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71

Synthesis and characterisation of a novel poly(amidoamine)s for use as a potential protein delivery system

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Introduction and Objectives

In recent years, gene, antisense and ribosyme therapies have been explored. All these systems share one common challenge, that of efficient delivery into the cytoplasm of the cell. Synthetic polymers have been developed as an alternative to viral gene delivery systems, which have brought some safety concerns in clinical trials. They may be tailored, through the application of rational design, to improve cytoplasmic access and modulate cell-specific targeting. Poly(amidoamine)s (PAA) are a family of synthetic functional polymers developed for use as polymer therapeutics. They were selected for this study as a potential protein delivery system.

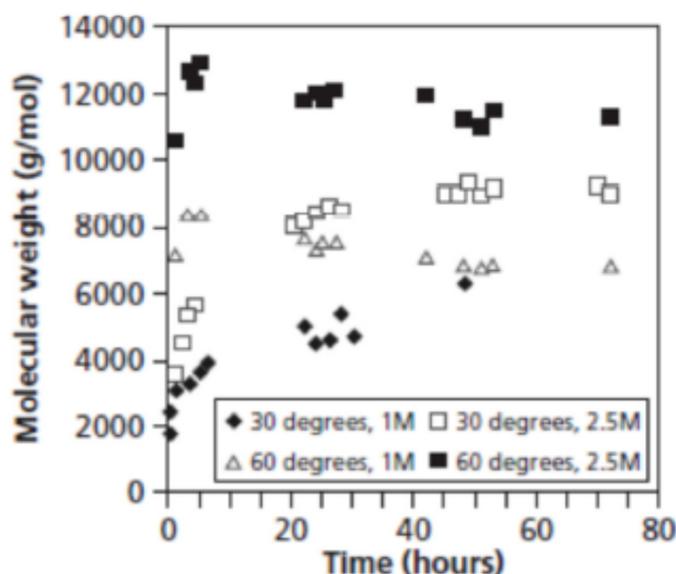


Figure 1 Evolution of PAA molecular weight (Mw) as a function of reaction time in water using different monomers' concentrations and temperatures.

Method

The general procedure for the polymerisation was as follows: equimolar amount of 6-amino-1-hexanol and 2, 2' bis(*N*-acrylamido)acetic acid was used. The kinetics of polymerisation was carried out at different temperatures (30 and 60°C) using different concentrations of monomers (1 and 2.5M) in different solvents (water, methanol and dimethyl sulfoxide (DMSO)). Structure of the polymers was identified by ¹H NMR and Fourier transform infrared (FTIR) spectroscopy. Molecular weight and polydispersity were determined by gel permeation chromatography using poly(ethyleneglycol) as standards. Thermal analysis was carried out using differential scanning calorimetry.

Results and Discussion

The polymerisation mechanism of poly [2, 2' bis(*N*-acrylamido)acetic acid-*alt*-(6-amino-1-hexanol)] was studied under different reaction conditions by varying the concentration of the monomers, temperature and the solvent. The kinetics of the polymerisation was characterised in terms of percentage conversion and building up of the molecular weight of the polymer (Figure 1).

Best results were obtained when carrying out the polymerisation reaction using higher concentration of monomers and water. The yield of the polymerisation was 76% and that of the molecular weight of the polymer was 14 200 g/mol. However, degradation occurred at higher temperature. Structure of the synthesised polymer was confirmed by infrared (IR) and nuclear magnetic resonance (NMR) spectroscopy. These results correlate well with that of previous studies.

Conclusion

Concentration of monomers and the temperature used in the polymerisation reaction were found to have a profound effect on the molecular weight and the percentage conversion. As this polymer is intended to be used as a protein delivery system, its cytotoxicity and delivery efficiency are currently under investigation.