Mechanical Properties of and *In Vitro* Response to a Novel Resorbable Biomaterial

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Statement of Purpose: A number of research groups have investigated the possibility of producing a liquid-crystalline bioresorbable polymer with varying success.[1,2] Dagger *et al*. have produced a series of bioresorbable liquid-crystalline polymers from varying quantities of 4-hydroxybenzoic acid (HBA), vanillic acid (VA), dimethyl bisphenol S (d-BPS) and adipic acid (AA) which have excellent mechanical properties.[3,4] This research describes the results obtained from mechanical property investigations and initial *in vitro* biocompatibility testing on poly$(HBA)_{50}(VA)_{25}(d\text{-}BPS)_{12.5}(AA)_{12.5}$ (LCP) in comparison with PLLA.

Methods: Biocompatibility Testing: The materials used during testing were poly$(HBA)_{50}(VA)_{25}(d\text{-}BPS)_{12.5}(AA)_{12.5}$ (Victrex PLC), PLLA (PURAC), PVC-tin (Raumedic), low density polyethylene (Smith & Nephew) and Thermanox™ (NUNC). Throughout the assays murine pre-osteoblast cells (MC3T3-E1 Subclone 14, ATCC) were expanded in αMEM and cultured in direct or indirect contact with the test material. Live/dead staining was carried out on all assays at 24 hours and 7 days. Samples were analysed at the appropriate wavelengths. ISO10993 Part 5 testing was conducted using media conditioned in the presence of PLLA, LCP, PVC-tin and low density polyethylene (LDPE) for 7 days (37 ^{o}C, 5% CO_2). The media was added to cell cultures for 24 hours at dilutions of up to 1/16. Testing was carried out using WST-1 cell metabolism reagent. Values of less than 70% indicate a cytotoxic potential of the material compared to the non-toxic control.

Mechanical testing: The polymer was injection moulded on a Fanuc 5T machine. The test samples had a gauge section of 11.95 x 2.31 mm and an overall specimen length of 70 mm. Mechanical testing to determine tensile and flexural properties was carried out on an Instron 5564 system.

Results: Live/dead staining of the direct contact assay after 24 hours indicated that the controls behaved as expected. Increased cell death was observed for the PLLA control in comparison to Thermanox™, whereas the quantity of live cells present on the LCP appeared more comparable to those on Thermanox™. After 7 days there was a similar level of cell survival observed for PLLA and LCP.

In the in-direct contact assays healthy cells were observed in close proximity to both PLLA and LCP with a number of healthy cells visible surrounding LCP.

Analysis of the data gained from the ISO 10993 testing indicates that the samples exposed to LCP had greater than 98% viability at all times compared to the control, indicating that this material is not considered to have cytotoxic potential. Cells cultured in media conditioned with PLLA showed viability as low as 81.9% as shown in Figure 1.

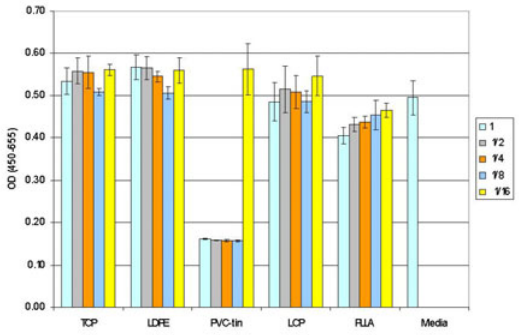

Figure 1: *Optical densities measured to determine cell viability in media conditioned in the presence of Thermanox (TCP), LDPE, PVC-tin, poly$(HBA)_{50}(VA)_{25}(d\text{-}BPS)_{12.5}(AA)_{12.5}$ (LCP) and PLLA.*

The mechanical properties determined for the LCP were higher than previously reported[3,4] and the optimum properties are detailed in Table 1.

Table 1: *Optimum Mechanical properties of LCP obtained during study.*

Property	Value
Tensile Strength	130 MPa
Tensile Modulus	2.6 GPa
Elongation	8.8%
Flexural Strength	220 MPa
Flexural Modulus	7.5 GPa

The properties detailed in Table 1 suggest that the LCP discussed herein has strengths comparable to market leading industrial and non-resorbable LCPs such as Vectra.[5] In the medical arena the properties are much higher than for current resorbable materials and more comparable to those quoted for PEEK-OPTIMA®[6] a permanent thermoplastic implant material. This novel LCP may provide benefits for medical applications requiring a high strength resorbable biomaterial.

Conclusions: Initial biocompatibility testing on poly$(HBA)_{50}(VA)_{25}(d\text{-}BPS)_{12.5}(AA)_{12.5}$ (LCP) has indicated that the cell response to this novel material is similar to that observed for PLLA. The excellent mechanical properties determined for this material are significantly higher than those for injection moulded PLLA.[7] Therefore, based upon the results of these studies this material may have potential for use in the production of load bearing bioresorbable implants.

References: [1]Chen Y., *Biomacromolecules*, 2003:4:974-980, [2]Du J., *Polym. Degrad. Stabil.*, 2008:93:838-845, [3]Dagger A.,WO 2007/110609, 2007, [4]Montes de Oca H., *Biomaterials*, 2010:31(30):7599-7605. [5]www.ticona.com, [6]www.invibio.com, [7]Perego G., *J. Polym. Sci.*, 199:59:37-43