Editorial

Dendrimers in medicine

Dendrimers are repeatedly branched new class of macromolecules which have found vast variety of applications in the field of engineering, medicine, and nano-biotechnology. They are typically symmetric around the core and often adopt a spherical three-dimensional morphology in a fashion that a particular function can be unveiled or enriched. In fact, by applying this dendritic pattern in any macromolecule, the enhancement of a certain function can sometimes be synergistically increased. Moreover, nature has already applied the use of these remarkable dendritic networks, such as in lungs where bronchioles and alveoli which provide a maximum surface for the transfer of oxygen into the bloodstream or in the central nervous system where dendrites can act as the receptive site of the neurons. However, the medicinal application of novel synthetic dendrimers is a relatively new field. In reality, the current nano-biotechnology research has seen enormous utilization of dendrimers in protein mimics, drug and gene delivery agents, anticancer and antiviral therapeutics, and in biomedical diagnostic applications. As a matter of fact, a dendrimer-based diagnostic tool for detecting cardiac damage is being developed by Dade Behring, which is one of the world's largest medical diagnostic firms. Similarly, Australian based StarPharma is in the process of developing a topical gel for use as a "liquid condom" called "VivaGel" which reduces the risk of HIV infection in women. In addition, the US Army Research Laboratory is developing a dendrimer-based diagnostic agent dubbed "Alert Ticket" to detect anthrax.

This intensified interest in dendrimers is due to their unique characteristics, which include excellent structural uniformity, multivalency, high degree of branching, well-defined molecular architecture, and highly variable chemical composition. Indeed, dendrimers can possess many terminal functional groups that can chemically be linked to other moieties in order to adjust their surface properties for applications such as biomimetic nano-devices. Besides, dendrimers can easily move across biological membranes and they can store a wide range of metals, organic or inorganic molecules among their branches which are of interest to us. The nano-drugs or devices made from dendrimers do not trigger the immune system when injected or used topically and have low cytotoxicity. More importantly, the amino groups that cover the dendrimeric molecule are not recognized as foreign by the immune system. However, some forms of dendrimers can induce clotting in the bloodstream, inducing a potential concern for *in vivo* applications. Thus, by customizing and controlling its architecture, nanotechnologists are developing dendrimers for drug delivery, diagnostic imaging and as carriers of genetic material. The advances in the field of synthetic chemistry made this task much easier. In fact, after the first successful synthesis of dendrimers by Tomalia's group from Dow Chemicals in 1983, their popularity grew a lot. Trying to imitate the branching in trees, they developed a new class of amide containing cascade polymers into a well-defined macromolecular dendritic structure. Since then, more than 5000 patents and publications have been presented to itemize various types of dendrimers, their mode of preparation and their potential applications.

Perhaps, the most prominent application of dendrimers in medicine is for gene and drug delivery. Despite its immense promise in gene therapy, carrying the gene into the cells as part of a virus has been thwarted due to the lack of getting genes into enough cells to make a therapeutic difference. Additionally, it has the serious disadvantage that even if the virus is benign, it can trigger an immune reaction in the body, leading to serious consequences at higher doses. In contrast, dendrimers are regarded as stealth molecules which are big enough to carry genetic material to mimic a virus. Moreover, the amine groups protruding out from the dendrimeric surfaces help to evade body's immune system. This allows dendrimers to carry large amounts of genetic load into the body with ease. The amount of the load depends on the size of a dendrimer, which can easily be adjusted depending on how many shells they have. So far, the dendrimer-based delivery or transfection of genes has been successfully demonstrated *in vitro* and is now being evaluated for its efficacy and toxicity *in vivo*.

Similarly, dendrimers have also shown aptitude as a

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potential MRI contrast agent for the diagnosis and therapy of tumors. In fact, the researchers at the University of Michigan have developed and successfully imaged a stable MRI contrast agent made up of the shell of dendrimer and polymer on an iron oxide nanoparticle core. This stable dendrimeric complex selectively targeted tumors in animal models and was successfully imaged using MRI vouching its ability as a potential MR contrast agent for targeting tumors. These potential applications of dendrimers in the field of nano-biotechnology and medicine described here represent a mere latent image of what has been developed so far. Several hurdles will have to be overcome to reach the goal of a general purpose using dendrimers. Moreover, this novel therapeutics can be easily managed if their delivery rate, biodegradation, and site-specific targeting can be predicted, monitored, and controlled. This will not only be beneficial from a global health care perspective, but also plays a constructive role in reducing the cost of traditional time consuming long-term treatments.

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