

Development of Poly(N-vinylpyrrolidinone) hydrogels for treatment of skin graft contracture

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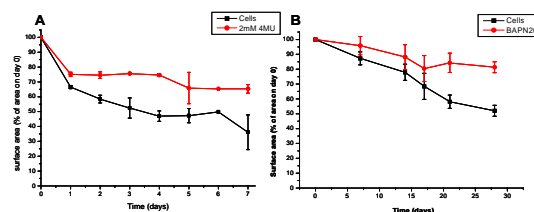
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INTRODUCTION: Skin graft contracture is a major post healing complication associated with burns treatment. The aim of this project was to develop and characterize a hydrogel wound dressing that could be used to deliver potential anti-contraction agents. Poly(N-vinylpyrrolidinone) (PNVP) was chosen to form the hydrogel due to its long history in biomedical applications. Two different crosslinking agents, ethylene glycol dimethacrylate (EGDMA) and diethylene glycol bisallylcarbonate (DEGBAC) were used to produce two different hydrogels with very different material properties. The agents selected to reduce contraction were β -aminopropionitrile (β APN), a competitive lysyl oxidase inhibitor which has been shown to significantly reduce contraction of a human reconstructed skin model and 4-methylumbelliferone, a hyaluronan synthase inhibitor.

METHODS: For details of hydrogel synthesis, material characterisation and cell culture see [1]. **Contraction models.** Collagen gels are formed from a stock solution of 5mg/ml rat tail collagen I in 0.1M Acetic acid to a final concentration of 1.5mg/ml in standard Greens medium and cast into a 24 well plate. Gels were cast containing 12,500 fibroblasts with 37,500 keratinocytes in 20 μ l medium added to the culture system after the gels had set. After 1 hour the gels were released from the sides of the well and 1ml of cell culture medium added. The reconstructed skin model was formed from seeding de-epithelialised acellular donor dermis with cultured fibroblasts and keratinocytes and was cultured submerged for two days. After two days the seeded area was excised and raised to an air liquid interface. At this point treatment with β APN and 4MU commenced. For both models contraction was measured using image analysis at regular time points.

RESULTS AND DISCUSSION: The two different crosslinkers used enabled us to produce two classes of polymer network with different material properties. Culture of fibroblasts in indirect contact with the hydrogels showed them to be non-cytotoxic and even stimulatory to cell viability and this effect was not altered by the presence of fetal calf serum in the culture system. [1]. 4-MU decreased contraction in both the collagen gels (Figure 1A) and the reconstructed



skin model however β APN was found to decrease contraction only in the reconstructed skin model (Figure 1B).

Fig. 1: Effect of 4-MU on contraction of collagen I gels (A) and effect of β APN on contraction of reconstructed skin (B)

Preliminary data for the release of 4MU from P(NVP-co-DEGBAC) showed that after an initial burst the release rate dropped to negligible levels. Hydrogels could provide release of potential anti-contraction agents for up to 48 hours.

CONCLUSIONS: Results to date suggest that this hydrogel can successfully take up and release these two agents which have been shown to moderate contraction in both models. The challenge now will be to evaluate the drug releasing hydrogels against both contraction models to develop an approach for topical clinical use following skin grafting.

REFERENCES: ¹ L.E. Smith, S. Rimmer, S. Mac Neil, (2006) *Biomaterials* **27**: 2806-2812.

ACKNOWLEDGEMENTS: We would like to thank the EPSRC for a doctoral training award for L. Smith.