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Guest Editorial

Dendrimer evolution timeline: Ground-breaking progress in cancer treatment

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ABSTRACT

Dendrimers holds potential in abating restrictions of other available treatments through the development of functionalized particles for targeted treatment. By developing functionalized particles for targeted treatment, dendrimers have the ability to reduce the limitations of other available therapies. Dendrimers have many advantages over other nanoparticles, making them perfect candidates for more efficient and targeted drug delivery. Dendrimers have the ability to deliver vast quantities of drugs to particular locations. They can also be used to monitor the progress of the procedure, giving them a theranostic capability that has never been seen before. Dendrimers show their potential applicability for effective cancer treatment for the near future. This article highlights the evolution timeline of dendrimers and various related aspects of the past four decades. These also involve the basic structure and information of dendrimers along with the current and future perspective. As a result, it is important to study dendrimers in order to keep up with recent developments.

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1. Editorial

Dendrimers can be seen as a bud that will soon flower and have a stronger effect for cancer care.¹ The current cancer treatments provide relief, but they can have unfavourable side effects on normal cells. The ability to effectively deliver anti-cancer drugs to the desired area while avoiding harm to normal cells is critical in cancer care. Dendrimers have excellent drug-carrying properties, and their biocompatibility can also be improved. Targeting ligands can be added to the surface of dendrimers for improved cancer cell selectivity, allowing cancer cells to reorganise without damaging healthy cells.² Dendrimers are a spherical three-dimensional nano-sized strongly branched tree-like architecture. The word dendrimer was derived from the Greek word dendron, which is another name for a tree, since it has the same branching structure as a tree.³ Buhleier

et al. succeeded in synthesising a cascade-like repetitive structure of mono and diamine at the periphery of the central core in 1978, and this was the first dendrimer.⁴ In 1985, Tomalia et al. created a new class of polymer known as starburst macromolecule, in which they synthesised star polymer with excellent structural symmetry, strongly branched and maximum terminal functional density, as well as monodispersed, regulated branching, and reproducibility. Hiroaki et al. created silicone dendrimer in 1990, which is made up of hyperbranched polysiloxanes with silicone hydrogen at the dendrimer's end. The lack of the solvent effect was studied on the dendrimers by the bilayer interaction by Kelly et al. in year 2009. Later in year 2011, the use of dendrimers was done in drug and gene delivery into the cells by Liu et al. In year 2013 Kasturirangan et al had premeditated multifunctional composite nanodevice which was used for cancer therapy and cancer imaging. In year 2014, Jin et al developed commercially available

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transfection reagent like profect and superfect that were used to form a stable dendrimer. The rigid structure of dendrimers like polyphenylene dendrimers by studied by Hammer et al in year 2015. Additionally, in year 2016 the linear polymers with higher viscosity than analogue dendritic were studied by Ren et al. To investigate the effect of the form of chemical modification, first- and second-generation dendrimers were synthesised with sulfonic, carboxylic, or phosphonic acids as the polar group and n-propyl, butyl, hexyl, or isopropyl chains as the nonpolar functionality. These chemical modifications were studied by Hammer et al. in year 2017. In year 2018 Zhong developed inhalable pH-sensitive PAMAM dendrimer. Santos et al. discovered that the central core, which is also a dendron, radiates outwards, resulting in a homo-structural layer, in the year 2019. In the year 2020, Huang et al. and Fana et al investigated nanotechnology, which includes various nanomaterials and nanocarriers such as dendrimers, for various applications in medicine and drug delivery to treat serious and lethal diseases such as visceral leishmaniasis, triple negative breast cancer, AIDS, and others. Niu et al. reviewed the applicability of dendrimers with saccharides in their structure in 2021.⁵ Dendrimers for co-delivery were the subject of the research. Dendrimers are well-known for their special properties, such as monodispersed, which allows them to be replicated at a large scale. The nanoscopic size of dendrimers not only increases surface area but also aids permeation in cells without a barrier. Dendrimer biocompatibility is improved by PEGylation and glycosylation because cationic dendrimers cause cell lysis due to interactions between the cell membrane (negatively charged) and the dendrimer surface (positively charged) that damage the cell membrane.^{6,7} According to the World Cancer Report 2020, there were 19.3 million new cancer cases and almost 10.0 million cancer deaths worldwide (excluding nonmelanoma skin cancer).⁷ Lung cancer, colorectal cancer, breast cancer, and mesothelioma were the cancers with the highest recorded treatment costs. Lung cancer was expected to cost \$282,000 over a lifetime, while mesothelioma was estimated to cost \$150,000.⁸ The overall annual economic cost of cancer in 2010 was approximately US\$ 1.16 trillion; thus, lowering the cost of promising cancer treatments is expected to be developed in the near future. The current cancer treatment/therapy provides relief, but it also has unfavourable side effects on healthy cells. The ability to effectively deliver anti-cancer drugs to the desired area while avoiding harm to normal cells is critical in cancer care. Liposomes, polymeric nanoparticles, and dendrimers are currently used as drug carriers, with dendrimers having superior properties such as monodispersed, nanoscopic size, multiple functional groups at the periphery, tunable size, reproducibility, and biocompatibility. The tumour has an acidic pH (5–6), while the body system circulation has a neutral to alkaline pH (7.4); this pH discrepancy will be a key factor in designing

next-generation stimuli-responsive dendrimer nanocarriers. Dendrimer-based nanocarriers can be used not only for treatment but also for cancer cell detection by encapsulating imaging probes such as fluorescent dye, magnetic resonance imaging contrast, and radionuclide. The majority of the research was done with PAMAM dendrimer, but other dendrimers will be investigated and compared to PAMAM dendrimer in the near future for effective cancer treatment.⁹ Despite their multifunctional properties, dendrimers have been shown to be toxic to biological membranes due to interactions between the negative charge of the biological membrane and the positive charge of dendrimers, resulting in nanoholes in the membrane. However, researchers have overcome this obstacle by developing biocompatible dendrimers and using dendrimer surface engineering to create nanoholes in the membrane. The perfect medication is Hydrophobic drugs can be encapsulated in the internal voids of biocompatible dendrimers, while hydrophilic drugs can be functionalized at the surface with pH-sensitive hydrolysable linkages. Biomarkers can also be conjugated on top of hydrophilic drugs for identification and attachment at tumour sites.¹⁰

2. Conclusion

Dendrimers have unique properties that make them a promising candidate for a variety of applications. Dendrimers can also help with drug delivery system optimization. Dendrimers may be a breakthrough success for the treatment and diagnosis of various diseases, especially cancer, according to a study that looked at their evolution over nearly four decades. Dendrimers, with their diverse properties, would have a significant effect on future research and offer a more advanced alternative for diagnosis and treatment of multiple cancer.

3. Source of Funding

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4. Conflict of Interest

None.

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