**Bioinspired Silicate Nanocomposites for Osteoarthritis Therapy**

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**INTRODUCTION:** A reduction of cartilaginous matrix can generate an arthritic response, which can reduce orthopedic joint function. This leads to impaired movement and pain, due to bone-on-bone contact. While conservative treatments exist to relieve symptoms, few therapies target the source of dysfunction by regenerating functional tissue. Our objective was to integrate differentiation-inducing material to provide a versatile scaffold system with desired functional tissue generation. A main criterion, however, was to do so without growth-factor involvement. Silicate nanoplatelets demonstrate good cytocompatibility as well as bioactivity to induce differentiation of human mesenchymal stem cells (hMSCs) into both osteogenic and chondrogenic lineages, vital for interfacial repair of the joint.

**EXPERIMENTAL:** hMSCs were incubated with a range of nanosilicate concentrations under both normal and chondroconductive media conditions. A nanoclay-rich kappa-Carrageenan composite hydrogel was fabricated to promote chondrogenic differentiation of hMSCs. A 1% solution of kappa-Carrageenan was prepared with and without nanosilicates and subsequently crosslinked with a 5% potassium chloride solution. *In vitro* characterization was performed through alamar blue staining to quantify metabolism of seeded cells, alcian blue and safranin O stains for visualization and quantification of glycosaminoglycans (GAGs) for preliminary evaluation of differentiation potential. Physical properties and structure were determined using mechanical compression analysis and scanning electron microscopy.

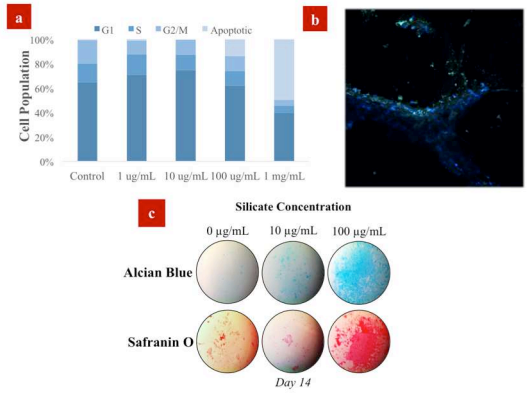


**Figure 1.** (a, b) Cell cycle analysis and internalization (blue) of silicate nanoparticles demonstrate cytocompatibility with hMSCs. (c) The addition of silicates results in an increase of GAG production by Day 14 of culture.

**RESULTS:** Internalization of nanosilicates, as evaluated by flow cytometry, was determined to follow a primarily clathrin-mediated mechanism. Additionally, cell cycle analysis demonstrated minimal adverse effects and enhanced proliferation, as seen by an increased population in the G1 phase, where only the largest concentration evaluated (1 mg/mL) displayed cytotoxicity. Integration of nanosilicates within kappa-Carrageenan hydrogels resulted in significant improvement of mechanical stability, demonstrating a two-fold increase in modulus for nanocomposite scaffolds. Likewise, cell adhesion was improved due to the additional binding sites provided by the silicates within the polymeric matrix. This trend directly correlated to concentration of nanoparticles added. Significant cartilaginous matrix production was documented at higher concentrations, indicating differentiation of hMSC's into chondrocyte lineage.

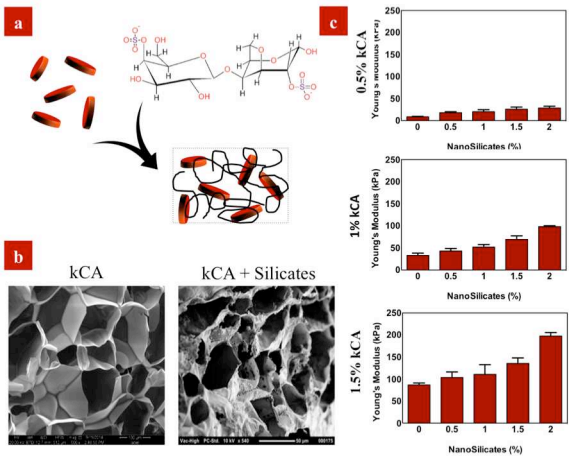


**Figure 2.** (a, b) Integration of nanosilicates into kCA matrix provides additional binding sites for encapsulated cells. (c) Polymer-nanoparticle interactions generate beneficial mechanical responses via control of polymer or nanoparticle concentration.

**CONCLUSION:** Bioinspired nanosilicates demonstrate induction capabilities, illustrated through GAG staining, in addition to cytocompatibility up to considerable concentrations. The incorporation of nanosilicates within the kappa-Carrageenan matrix enhanced the mechanical integrity of the hydrogel while providing adhesion sites for cellular proliferation. This nanocomposite system has the potential for use in osteochondral tissue engineering applications in which cartilage wear impairs joint function.