Electroconductive hydrogels for spinal cord regeneration

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INTRODUCTION

Spinal cord injury (SCI) is a devastating condition that disrupts the central nervous system, leading to disability and several associated medical complications [1]. Current treatments cannot fully address the complex pathophysiology of SCI due to the limited regenerative capacity of nervous tissue and the multifaced nature of the disease. In contrast, neuronal stem cells (NSCs) transplants offer therapeutic potential, as these cells can proliferate and differentiate helping to repopulate the damaged tissue [1-2]. However, direct NSCs injections into the injury site often fail to restore functionality, mainly due to low cell survival and integration [2]. To improve transplantation outcomes, hydrogels can be introduced as supportive scaffolds with physical and biochemical properties similar to those of neural tissue [2-3]. Furthermore, by incorporating electroconductive polymers into the hydrogel matrix, NSCs differentiation can be preferentially directed towards neurons, enhancing the therapeutic benefit [3]. This work proposes the design of an electroconductive hydrogel scaffold tailored for NSCs transplantation to promote spinal cord regeneration. Agarose and gelatin were selected as the base polymeric matrix to enhance biocompatibility, while in situ polymerized polypyrrole (PPy) or polyaniline (PAni) were introduced for their conductive and antioxidant properties [3-4].

MATERIALS AND METHODS

Agarose-gelatin (AgaGel) hydrogels were prepared by mixing both polymers at 60°C and then cooling the blend to room temperature. Electroconductive AgaGel hydrogels were obtained by adding either aniline or pyrrole to the hot blend, followed by in situ oxidative polymerization at 4°C. Unreacted monomers were then removed through washing. Hydrogels characterization included oscillation rheology, swelling tests, conductivity measurements, FT-IR spectroscopy, and scanning electron microscopy (SEM).

RESULTS

Several AgaGel formulations were developed by varying the concentrations of both polymers. Agarose primarily influenced mechanical strength, while gelatin improved stiffness and elasticity but, at high concentrations, reduced network stability. Therefore, the optimal agarose-gelatin ratio was defined



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based on mechanical properties considering an ideal storage modulus (G') between 100–1000 Pa to support NSCs viability. Conductivity was enhanced by incorporating PPy or PAni without compromising structural integrity. SEM analysis revealed interconnected porosity and visible collagen fibers, promoting cell attachment and growth.

CONCLUSION

The strategy proposed enabled the design of electroconductive hydrogel scaffolds tailored for cellular therapies for spinal cord regeneration. Furthermore, the combination of electroactive and antioxidant activity offers a promising platform for improving NSCs-based therapies and addressing key challenges in SCI treatment.

REFERENCES

- [1] Hu, X., Xu, W., Ren, Y. et al., 2023, 10.1038/s41392-023-01477-6.
- [2] Giorgi Z. et al., 2024, 10.1021/acsabm.3c01058.
- [3] Qin C. et al., 2023, 10.2147/IJN.S436111.
- [4] Raguraman M. et al., 2024, 10.1016/j.mtcomm.2024.109775.

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