Polymer Sciences
ISSN: 2471-9935

Open access Short Communication

Redefining the Importance of Polymers in Gene Therapy

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INTRODUCTION

A biocompatible polymer with a main chain structure like that of poly(ethylene oxide), polyglycidol (or polyglycerol) has a -CH_2OH reactive side group in each structural unit. The hydroxyl groups in polyglycidol not only make this polymer more hydrophilic, but they also give rise to polymers containing carboxyl, amine, and vinyl groups, as well as polymers with bound aliphatic chains, sugar moieties, and covalently immobilised bioactive chemicals in certain proteins. The present state of knowledge about the synthesis of polyglycidols with various topologies-including linear, branching, and star-like and with varied molar masses is discussed in the study. We discuss surfaces with high polyglycidol content and protein-repelling capabilities. We also go through how to make polyglycidol-containing copolymers as well as how to make the nano-and microparticles that may come from them. The utilisation of polyglycidol and polyglycidol-containing polymers as drug carriers, diagnostic system reagents, and biosensor components is summarised in this work.

The effective transport of nucleic acids into a target cell is essential for the treatment of genetic problems, which makes gene therapy an appealing therapeutic approach. The goal of the current study is to assess the ability of copolymers based on linear polyglycidol to function as nucleic acid carriers. Using previously synthesised poly(allyl glycidyl ether)-b-polyglycidol block copolymers as precursors, functional copolymers carrying linear polyglycidol as a non-ionic hydrophilic block and a second block having amine hydrochloride pendant groups were created. Through the extremely effective radical addition of 2-aminoethanethiol hydrochloride to the alkene side groups, the amine functionalities were introduced [1,2].

DESCRIPTION

The presence of dodecyl residues at the ends of the modified copolymer structures and the hydrogen-bonding interactions in the polyglycidol segments maintained the loose aggregates with a significantly positive surface charge in aqueous conditions. Through electrostatic interactions, the copolymer aggregates could compact and stabilise DNA into nanosized polyplex particles. A panel of human cancer cell lines exposed to the copolymers and matching polyplexes revealed low to moderate cytotoxicity. The examination of cell internalisation showed that the polyplexes could successfully transport DNA to the cancer cells. The fundamental idea behind gene therapy is to add, replace, or alter a gene that is missing or defective, or to prevent the expression of a mutant gene from being expressed, in order to induce a therapeutic impact in patients. It has the potential to alter the management and treatment of a variety of acquired and inherited genetic illnesses, in which the transport of nucleic acids is essential. The earliest gene delivery systems were created viruses. They were effective, but their high toxicity, significant side effects, and intrinsic immunogenicity made them appear to be highly dangerous for the patient, which limited their clinical usage.

The investigation of alternate forms of gene transfer based on lipids, polymers, and inorganic materials, which are safer, less pathogenic, and less immunogenic, is driven by the known hazard of viral carriers. Polymer-based vectors are one of them that have sparked a lot of scientific attention. In addition to the potential benefits for safety, polymers provide excellent structural and chemical versatility for modifying the physicochemical properties, access to large-scale production, batch-to-batch reproducibility, a high capacity for loading nucleic acids, stability upon storage, and low cost of treatment all of which are beneficial for such a complex and difficult process as gene therapy. The anionic character of DNA is often taken advantage of by polymeric vectors to promote complexation through electrostatic interactions. The bulky DNA structure may be compressed into nanosized complexes by cationic polymers such

Received:	02-January-2022	**Manuscript No:**	IPPS-23-15673
Editor assigned:	04-January-2022	**PreQC No:**	IPPS-23-15673 (PQ)
Reviewed:	18-January-2022	**QC No:**	IPPS-23-15673
Revised:	23-January-2022	**Manuscript No:**	IPPS-23-15673 (R)
Published:	30-January-2022	**DOI:**	10.36648/2471-9935.23.8.001

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Citation Roy D (2023) Redefining the Importance of Polymers in Gene Therapy. J Polymer Sci. 8:001.

polyethyleneimine (PEI), poly(L-lysine), poly(2-(dimethylamino) ethyl methacrylate), and polyamidoamine, as well as natural polymers like chitosan, dextran, and pullulan (polyplexes). The neutralisation of DNA's negatively charged phosphate backbone and protection from both extracellular and intracellular nuclease degradation are further benefits of condensation. DNA should ideally continue to be active and capable of transfecting cells. However, there is still a problem with the cationic polymers' high cytotoxicity, quick detection by the reticuloendothelial system (RES), and quick blood clearance [3,4].

Hydrophilic, flexible polymer moieties or segments can be added to minimise cytotoxicity while suppressing RES absorption. In addition, they can include functions that can aid in overcoming biological obstacles to gene transport, improve colloidal stability, and have a positive impact on physicochemical characteristics. However, the widespread decrease in efficiency usually outweighs all those advantages of inclusion of new moieties, therefore it is always important to strike a fine balance between functions and features that appear to be in opposition to one another.

CONCLUSION

Protective and stabilising substances in medicine include poly(ethylene oxide) and polyglycidol. Many bioactive pharmacological components, notably nucleic acids and practically all types of proteins, are useless when administered directly intravenously or orally. These species are degraded and eliminated from the circulation by a variety of hydrolases and molecular and cellular immune system components. Oral delivery of unprotected nucleic acids and proteins results in digestion. Furthermore, the immune system would further destroy and remove any big fragments of partly damaged proteins or nucleic acids that managed to pass through the endothelial barrier of the gut after being consumed. Protein and nucleic acid covalent binding of poly(ethylene oxide) prevents their destruction by shielding them from enzymes, antibodies, and macrophages. As a result, immobilising poly(ethylene oxide) modifies proteins, nucleic acids, and their carriers, greatly increasing the circulation of these species in the blood. The word "pegylation" refers to this procedure and refers to low molar mass poly(ethylene oxide), which is what this technique is typically known as.

ACKNOWLEDGEMENT

Authors do not have acknowledgments currently.

CONFLICT OF INTEREST

There are no conflicts of interest.

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