Development of Novel Polyethylene Glycol Dimethacrylate (PEGDMA)-based Hydrogels for Nerve Regeneration

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Introduction:

Injury to the peripheral nervous system (PNS) affects more than 1,000,000 people worldwide a year. It is estimated that ~ $150 billion is spent on nerve injury repair in the USA alone each year. The current surgical methods have several disadvantages, such as limited recovery, which presents a need for improved peripheral nerve repair[1].

Nerve guide conduits (NGCs) have been developed to overcome this problem by protecting the nerve from the surrounding tissue and promoting successful nerve regeneration. Synthetic polymers may be used to produce NGCs and must possess certain characteristics to be considered as a suitable material for nerve regeneration[1][2] (see figure 1).

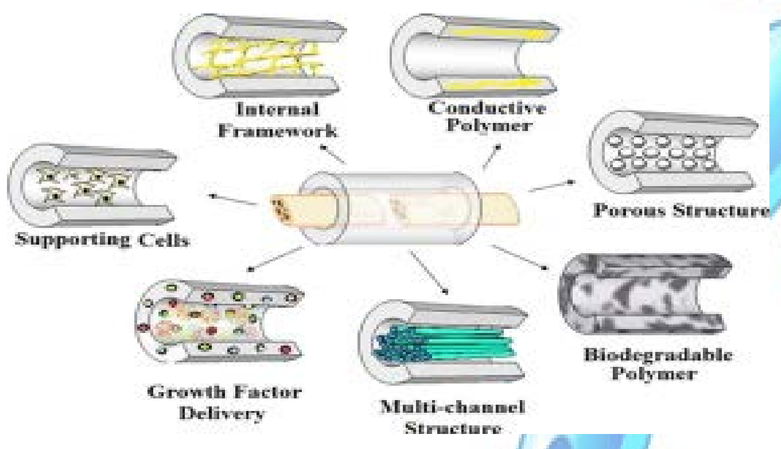

Figure 1: Ideal properties of a nerve guide conduit[3]

In this study, PEGDMA was chemically crosslinked with temperature sensitive poly (N-vinylcaprolactam) (PNVCL) to produce novel hydrogels. Charaterisation tests were carried out to determine if these novel biomaterials could potentially be used for the development of a novel NGC for peripheral nerve repair. 4-aminopyridine (4-AP), a neuroregenerative drug for acute traumatic nerve injury, was incorporated into the gels.

Experimental details:

PNVCL was chemically crosslinked with PEGDMA at various monomer concentrations (see table 1) *via* photopolymerisation by UV curing.

Table 1: Composition of PNVCL-based hydrogels

Hydrogel code	PNVCL (wt%)	PEGDMA (wt%)	Irgacure® 2959 (wt%)
PNVCL 100	100	0	0.1
PEGDMA 30- PNVCL 70	70	30	0.1
PEGDMA 70- PNVCL 30	30	70	0.1
PEGDMA 100	0	100	0.1

Characterisation studies:

Degradation Studies
-8 week degradation study
-Conditions: pH 7.4 at 37°C

Drug Release Studies
-5-day dose of 4-AP
-Drug dissolution at 37°C at pH 7.4

Results and Discussion:

Degradation Studies:

The main function of a NGC is to act as a channel to provide guidance for axons to regenerate and then eventually degrade from the site. If a NGC degrades too quickly, it can result in low mechanical support thus leading to poor axonal regeneration. However, slow degradation may compress nerves causing more damage to the injured site. In this study, PEGDMA 100% only showed a maximum of 4.83% weight loss after 8 weeks. The incorporation of PNVCL increased the degradation rate of the hydrogels, thus enhancing the properties of the hydrogels for nerve regeneration (see figure 2).

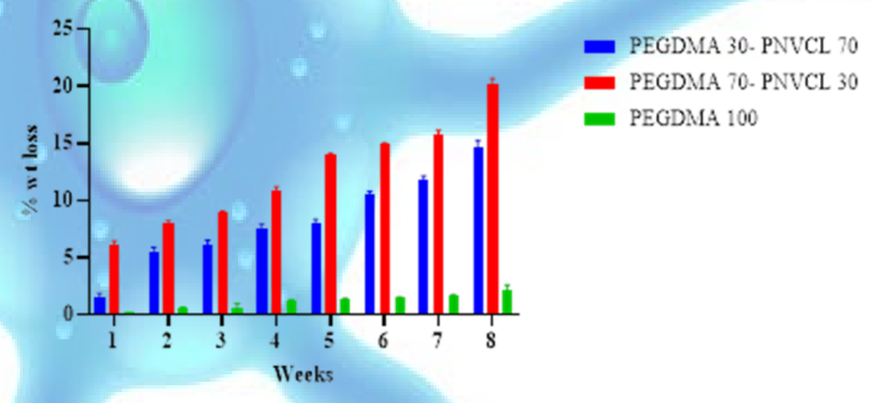

Figure 2: Degradation profile of PEGDMA-based hydrogels

Drug Release Studies:

A 5-day dose (100 mg) of 4-AP was incorporated into the gels and their drug release profile was established, see figure 3. 4-AP has been proven to improve the conduction of nerve impulses, thus improving nerve repair. The daily dose of 4-AP for human treatment varies from 10-30 mg, anything above has proven to be toxic. Therefore, it is critical to develop a drug delivery system which can successfully administer ~20 mg of 4-AP daily. In figure 3, it was found that the addition of PNVCL successfully controls the delivery of 4-AP from the gels with ~15-30 mg of the drug released daily over a 5-day period.

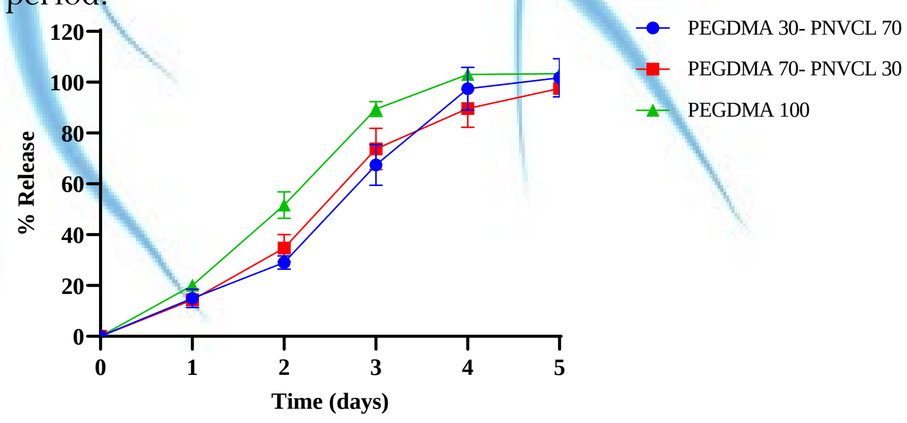

Figure 3: Dissolution profile of PEGDMA-based hydrogels

Conclusion:

The synthesis of novel PEGDMA-based hydrogels was successful. The thermo-sensitivity of PNVCL has proven to enhance the properties of the biomaterial. The hydrogels displayed favourable degradation profiles and have proven to be successful drug delivery systems by controlling the release of the neuroregenerative agent 4-AP.

References:
[1] Daly, W. et al. "A Biomaterials Approach To Peripheral Nerve Regeneration: Bridging The Peripheral Nerve Gap And Enhancing Functional Recovery". Journal of The Royal Society Interface 9.67 (2011): 202-221.
[2] Pinho, Ana C., et al. "Peripheral nerve regeneration: current status and new strategies using polymeric materials." Advanced healthcare materials 5.21 (2016): 2732-2744.
[3] Dalamagkas, K. et al. "Advances in peripheral nervous system regenerative therapeutic strategies: a biomaterials approach." Materials Science and Engineering: C 65 (2016): 425-432.