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A biocompatible polymer for non-viral gene delivery

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In recent years, there has been an increase in the development of non-viral gene delivery systems using cationic polymers for various types of diseases. As an alternative to high molecular weight poly(L-lysine) (PLL), a biocompatible, reducible and effective non-toxic gene delivery system using linear L-lysine copolymers (LLCs) has been developed. The importance of the development of biodegradable and biocompatible polymers is to maintain cell viability as well as improve transfection efficiency. These biodegradable polymers can be developed by introducing disulphide bonds in the backbone of polymers which help in reducing the molecular weight of the polymer as well as in the release of DNA into the cytoplasm. This novel reducible linear L-lysine copolymer is made of repeating units of cystamine bisacrylamide (CBA) and L-lysine. Additionally, for efficient DNA condensation, there is a need to introduce primary amines; this is done by modifying LLCs with ethylenediamine. To understand the mechanism in detail, several comparative studies have been performed by the researchers. One example is the study of the mechanism of DNA release into the cytoplasm by fluorescence spectroscopy performed using 1,4-dithio-DL-threitol (DTT). Its results revealed that there is a lot of decrease in fluorescent intensity when the LLCs are added and on DDT addition there is a nearly 95% increase in intensity. This demonstrated that the decrease in the number of disulphide bonds result in the release of DNA. Additionally, the results obtained from the study pertaining to LLCs gel retardation assays and their transfection efficiency were found to be favourable. Following these results, LLCs have been used as a nonviral gene carrier system to generate genetically modified stem cells that produce sufficient amounts of the vascular endothelial growth factor (VEGF165), which is an angiogenic cytokine. These stem cells are then used to generate revascularisation of an infarcted region of the heart, which can reduce myocardial damage and scar formation. Hence, LLCs have a great potential for the treatment of myocardial infarction and can have significant applications in the field of therapeutics and medicine.

Keywords: Non-viral gene delivery, Biodegradable polymers, DNA transfection, L-Lysine copolymers, Myocardial infarction

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