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Polymeric Nanocarriers, Gene Delivery and siRNA Therapeutics

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Editorial

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Introduction

Gene delivery is a rapidly advancing field aimed at treating diseases at the genetic level by introducing nucleic acids into target cells. Small interfering RNA (siRNA) has emerged as a powerful therapeutic tool because it can selectively silence disease-causing genes through RNA interference. However, siRNA is highly unstable in biological fluids and cannot easily cross cell membranes. These limitations have driven the development of advanced delivery systems. Polymeric nanocarriers have gained major attention as non-viral vectors due to their safety, flexibility, and ability to protect and transport siRNA effectively [1-4].

Discussion

siRNA-based therapy offers great potential for treating cancer, viral infections, and genetic disorders by specifically downregulating harmful gene expression. Despite this promise, naked siRNA is rapidly degraded by nucleases in the bloodstream and is cleared quickly by the kidneys. In addition, its negative charge and large molecular size prevent efficient cellular uptake. Therefore, a suitable carrier system is essential for successful gene delivery.

Polymeric nanocarriers are nanoparticles made from natural or synthetic polymers such as chitosan, polyethyleneimine (PEI), poly(lactic-co-glycolic acid) (PLGA), and polycaprolactone. These polymers can form complexes with siRNA through electrostatic interactions, creating stable nanostructures that protect siRNA from enzymatic degradation. Encapsulation also improves circulation time and allows controlled release at the target site [5].

A key advantage of polymeric nanocarriers is their tunable physicochemical properties. Particle size, surface charge, and hydrophilicity can be adjusted to optimize pharmacokinetics and biodistribution. Surface modification with polyethylene glycol reduces recognition by the immune system, prolonging blood circulation. Targeting ligands such as antibodies or peptides can be attached to direct nanocarriers to specific cells, increasing gene silencing efficiency while minimizing off-target effects.

After cellular uptake, siRNA must escape from endosomes to reach the cytoplasm, where gene silencing occurs. Certain polymers, such as PEI, facilitate endosomal escape through the “proton sponge” effect, enhancing therapeutic activity. Biodegradable polymers further improve safety by breaking down into non-toxic byproducts after delivery.

Despite these advantages, challenges remain. Some polymers exhibit cytotoxicity at high concentrations, and large-scale manufacturing with consistent quality is complex. In vivo stability, long-term safety, and regulatory approval also require further investigation.

Conclusion

Polymeric nanocarriers represent a promising platform for efficient and safe siRNA-based gene delivery. By protecting siRNA from degradation, enhancing cellular uptake, and enabling targeted delivery, these systems overcome major biological barriers. Continued advancements in polymer design and nanotechnology are expected to accelerate the clinical translation of siRNA therapeu-

tics and expand their role in precision medicine.

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