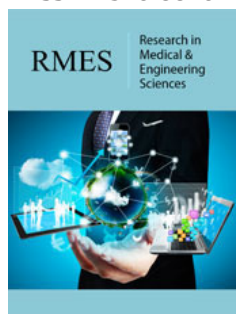
Dendrimers: Exploring the Molecule of the Millennium

Surya Prakash Gautam^{1*}, Arun Gupta² and Tapsya Gautam¹

¹Department of pharmaceuticals, India

²Chameli Devi Institute of Pharmacy, India

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*Corresponding author: Surya Prakash Gautam, Department of pharmaceuticals, India

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Abstract

Dendrimers has proved to be the molecule of the millennium. It acclaimed to this fascinating position is in the nanoworld. Despite of short history of nearly three decades, it has proved itself in the market as dendrimers-based products are contributing significantly and efficiently. Top leaders and Pharma giant companies are further strengthening their global presence by launching dendrimer-based products. Star pharma solely dedicated to dendrimers-based product have launched couple of products in the market and many more are in clinical trials. Scientists actively involved in research, number of patents filed every year; new drug applications submitted to FDA are witnessing and forecasting the future of dendrimers. Dendrimers if trusted will surely address the challenges of medical science. Dendrimers may address the problems in healthcare and feasibly our beloved ones may live long, or we may provide them the better quality of life.

Keywords: Clinical trial; Dendrimers; Drug Delivery; Nanoworld; Targeted

Introduction: Journey of Molecule of Millennium (Dendrimers)

In early 1980 Donald A. Tomalia started and published the birth of new member of Nano family. Vogtle, Jean Fréchet, Newcome have initiated and dedicated their work for dendrimers and have contributed scientifically [1,2]. The journey has started from providing proof of concepts and the number of research publications, patents filed every year is justifications of its global presence. The science of miniature has gained attraction of both beginners and advanced scientists (Figure 1).

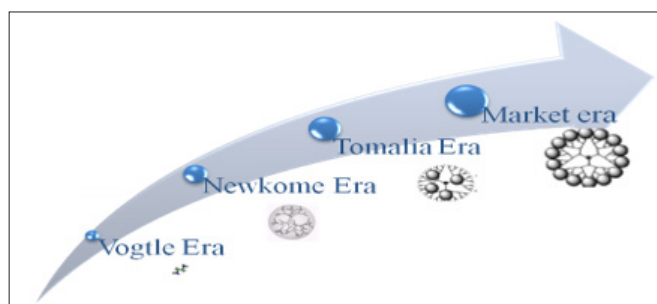


Figure 1: Growth track of Dendrimers.

Dendrimers Global Presence: Proved Itself to be Molecule of Millennium

Dendrimers proved itself to be molecule of millennium. Potted seeds in early 1980 have started giving fruits (dendrimer-based products). More than 10 products are commercialized and are doing well in market. Top dendrimers-based products Vivagel, Stratus CS®, SuperFect®, Starburst®, Priofect®, SPL7013, Nano-Juice™ and many more are proving themselves to be the products of choice [3]. Continuously increasing number of IND application is forecasting the future of this magical segment of drug delivery. Dendrimers being an architecture of functional groups mimicks natural material such as amylopectin (natural dendrimer) and proteins as well as the drug candidates already in the market. Star pharma commences Dendrimer-Docetaxel clinical trial and working with full potential especially in cancer segment. Dade Behring, Qiagen, Sigma Aldrich, Starpharmassl, Starpharma,

Baker, Stiefel, EMD Chemicals are the top leaders engaged with dendrimers-based formulation development especially in drug delivery (Table 1) [1,4,5].

Table 1: Dendrimers based products and market prospects.

S. No.	Dendrimers Products	Application	Company
1	Stratus CS®	Cardiac Marker diagnostic	Dade Behring
2	SuperFect®	Gene Transfection technology	Qiagen
3	Starburst®	Dendrimers commercial	Sigma Aldrich
4	Priofect®	SiRNA & DNA transfection reagents	MERCK
5	Vi-vaGel®SPL7013	HIV and genital herpes Condom coating	Starpharmassl
6	SPL7013	Arthritis and cosmetic treatment	STARPHARMA
7	Nano Juice™	DNA transfection agent kit	EMD Chemicals
8	Targeted	MRI imaging Contrast agent	Baker
9	Drug Delivery	Cancer, Dermatological	Stiefel

Dendrimers in Laboratory Providing the Proof of Concept

Dendrimer based products hitting the market, number of patents every year, IND applications to FDA have strongly motivated the scientists across the globe to engage themselves in research dedicated to Dendrimers (Figure 2). Concepts/hypotheses are increasing day by day and getting converted to reality. The number of products in market and many more in clinical trial are explaining how this Nano-molecule is doing big things. Scientists are going from small to achieve big. Contextual reviews and comprehensive research work on dendrimers disclosed inherent properties especially its medicinal claims and health benefits.

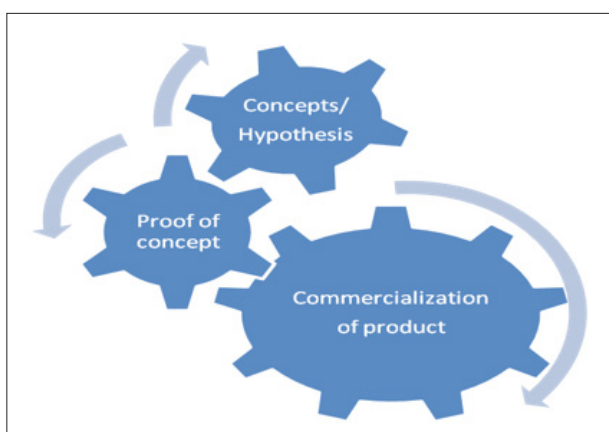


Figure 2: Dendrimers triangle domains.

Drug Delivery Applications of Dendrimers: Current Update

Dendrimers branches are emanating in all direction in almost every field. Major applications to drug delivery are highlighted in

present review. Dendrimers have disclosed inherent medicinal activities including antibacterial, antifungal, antiviral, wound healing and even in the Alzheimer's management. Artificial joints and bones are also utilizing dendrimers as a basic material of construction. Diagnostic applications are gaining much attraction. Purification of water using dendrimers is gaining commercial utility. These nanocarriers are used in drug delivery for plethora of drug candidates (Figure 3) [6-9]. Drug delivery and gene delivery aspects of dendrimer polymer reported by Yu Gao and his colleagues [10,11]. Antihypertensive and anticancer drugs can be used mostly by oral route with the help of Dendrimers [12-16]. Use of dendrimers in ocular region shows better results compare to the other methods of ocular delivery of drugs, because, dendrimers overcome the problems and complications which are associated with the other drug delivery systems [17,18]. Transdermal formulation of dendrimers shows better water solubility and plasma circulation time also enhanced and it can easily deliver the drug into the specific site [19-24]. Antihypertensive, antiviral, nonsteroidal anti-inflammatory and anticancer drugs are delivered via the transdermal route with the help of dendrimers [20,24]. Twibanire and co-worker reported the use of polyester dendrimer in drug delivery system [25] (Figure 3).

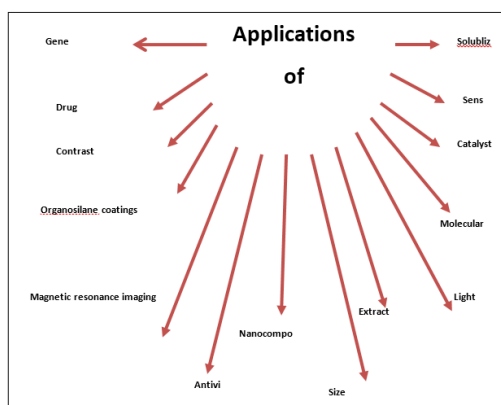


Figure 3: Dendrimers applications.

Receptor: Next Targets to Regulate

Interaction with receptor regulates plethora of chemical pathways responsible for the clinical activity. Receptors are basically Nano units and it needs Nano compounds to activate or deactivate receptors and their functions. Dendrimers being Nano in size and are basically functional groups arranged in a systematic way and synthesized by iterative fashion. Literature claims dendrimers interacts with TLR4-MD-2-LPS receptor complex, Dendrimer-GPCR ligand complex from a receptor (AR) antagonist, P2Y Receptors, H₁ receptor [26-28]. Knocking the receptors by dendrimers is expressing the potential of new segment ready to treat the diseases regulated by these pathways. Dendrimer alone or in conjugated form if interacts with GPCR superfamily can offer new strategy for treatment of a number of diseases.

Need of Screening Studies to Explore Medicinal Activities

Closely structurally related drug molecules are showing the clinical value why not Dendrimers. Drug like ness, drug ability,

innovative nanomedicine terminologies are already assigned for these nanocarriers. Nature is working at Nano level and diseases are originating from level. To fight we have to go down to Nano level to have a healthy competition and to destroy the root cause of diseases. A number of drugs, having ethylene diamines core or starting material have diverse clinical applications are already in the market. PAMAM dendrimer are synthesized using ethylenediamine as core moiety. Drug candidates such as Ethambutol (Antituberculosis drug), Tripeleminine (Antipruritic) Ethylenediaminedisuccinic acid (Antiviral and immunomodulatory activity), Buspirone (psychoactive drug) and Pyrilamine (first generation antihistamine) have ethylene diamine in their basic backbone structure [29,30]. Already dendrimers are claimed for variety of medicinal activities. Dendrimers of different category and their surface modification capabilities can be used to synthesize and screening them against the diseases.

Future Prospects

Dendrimers unique feature and intrinsic qualities made it to capture global presence. They are impacting almost all the fields especially their contribution towards the health segment is really significant. They are mushrooming like anything as Concepts and hypothesis regarding them became reality and doing miracle in the market. In this era of innovation, the molecules have gained the most fascinating position in the nano world as a drug carrier, and as a molecule having inherent medicinal activities. Mingling with the receptor opened a new avenue of research, because interaction with the receptor may regulate the cascade of pathway that may regulate the plethora of clinical responses.

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