A NOVEL SELF-SINTERING MICROPARTICLE-BASED SYSTEM FOR REGENERATIVE MEDICINE

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INTRODUCTION: The use of injectable scaffolds has raised great interest as they minimise the need for invasive surgery and its associated complications, costs and discomfort to the patient. Furthermore, they can fill cavities of any size or shape as well as being able to deliver a localised therapeutic agent [1]. The aim of this study was to develop an injectable scaffold using PLGA microparticles which may be able to (i) carry cells and/or drugs to a site of injury (ii) be delivered via a narrow bore needle, and (iii) form a scaffold *in situ* with sufficient mechanical properties. The investigated system exploits a novel *in situ* solidification mechanism (liquid sintering) whereby the injectable microparticle-based precursors solidify into 3D constructs in response to thermal changes [2]. Thus, we demonstrate that PLGA microparticles incorporated with Triton X-100 are thermally responsive at body temperature (37°C) and may be exploited in regenerative medical applications.

METHODS: PLGA microparticles (<50µm and 50-100µm diameter) were fabricated using the single emulsion (oil-in-water; O/W) technique. Triton X-100 incorporated microparticles were fabricated using the double emulsion (water-oil-water; W/O/W) technique. Mechanical, rheological and injectability (27-gauge needle) characteristics of these microparticles were also documented. Fabricated microparticles were left to sinter at 37°C and 60°C (temperature above Tg) for 24h before being evaluated using a Joel 6060LV variable pressure SEM operating at 10kV. The attachment, spreading and proliferation characteristics of Swiss 3T3 cells on the microparticles were also investigated. Moreover, the biocompatibility of these scaffolds was assessed using the chick chorioallantoic membrane (CAM) assay.

RESULTS: Injectability of these microparticles (both size fractions) through the 27-gauge needle was feasible; although injectability of the suspension decreased with an increase in microparticle concentration. The rheological and mechanical profiles of the microparticles also expressed favourable transition characteristics. PLGA microparticles with Triton X-100 incorporated were found to sinter into matrices at both 37°C and 60°C while microparticles without Triton X-100 incorporated did not undergo liquid sintering at 37°C (Fig 1). Triton X-100 incorporated microparticles did not sinter at room temperature.

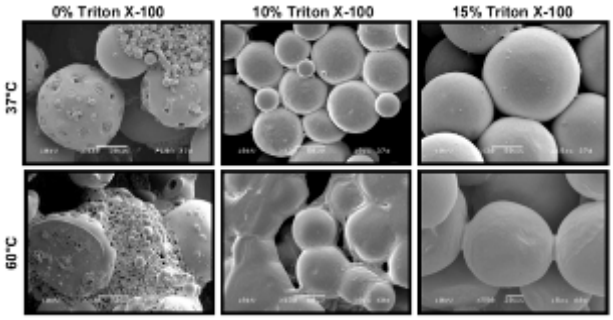

Fig. 1: SEM micrographs of PLGA microparticles with 0%, 10% and 15% Triton X-100 incorporated after liquid sintering at 37°C (top row) and 60°C (bottom row)

DISCUSSION & CONCLUSIONS: Injectability of the microparticles improved with higher liquid-to-particle ratio by mass. Interestingly the size fractions had no significant effects on their injectability through a 27-gauge needle ($p>0.05$). The sintering effect at both 37°C and 60°C was induced by the presence of Triton X-100 and the consequent fusing between neighbouring microparticles into a 3D construct. Moreover, due to the low concentration of Triton X-100 exploited, incorporation efficiency and also leaching characteristics, initial cell and CAM assay analyses indicate that this novel self-sintering system may be biocompatible and not inhibit angiogenesis.

REFERENCES: [1] Q Hou, PA De Bank and KM Shakesheff (2004) *J. Mater. Chem.* 14(13):1915-1923. [2] C Bouissou, J Rouse, R Price and C Van der Walle (2006) *Pharm Res.* 23(6):1295-1305.

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