Biocompatibility of Silicon Nitride Nanoparticles and Cobalt Chromium Wear Debris from THR

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Introduction: Silicon nitride (SiN) is a recently introduced bearing material for THR that has shown potential in its bulk form and as a coating material on cobalt-chromium (CoCr) substrates. Previous studies have shown that SiN has low friction characteristics, low wear rates and high mechanical strength. Moreover, it has been shown to have osseointegration properties. However, there is limited evidence to support its biocompatibility as an implant material. The aim of this study was to investigate the responses of peripheral blood mononuclear cells (PBMNCs) isolated from healthy human volunteers and U937 human histiocytes (U937s) to SiN nanoparticles and CoCr wear particles.

Methods: SiN nanopowder (<50nm, Sigma UK) and CoCr wear particles (nanoscale, generated in a multidirectional pin-on-plate reciprocator) were heat-treated for 4 h at 180°C and dispersed by sonication for 10 min prior to their use in cell culture experiments. Whole peripheral blood was collected from healthy donors (ethics approval BIOSCI 10-108, University of Leeds). The PBMNCs were isolated using Lymphoprep® as a density gradient medium and incubated for 24 h in 5% (v/v) CO_2 at 37°C to allow attachment of mononuclear phagocytes. SiN and CoCr particles were then added to the phagocytes at a volume concentration of 50 μm^3 particles per cell and cultured for 24 h in RPMI 1640 culture medium in 5% (v/v) CO_2 at 37℃. Cells alone were used as a negative control and lipopolysaccharide (LPS; 100 ng/ml) was used as a positive control. Cell viability was measured after 24h by ATPLite assay and tumour necrosis factor alpha (TNF-α) release was measured by sandwich ELISA. U937s were co-cultured with SiN and CoCr particles at doses of 0.05, 0.5, 5 and 50 μm^3 particles per cell for 24h in 5% (v/v) CO_2 at 37℃. Cells alone were used as a negative control and camptothecin (2 μg/ml) was used as a positive control. Cell viability was measured after 0, 1, 3, 6 and 9 days. Results from cell viability assays and TNF-α response were expressed as mean ±95% confidence limits and the data was analysed using one-way analysis of variance (ANOVA) and Tukey-Kramer post-hoc analysis.

Results and Discussion: At a high volume concentration of particles (50μm^3 per cell), SiN did not affect the viability of PBMNCs, while CoCr significantly reduced the viability over a 24 hour period [Figure 1A]. Similarly, SiN particles had no effect on the viability of U937s up to 9 days with a range of particle doses (0.05-50 μm^3 per cell) [Figure 2A]. In contrast, CoCr particles significantly reduced the viability of U937s after 6 days [Figure 2B]. Additionally, CoCr particles caused significantly elevated levels of pro-inflammatory cytokine TNF-α, whereas no inflammation was associated with SiN particles [Figure 1B].

Conclusion: This study has demonstrated the in-vitro biocompatibility of SiN nanoparticles. Therefore, SiN is a promising orthopaedic bearing material not only due to its suitable mechanical and tribological properties, but also due to its biocompatibility.

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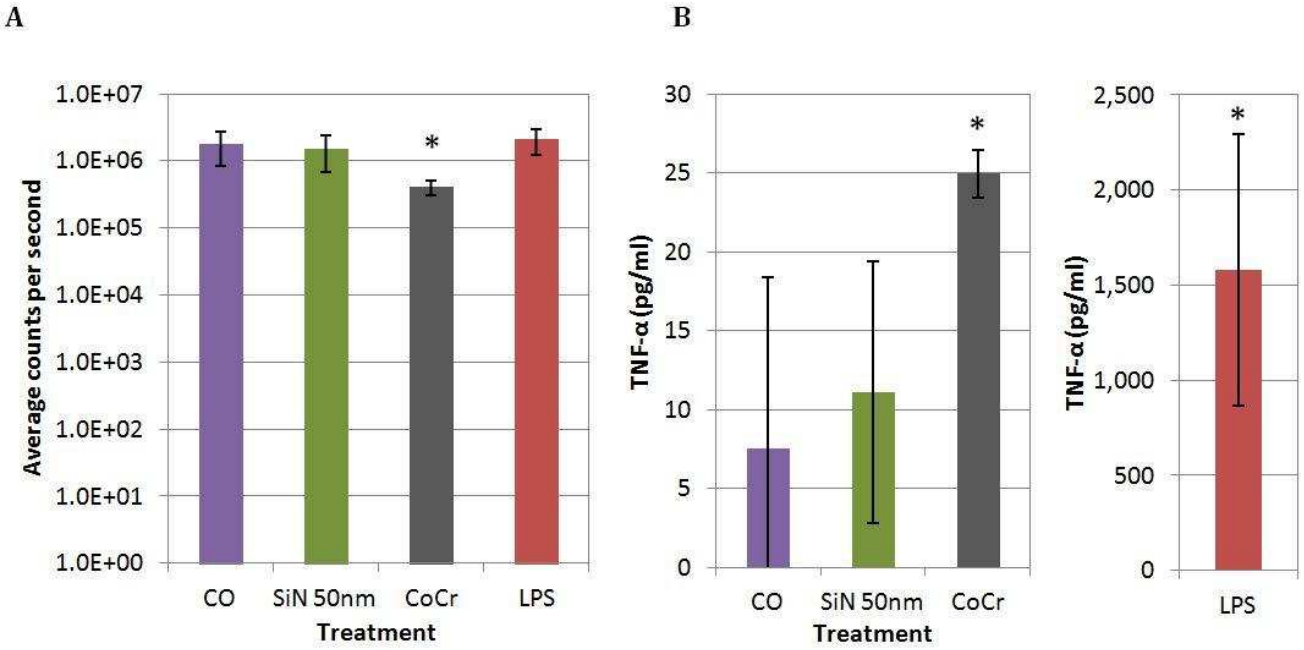

Figure 1. A) Viability of PBMNCs cultured with silicon nitride 50nm model particles and cobalt chromium (CoCr) wear particles at 50um^3 particles per cell. B) TNF-α release in PBMNCs co-cultured with silicon nitride 50nm model particles and cobalt chromium (CoCr) wear particles at 50um^3 particles per cell. CO: Cells only control, LPS: Lipopolysaccharide control. *Significant difference from the cell only control (ANOVA and Tukey-Kramer post hoc test, $p<0.05$).

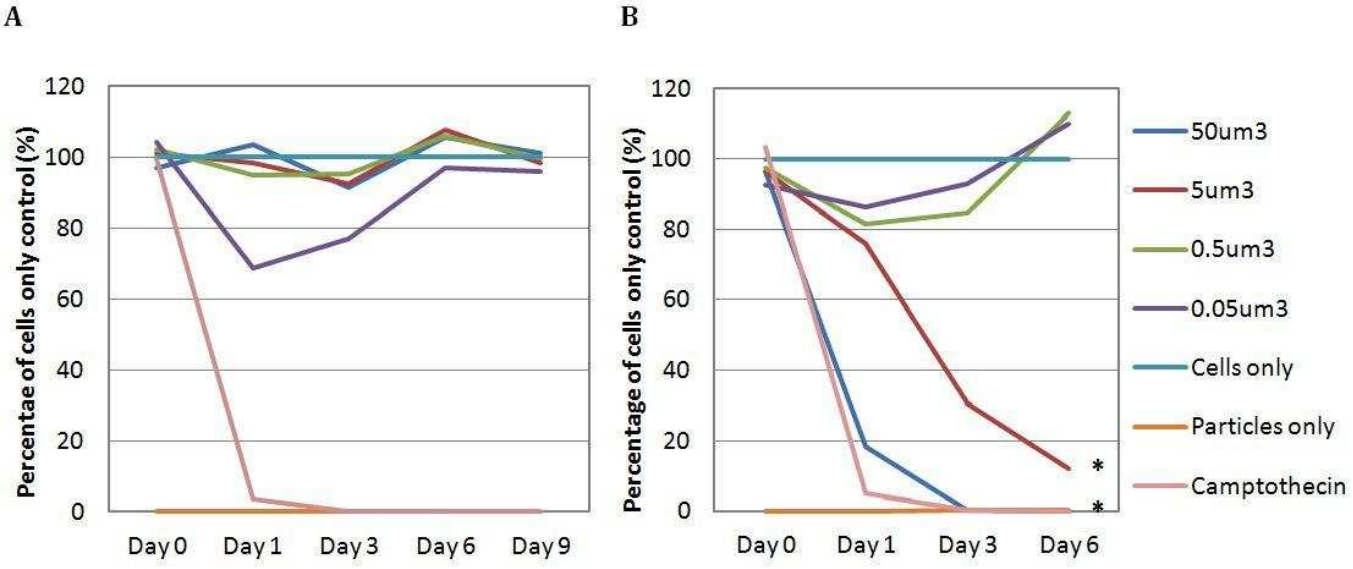

Figure 2. Viability of U937 cells co-cultured with 0.05um^3, 0.5um^3, 5um^3, 50um^3 of particles. A) Cells cultured with silicon nitride model particles. B) Cells cultured with CoCr wear particles. *Significant reduction in the cell viability on day 6. (ANOVA and Tukey-Kramer post hoc test, $p<0.05$).