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Investigation into the biocompatibility and antibacterial performance of TiO_2 silicone nanocomposites

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SUMMARY

Incorporation of nanoparticles into silicone elastomers to form silicone nanocomposites is an area of ongoing research, with a broad range of biomedical applications. Addition-cure silicone nanocomposite dispersions were prepared, containing TiO_2 of varying nanoparticle sizes and concentrations. All TiO_2 silicone nanocomposites remained biocompatible (cell viability >70% relative to control silicone) when assessed via direct contact MTT assay. However, results from bacterial adherence studies demonstrated that 1000 nm and 200 nm TiO_2 nanocomposites displayed a greater antibacterial effect in comparison to 100 nm and 20 nm TiO_2 nanocomposites. The data suggests TiO_2 silicone nanocomposites possess antibacterial properties (that is dependent on particle size) and are cytocompatible, warranting further research into potential uses for biomedical applications.

INTRODUCTION

The incorporation of nanoparticles (NPs) within silicone elastomers in order to form silicone nanocomposites is an area of active research, as may impart the elastomer with advantageous properties for particular applications (Binyu, 2011; Kumaravel, 2021). TiO_2 is inexpensive, biocompatible and possesses antibacterial properties (Lam, 2021). The effect of TiO_2 nanoparticle size and concentration within silicone nanocomposites was investigated.

MATERIALS AND METHODS

Preparation of silicone elastomer films

Silicone elastomer films containing 2.5% or 5% w/w TiO_2 of varying particle sizes (20, 100, 200 and 1000 nm) were prepared from medical grade addition-cure silicone elastomer dispersions (MED 6600, NuSil Technology LLC). Briefly, silicone parts A and B (1:1) were mixed (Speedmixer DAC-150) with the required quantity of NP for 5 min at 3000 rpm, left overnight for solvent evaporation, and then post-cured (3 h, 90°C) Circular discs of 1 cm diameter were cut from the resulting films.

Bacterial quantification and biofilm formation

Samples were incubated in a Mueller Hinton broth containing ~10^6 CFU/mL *Staphylococcus aureus* (ATCC 6538) or *Escherichia coli* ((ATCC 11303) for 4 h or 24 h. Bacteria were detached into quarter strength Ringer's solution by sonication at 37 KHz for 15 min and then placed into a vortex mixer for a further 1 min. Bacteria were then enumerated using the Miles & Misra technique.

Cytocompatibility studies

Under standard cell culture conditions, samples were incubated in direct contact with RAW 264.7 macrophages in a Dulbecco's Modified Eagle Medium (Gibco® DMEM) or L929 fibroblasts cells in a Minimum Essential Media (Gibco® MEM). All

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media were supplemented with 10% foetal bovine serum (Gibco®) and 1% (50U/mL) penicillin/streptomycin (Gibco®). MTT assays were then performed after 24 and 48 h to assess cytotoxicity.

Statistical analysis

A one-way ANOVA with Tukey's post hoc test, with α= 0.05 was used to analyse data. The statistical analyses were performed using GraphPad Prism, version 8.3.1.

RESULTS AND DISCUSSION

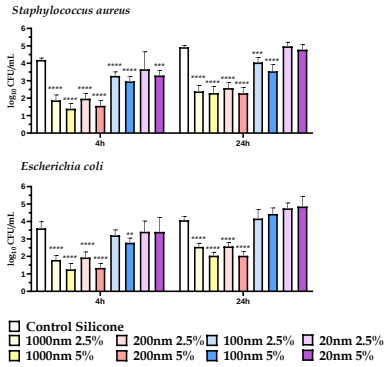

***Fig. 1**. Bacterial adherence of Staphylococcus aureus (top) or Escherichia coli (bottom) upon various silicone nanocomposites following 24h at 37°C in a gyrorotary incubator (n=3). Asterisks in fig. 1. indicate significant differences in relation to the blank control silicone (NS P > 0.05, * P ≤ 0.05, ** P ≤ 0.01, *** P ≤ 0.001, **** P≤ 0.0001).*

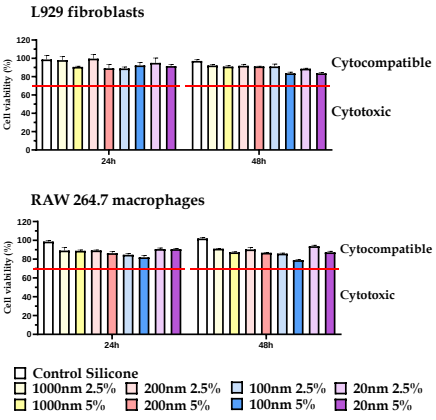

***Fig. 2.** Summary of MTT proliferation assays for L929 fibroblasts (top) and RAW 264.7 macrophages (bottom) following 24h incubation upon silicone nanocomposites (n=3). The red line at 70% signifies the ISO-defined boundary between cytocompatible and cytotoxic.*

As illustrated in *Fig. 1.*, nanocomposites containing 1000 nm and 200 nm exhibited the greatest antibacterial properties relative to their 100 nm and 20 nm counterparts. Increasing the TiO_2 concentration from 2.5 to 5% w/w caused a further reduction in CFU/mL in most samples apart from samples containing 20nm TiO_2 challenged with *Escherichia coli*.

The data highlighted in *Fig. 2.* demonstrates that the silicone nanocomposites can be considered cytocompatible, since cell viability of both L929 fibroblasts and RAW 264.7 macrophages exposed to nanocomposites remained above the 70% threshold, relative to cell lines exposed to blank silicone control.

CONCLUSIONS

Silicone nanocomposites containing TiO_2 of varying particle sizes and concentrations were synthesised and it was found that TiO_2 silicone nanocomposites offer antibacterial properties without compromising biocompatibility. Furthermore, TiO_2 NP size influenced the antibacterial properties of samples.

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