Synthesis of poly(ester-carbonate) with pendant acetylcholine analog for promoting neurite growth

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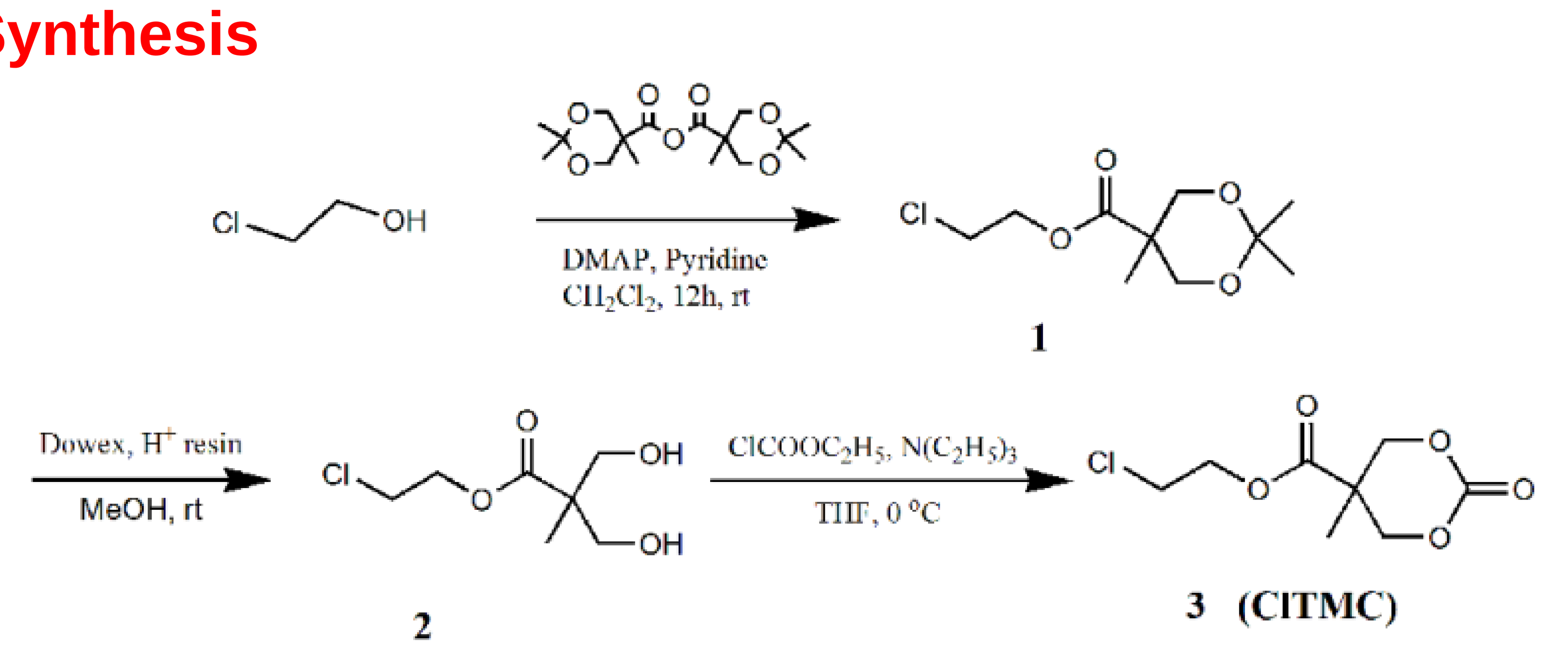
Introduction

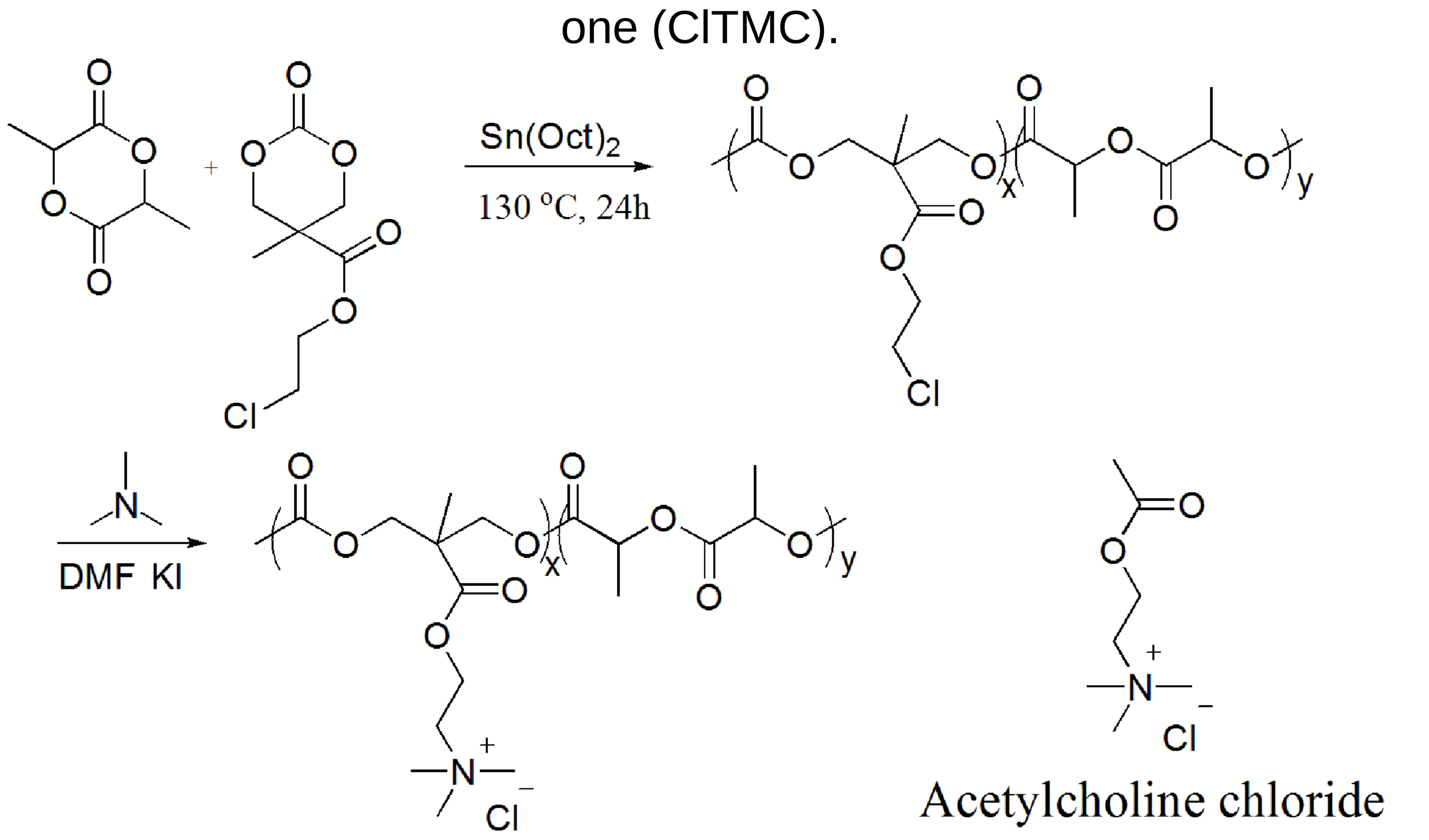
Peripheral nerve injuries caused by trauma or disease often lead to disabilities in patients. Rational biomaterial synthesis and functional interface construction are vital for successful nerve regeneration in terms of supporting neuron adhesion and proliferation, as well as guiding neurite outgrowth. Neurotransmitters are proved to play a key role in signal transduction and mediating cell behaviors in nervous system.

In this study, a biodegradable poly(ester-carbonate) with a pendant acetylcholine analog, which is expected to be presented as a neurotransmitter motif to positively interact with neural cells, is designed and synthesized.

Synthesis



Scheme 1. Synthesis of 5-methyl-5-chloroethoxycarbonyl-1,3-dioxan-2-one (ClTMC).



Scheme 2. Synthesis of P(LA-ClTMC) and its quaternization.

Characterization

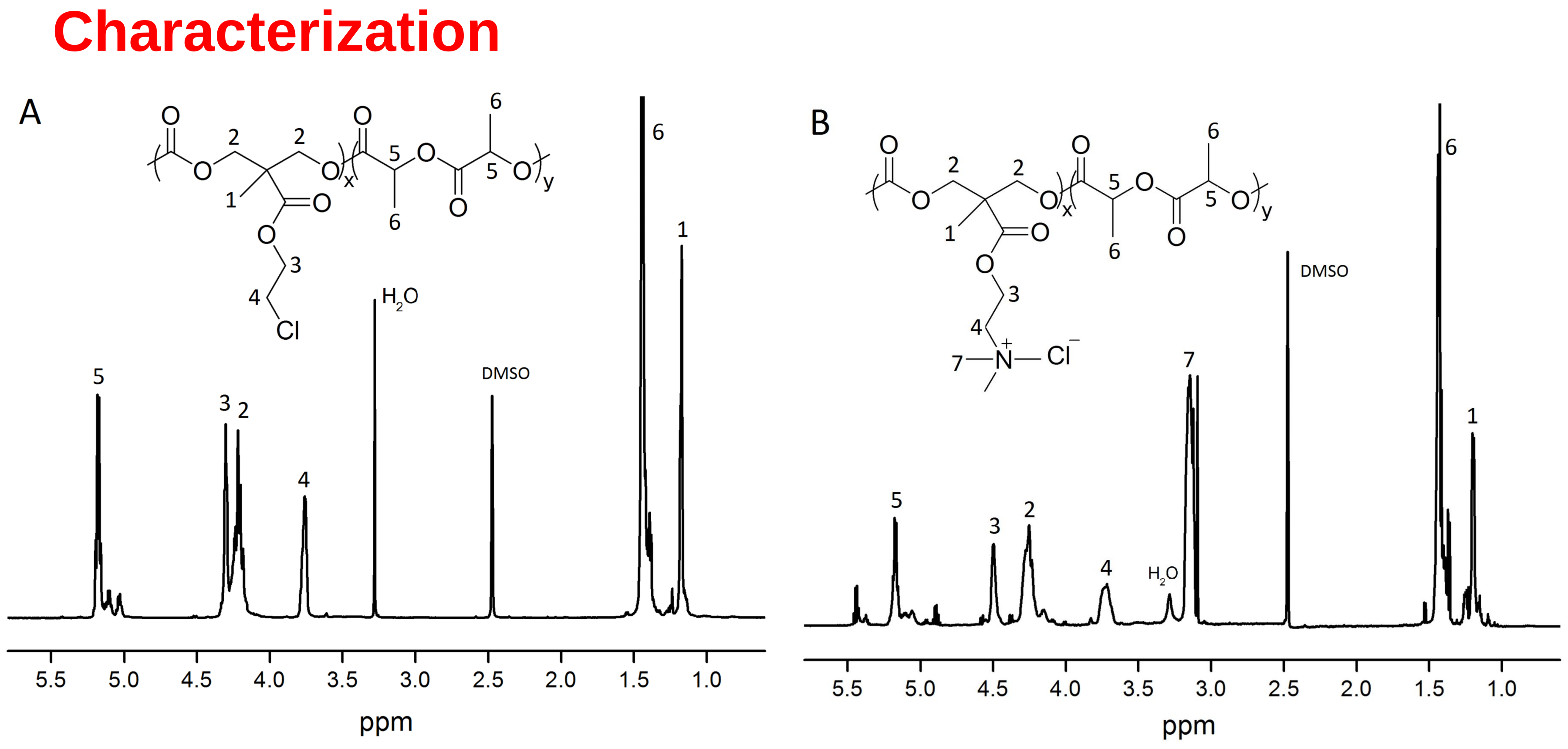


Fig. 1 ^1H NMR spectra (DMSO-d_6) of P(LA-ClTMC) copolymer before (A) and after quaternization Ach-P(LA-ClTMC) (B).

Poly(ester-carbonate)s with acetylcholine analogs were obtained, and the content of pendant acetylcholine analog on the polymer could be modulated by changing the molar feeding fraction of ClTMC

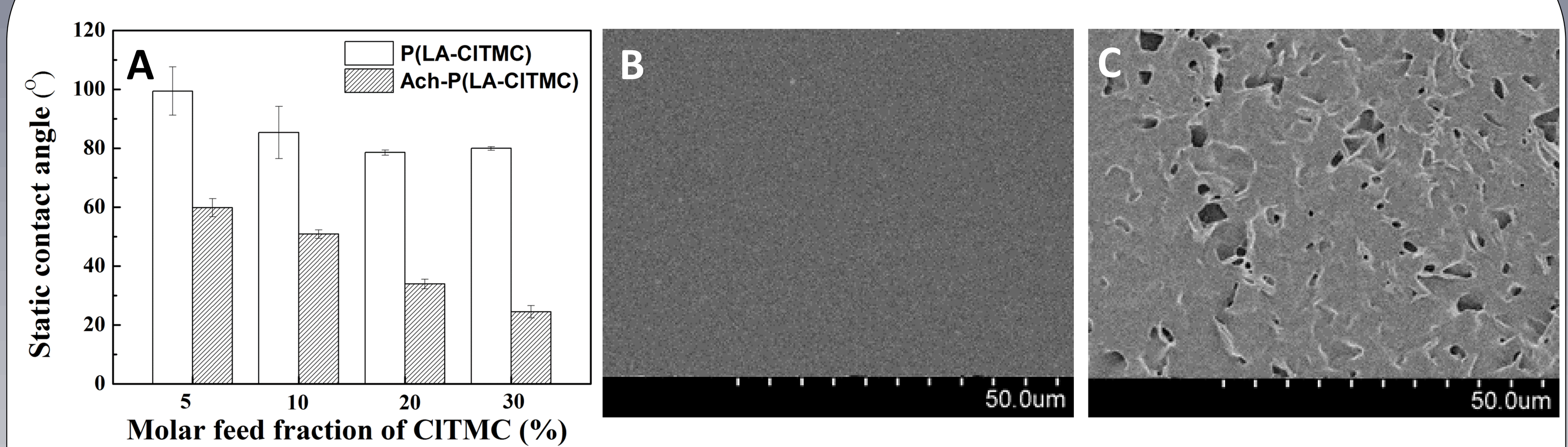


Fig. 2 (A) Static water contact angle of P(LA-ClTMC) films before and after quaternization as a function of ClTMC feeding ratio. (B) SEM images of films of P(LA-ClTMC)-5, and (C) Ach-P(LA-ClTMC)-5.

Compared to P(LA-ClTMC), the hydrophilicity of Ach-P(LA-ClTMC) was significantly enhanced, films of Ach-P(LA-ClTMC) copolymers showed a rather rougher surface than P(LA-ClTMC).

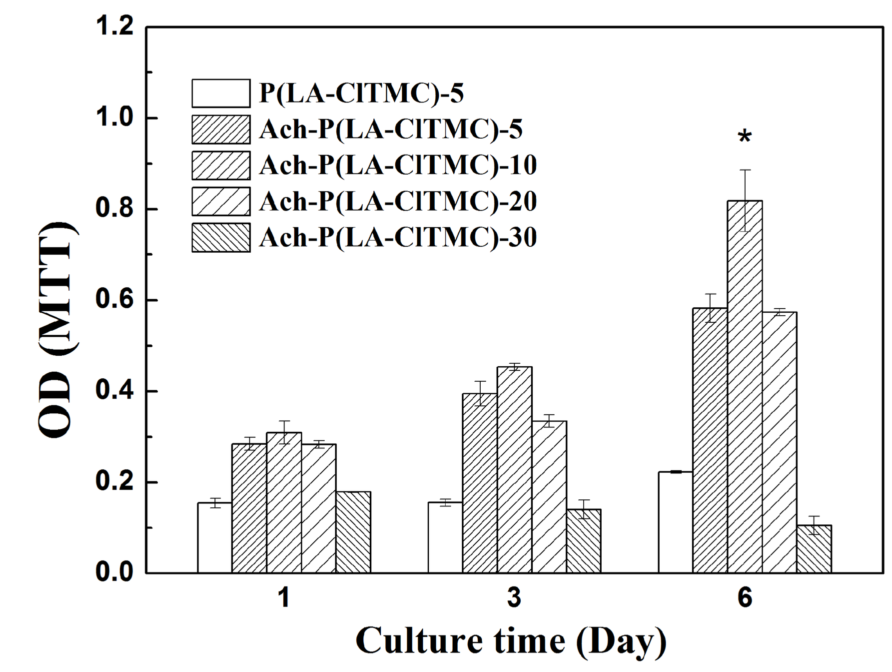


Fig. 3 MTT assay of PC12 viability on different films after being cultured for different time.

The highest cell viability appeared on the film of Ach-P(LA-ClTMC)-10 at the same culture time

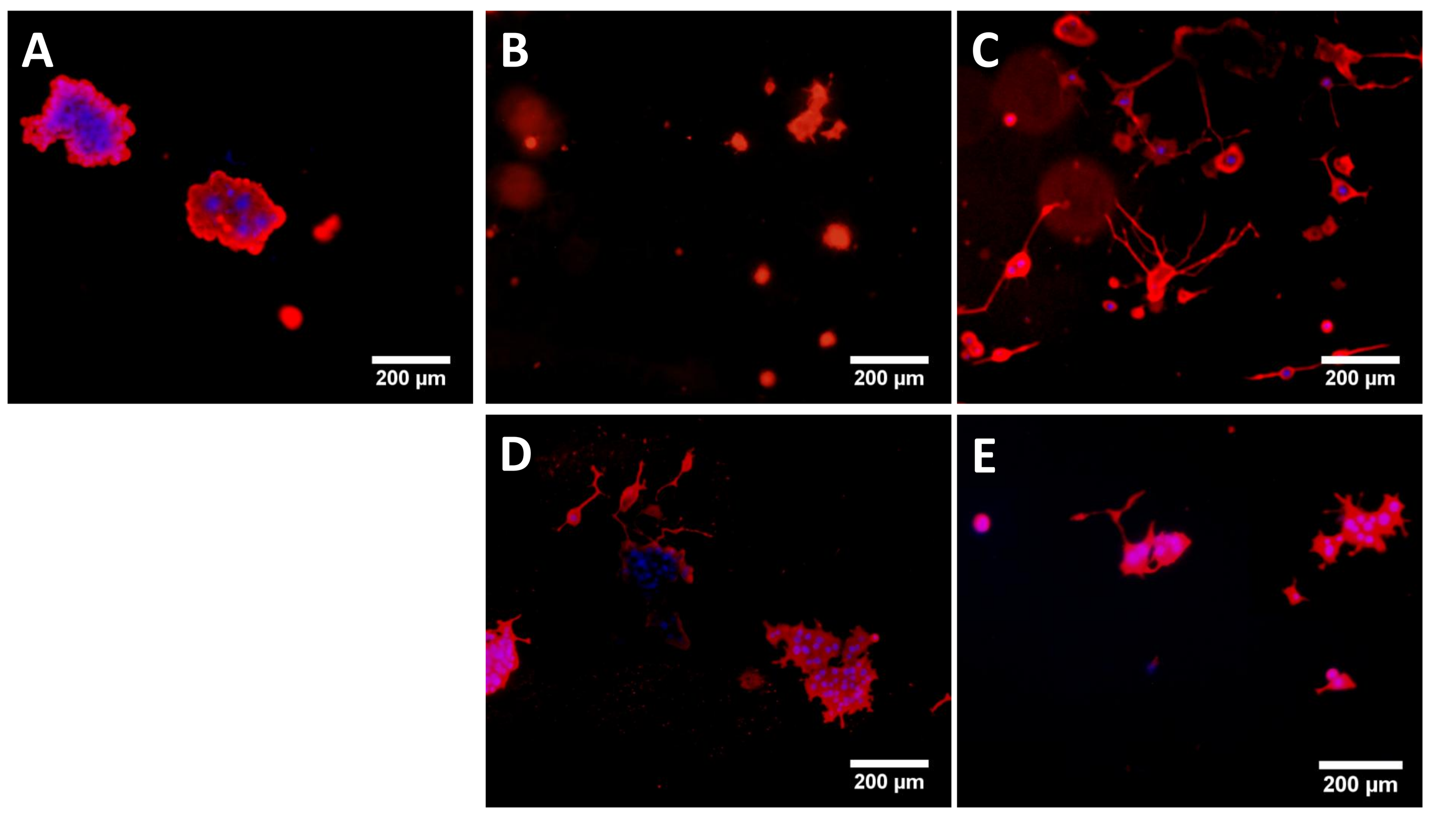


Fig. 4 Fluorescent images showing the neurite outgrowth of PC12 cells induced by NGF for 6 d on films of (A) P(LA-ClTMC)-5, (B) Ach-P (LA-ClTMC)-5, (C) Ach-P(LA-ClTMC)-10, (D) Ach-P(LA-ClTMC)-20, and (E) Ach-P(LA-ClTMC)-30.

Conclusions

A novel type of acetylcholine-functionalized poly(ester-carbonate)s were synthesized by copolymerization of LA with ClTMC, and subsequent quaternization with trimethylamine.

PC12 cells culture demonstrated that the acetylcholine analog affected cell behaviors such as cell viability and neurite outgrowth in a concentration-dependent manner. The Ach-P(LA-ClTMC)-10 showed the best performance in promoting neurite growth.

Acknowledgement

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