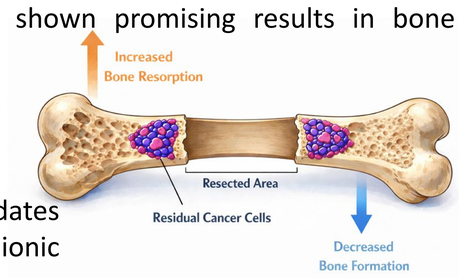
Selenium and Magnesium Functionalised Scaffolds for Dual Bone Regeneration & Anti-Cancer Therapy

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Introduction

- Cancer impairs bone remodelling resulting in reduced bone formation and increased resorption
- Tumour resection poses the risk of non-union defects alongside residual cancer cells remaining in the site
- Incorporation of bioactive ions into biomaterials has shown promising results in bone regeneration and anti-cancer activity
  - **Magnesium (Mg) -** Osteogenic and anti-resorptive[2]
  - **Selenium (Se) -** Anti-cancerous[3]
- Nanohydroxyapatite (nHA) particles are excellent candidates for ion delivery as their structure can accommodate ionic substitution



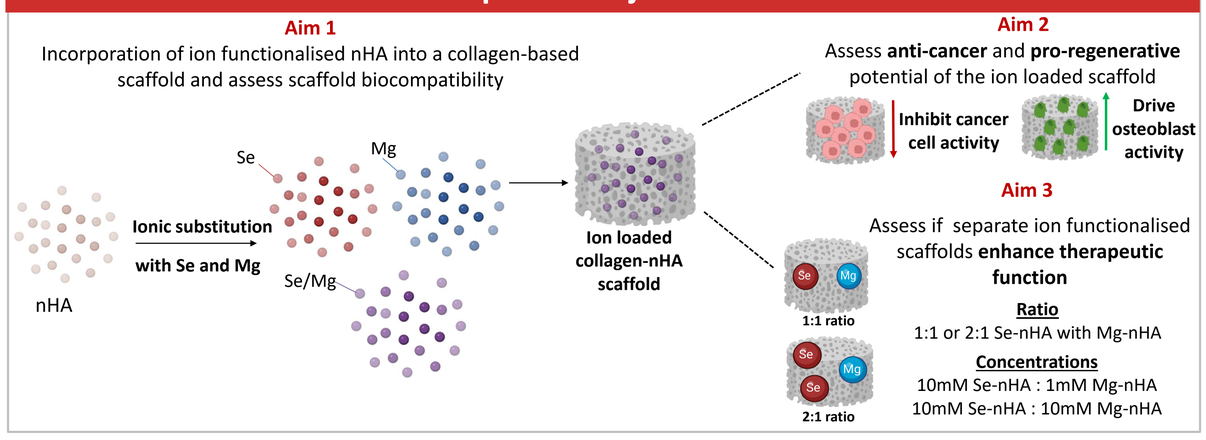
Hypothesis

By harnessing therapeutic qualities of Selenium and Magnesium, the scaffold will exhibit synergistic anti-cancerous properties (Se) while also promoting bone regeneration (Mg).

Overall Aim

The overarching aim of this project is to develop a dual functional, anti-cancer and pro-regenerative, scaffold for the treatment of bone defects resulting from tumour resection, by combining nano-therapeutics such as nHA and bioactive ions alongside biomaterial technologies.

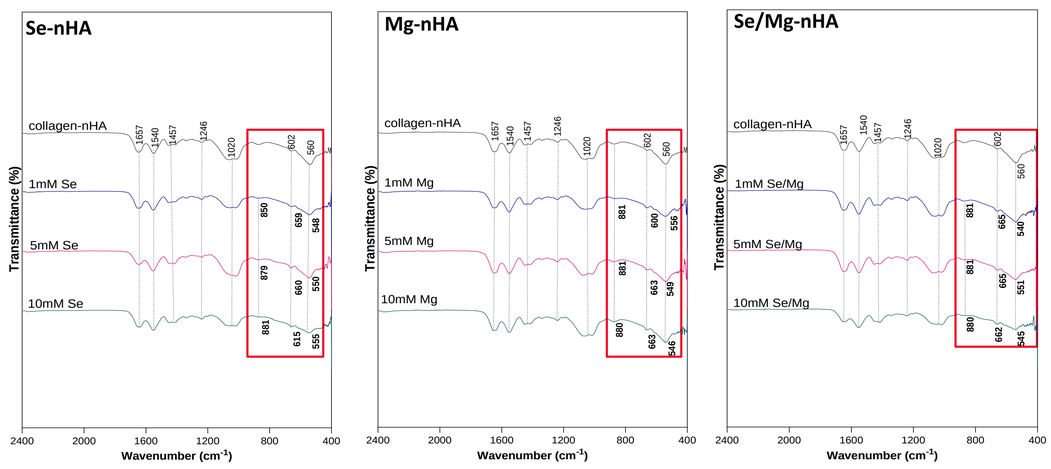
Specific Objectives



Results

Aim 1: Ion loaded collagen-nHA characterisation and biocompatibility

Aim 1.1 Physicochemical characterisation of ion loaded collagen-nHA scaffolds



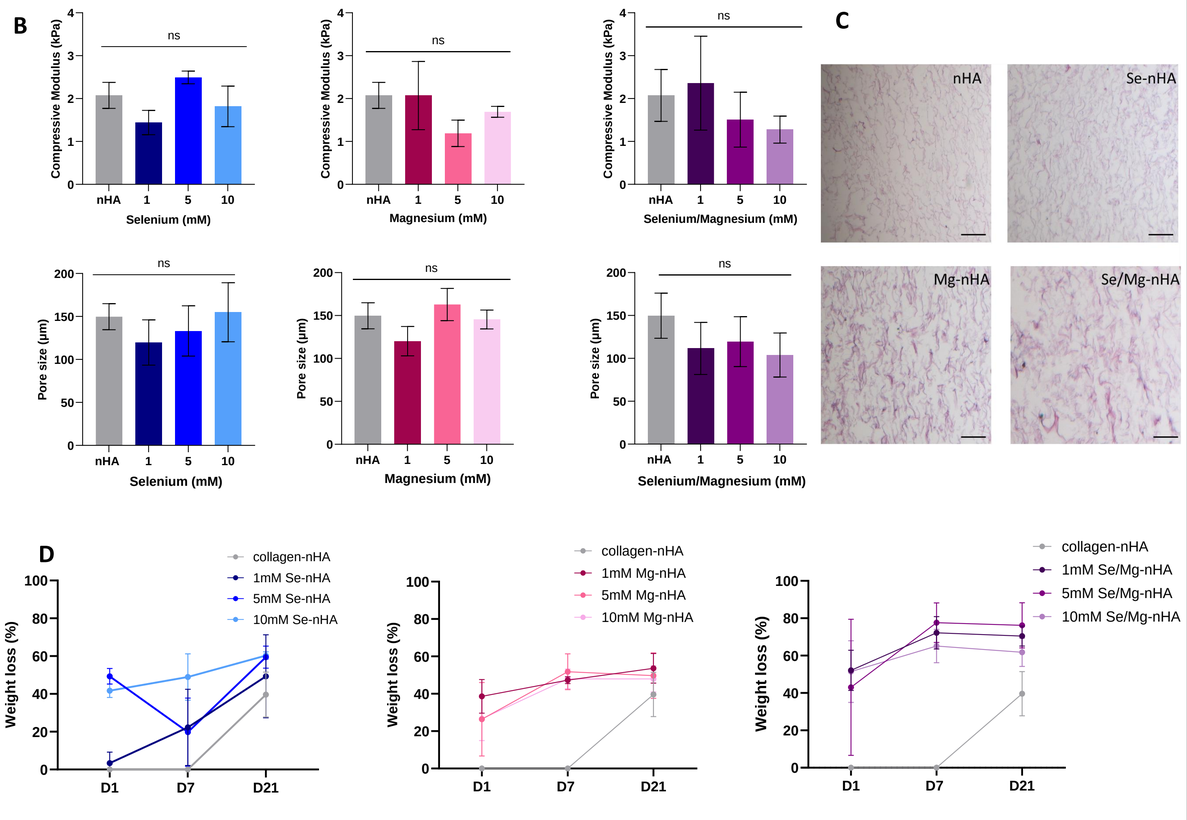


Figure 1. Fourier-Transform Infrared Spectroscopy (FTIR) spectra of Se, Mg and Se/Mg-nHA. Peaks observed around 560, 602 and 1000 cm^{-1} are characteristic of hydroxyapatite, with additional peaks at 700 cm^{-1}, 800 cm^{-1} and 1000-2000 cm^{-1}, demonstrating successful Se, Mg and Se/Mg incorporation (A). Compressive modulus and pore size was not affected by ion incorporation with average compressive modulus of 1.5kPa and pore size of 150μm (B+C). An increase in degradation was observed with increasing ion concentrations (D). Scale bar 100μm.

Results

Aim 1: Ion loaded collagen-nHA characterisation and biocompatibility

Aim 1.2 Biocompatibility of the ion loaded scaffolds on both osteoclasts and osteoblasts

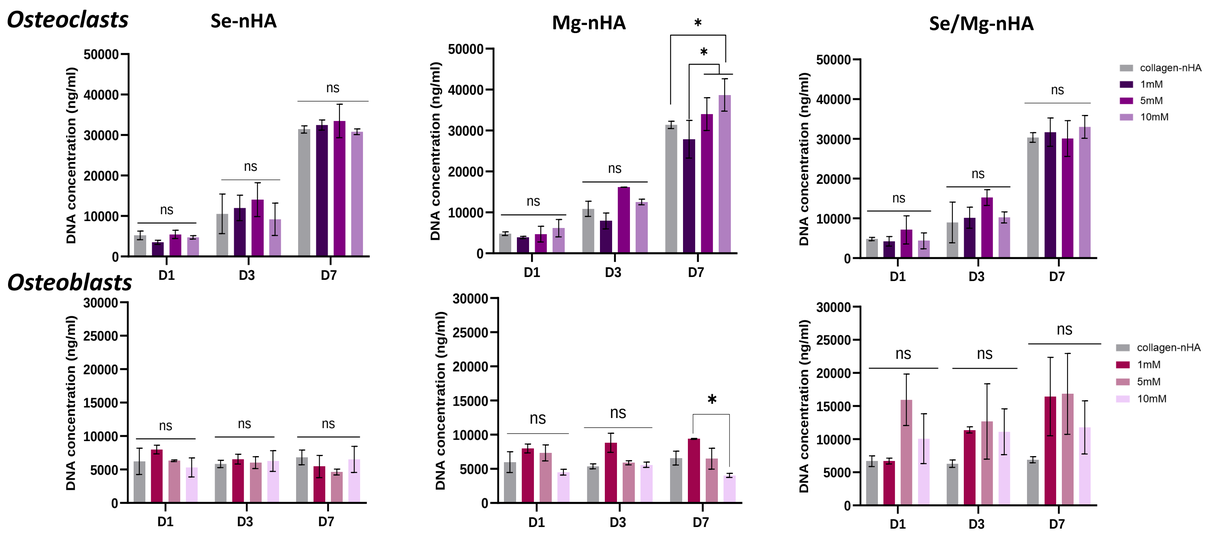


Figure 2. Se-nHA had no significant effect on both osteoclast and osteoblast activity while Mg-nHA (10mM) enhanced osteoclast activity while reducing osteoblast activity. Se/Mg-nHA enhanced osteoblast proliferation compared to both individual ions. *p<0.05 compared to nHA

Aim 2: Assess anti-cancer potential of the ion loaded scaffolds on cancer cell proliferation

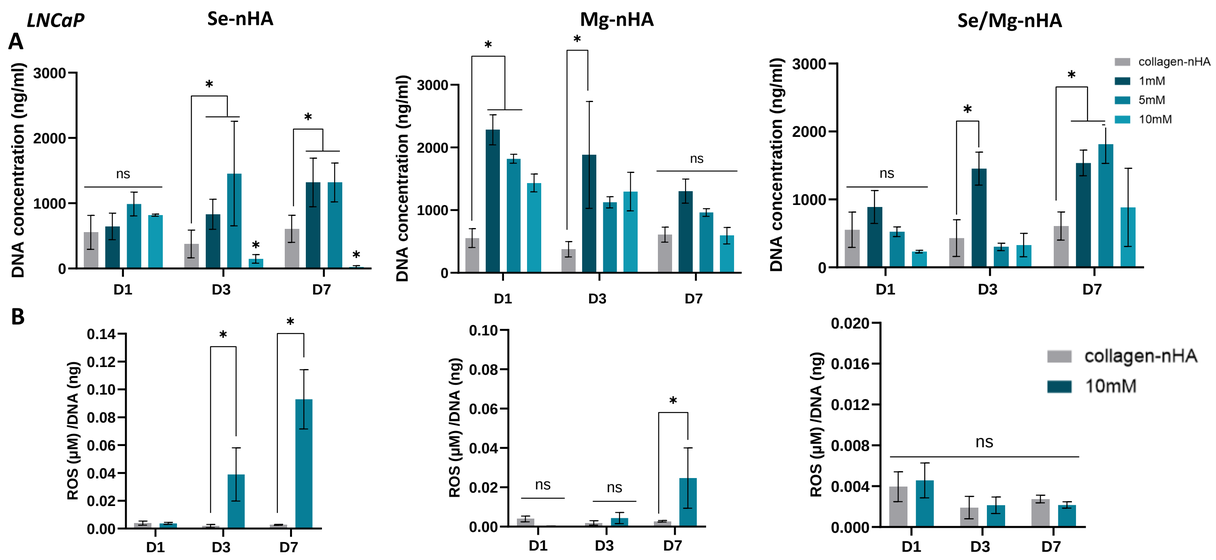


Figure 3. Se-nHA had a concentration dependent effect on LNCaP proliferation with 10mM significantly reducing proliferation while Mg had no significant effect. A reduction in LNCaP proliferation was observed in the Se/Mg-nHA (10mM) although not as significant as Se-nHA. compared to nHA (A). 10mM Se-nHA had a significant increase reactive oxygen species (ROS) measured indicating a pro-oxidative response (B). *$p<0.05$*

Aim 3: Enhancing therapeutic function through separate ion delivery

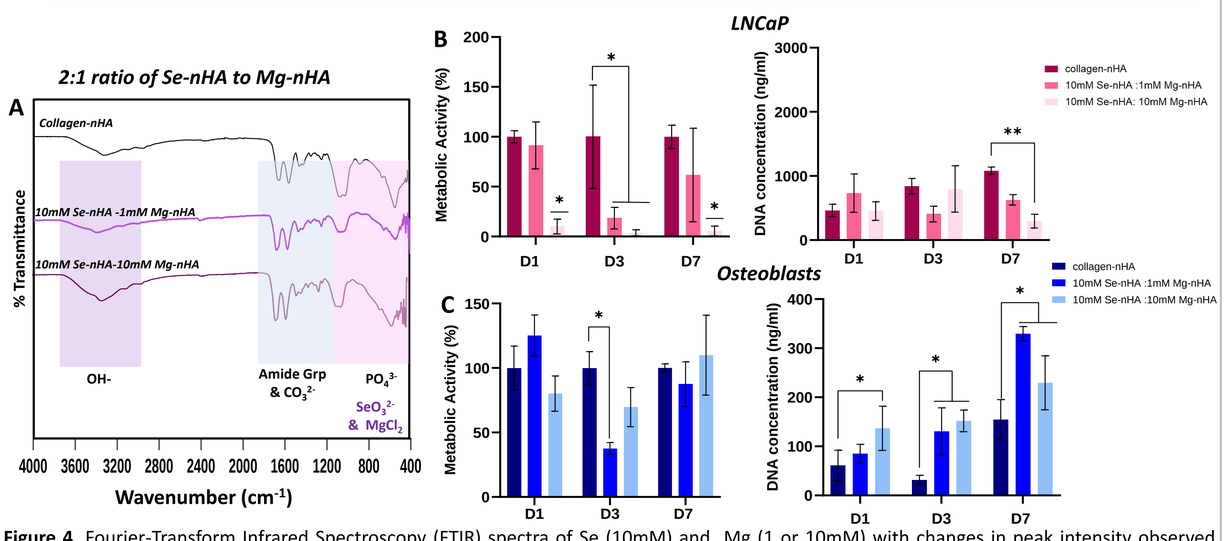


Figure 4. Fourier-Transform Infrared Spectroscopy (FTIR) spectra of Se (10mM) and Mg (1 or 10mM) with changes in peak intensity observed around at 700 cm^{-1}, 800 cm^{-1} and 1000-2000 cm^{-1}, demonstrating successful Se and Mg incorporation (A). At a 2:1 ratio of Se (10mM) to Mg (10mM) the scaffolds significantly reduced cancer cell proliferation (B) while enhancing osteoblast activity (C) retaining the dual functionality of the scaffolds. *$p<0.05$, **$p<0.01$* compared to collagen-nHA control.

Conclusions

- Incorporation of both Se and Mg did not affect the compressive modulus of the scaffolds
- Higher concentrations of Se, Mg and Se/Mg-nHA (10 mM) increased scaffold degradation rates
- Se/Mg-nHA, enhanced osteoblast activity while and inhibiting osteoclast proliferation, highlighting their potential for enhanced therapeutic efficacy
- 10 mM Se-nHA significantly inhibited LNCaP proliferation with an increase in ROS with this effect reduced in the Se/Mg-nHA scaffolds
- When delivered separately in the same scaffold at a 2:1 ratio of Se (10mM) to Mg (10mM) LNCaP proliferation is reduced while enhancing osteoblast activity.

Future work

- Current work is investigating if there is ROS dependent effect of Se, Mg and Se/Mg on LNCaP proliferation while also assessing LNCaP attachment and migration
- Future work will also assess the effect of Se, Mg and Se/Mg on osteogenic and osteoclastogenic differentiation and bone formation

References and Acknowledgments

1. Little (*et al.*), *Bone Jt. Surg. - Br. Vol.* **89–B:** 425–433, 2007.
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3. Fan (*et al.*), Materials Express. **12:** 1033-1041, 2022.

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