Polylactide Coated Hydroxyapatite Nanoparticles for Reinforced Biodegradable Polymer Scaffolds

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Abstract

Tissue engineering involves combining cells and biomaterials to generate scaffolds that act as templates for tissue regeneration. Polylactide (PLA) is a biocompatible and biodegradable polymer, but critical problems are associated with it due to its hydrophobicity and its inadequate mechanical properties. Hydroxyapatite (HA) nanoparticles ($Ca_{10}(PO_4)_6(OH)_2$) exhibit chemical similarity to the main mineral component of bone, and promise to provide strength to compensate for the low durability of PLA. Due to the incompatibility of unmodified hydroxyapatite nanoparticles and PLA, PLA-coated hydroxyapatite will be synthesized in order to promote successful interaction with the PLA fiber. Once the PLA-coated hydroxyapatite is integrated successfully and is dispersed evenly into the PLA fiber, it will provide strength throughout the scaffold in a uniform manner. As the PLA surrounding the PLA-coated HA nanoparticles degrades, the remaining HA will incorporate itself into the bone naturally, filling the targeted defect while preventing an immunogenic response from occurring in the body.

Introduction

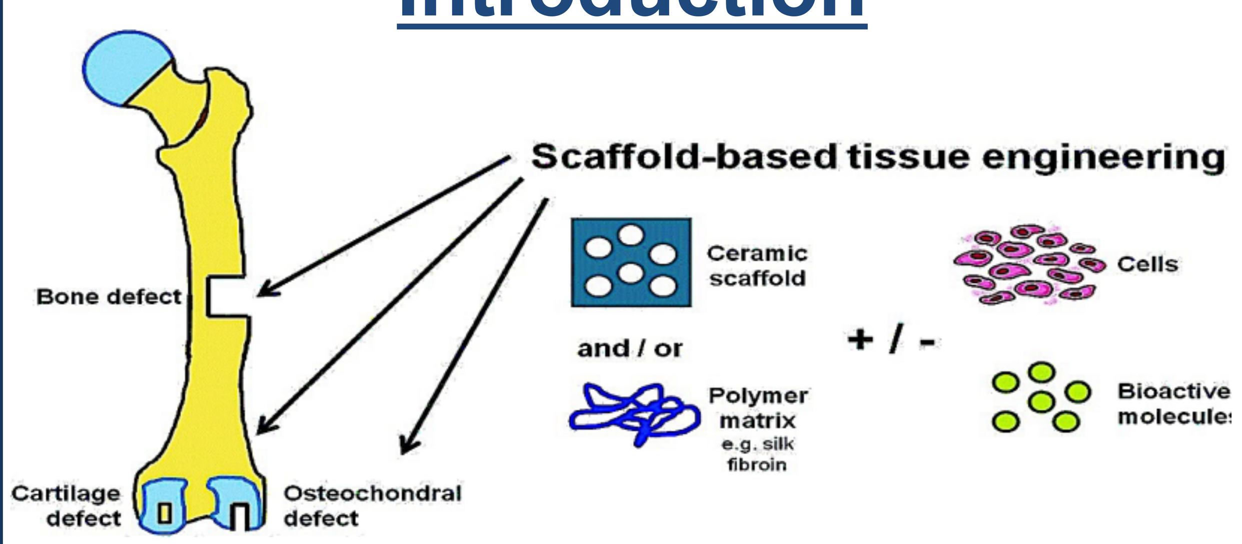


Figure 1. Components of the biodegradable scaffold[2]

- Properties such as porosity, strength, and biodegradability can be manipulated in polymeric scaffolds.

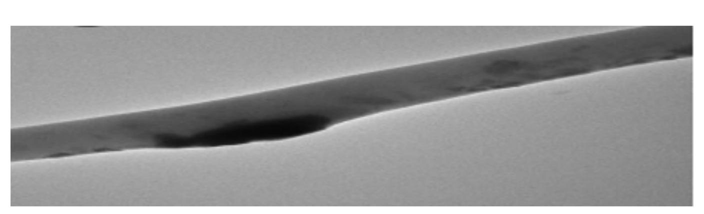


Figure 2. Clumping of HANP's on PLA fiber[3]

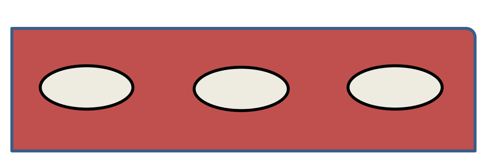
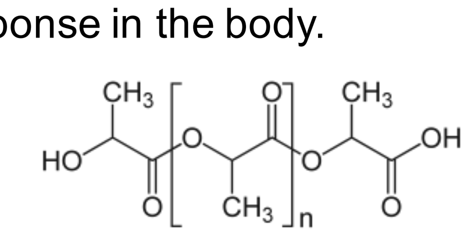


Figure 3. Even distribution of coated HANP's inside PLA fiber

- HA nanoparticles and PLA have different inherent properties; thus, the interaction between these two components has been unsuccessful, resulting in inhomogeneous composites with a formation of HA aggregates and inadequate mechanical properties due to distinct phase separation[7]
- Generating optimal scaffolds by incorporating PLA-coated hydroxyapatite into the PLA fiber will provide strength uniformly throughout the scaffold while also allowing tissue to naturally regenerate after the surrounding PLA degrades, without triggering an immunogenic response in the body.

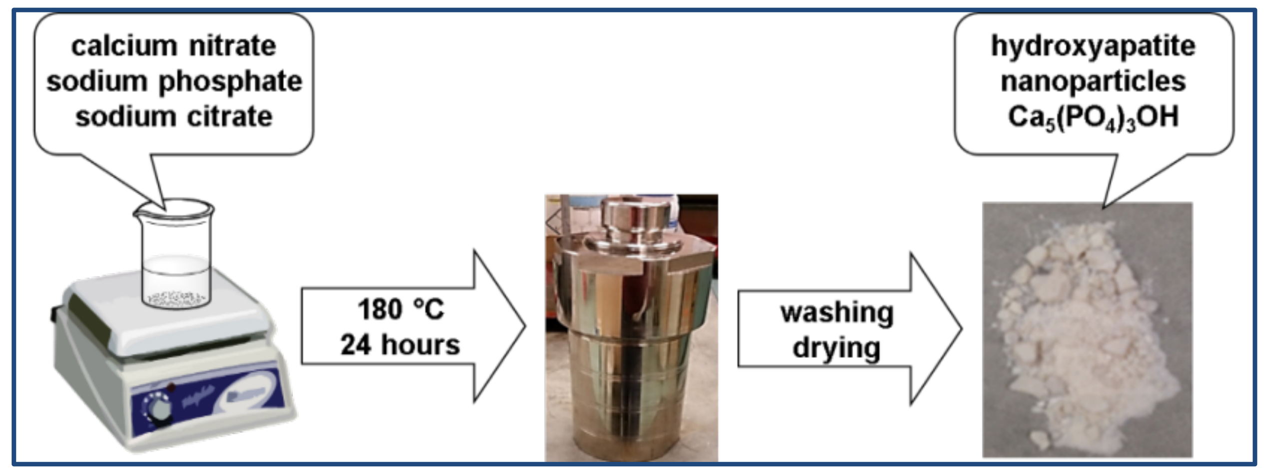
Figure 4. PLA Structure



- Composite scaffolds exhibiting sufficient biocompatibility and biodegradability allow for successful cell proliferation and cell interaction at the defect site with a decrease in implant complications, eventually leading to natural, successful tissue regeneration.

Materials and Methods

Hydrothermal Method for Hydroxyapatite Nanoparticle Synthesis:



Scheme 1. Hydrothermal Synthesis

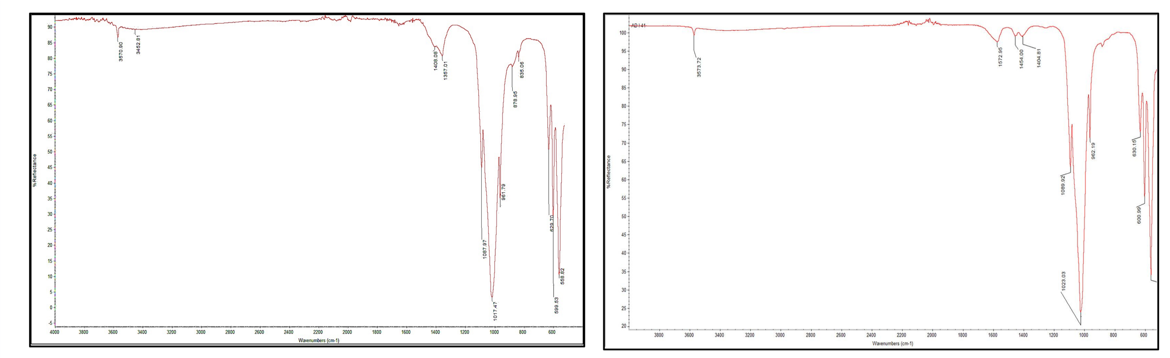


Figure 6. IR spectrum of unmodified HA (50x without citrate)and unmodified HA (50x with citrate)

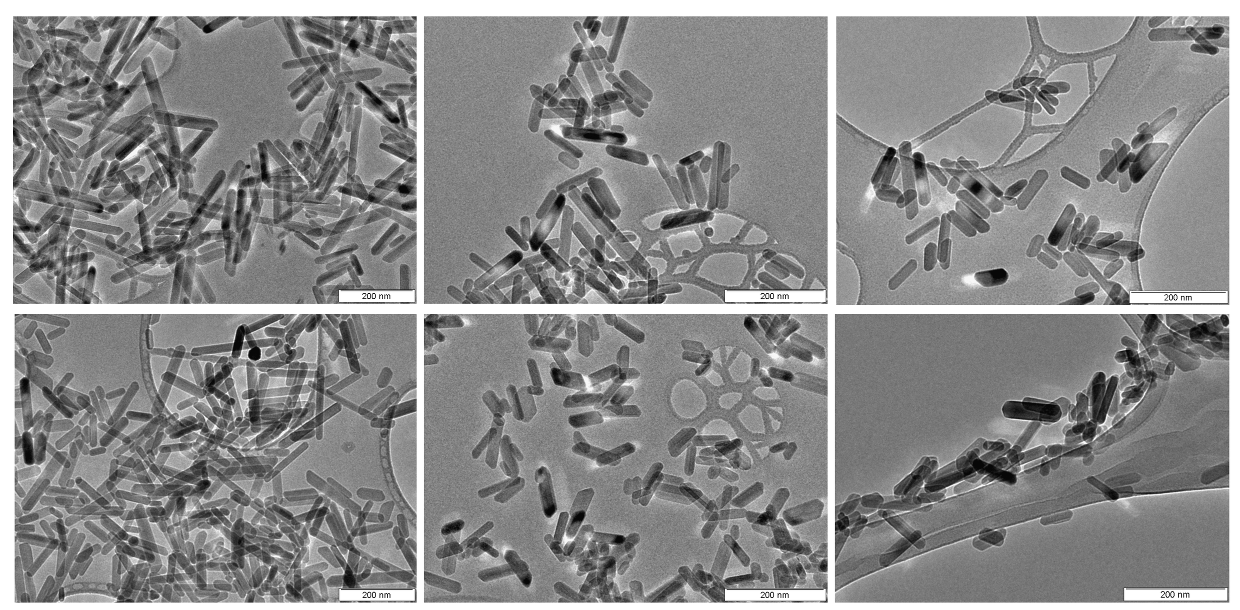


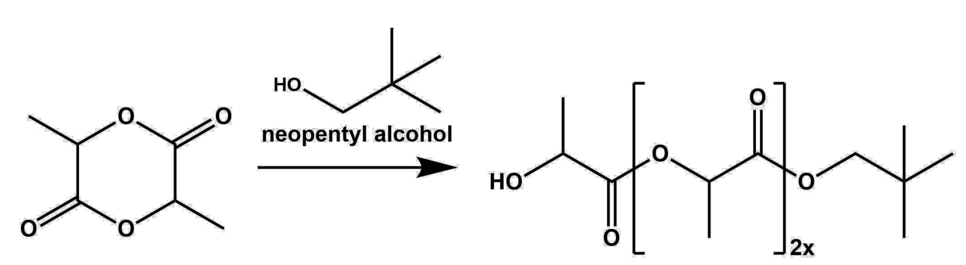
Figure 5. Unmodified hydroxyapatite nanoparticle morphology with varying concentrations(1x,5x,25x,50x with citrate, 25x,50x without citrate)

Reactants concentration	Average length(nm)	Average width(nm)
1x	159 ± 70	30 ± 7
5x	103 ± 32	24 ± 6
25x without citrate	72 ± 22	23 ± 5
25x with citrate	77 ± 22	21 ± 5
50x without citrate	71 ± 22	23 ± 6
50x with citrate	72 ± 23	22 ± 5

Table 1. Hydroxyapatite nanoparticle average length and width with varying reactant concentrations

Surface Modification of Hydroxyapatite Nanoparticles with L-lactide:

Ring-Opening Polymerization



Scheme 2. Ring Opening Polymerization

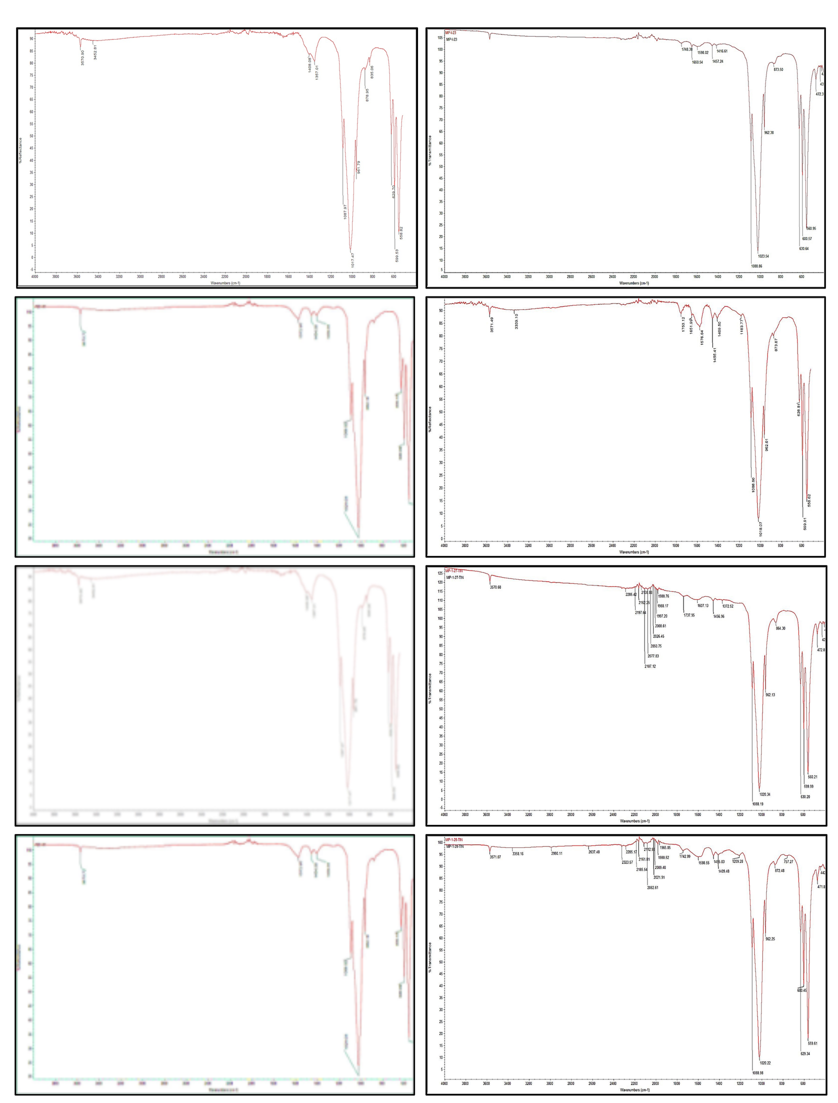


Figure 7. IR spectra of unmodified HA (50x without and with citrate) (on the left) versus surface-grafted HA nanoparticles mediated by DMAP and the Tin catalyst respectively (on the right)

Catalyst

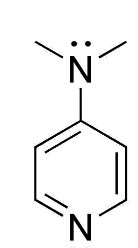


Figure 8. 4-Dimethylaminopyridine (DMAP)

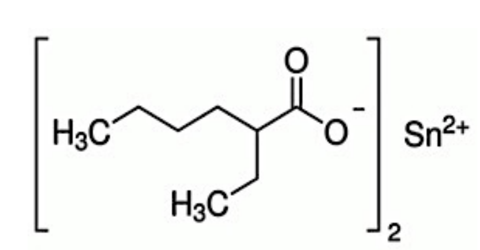


Figure 9. Tin(II) 2-ethylhexanoate

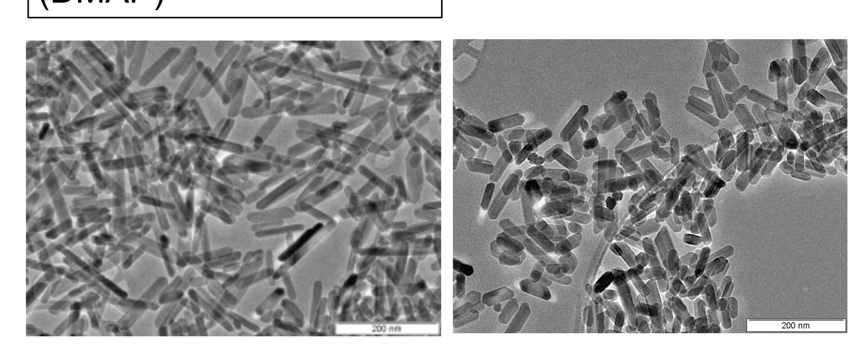


Figure 10. TEM images of unmodified HA particles

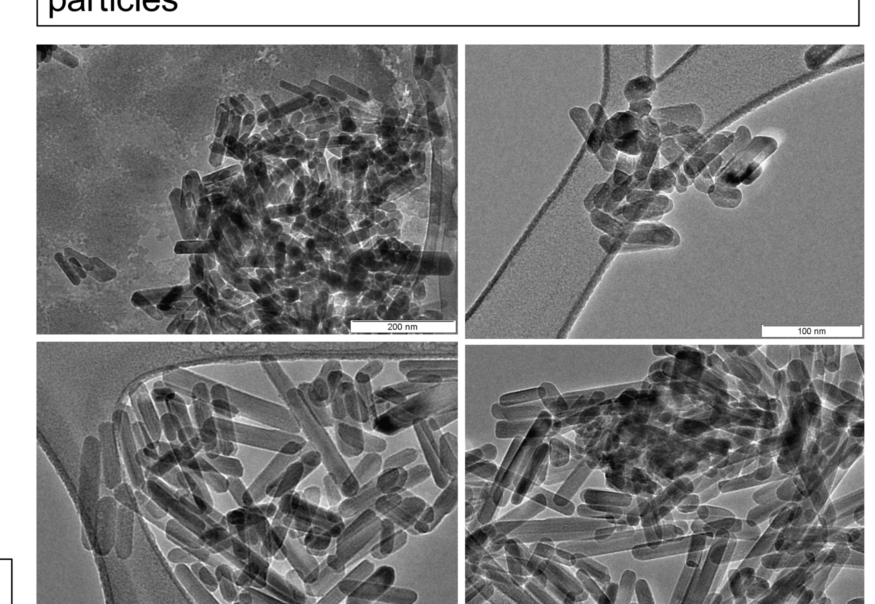


Figure 11. TEM images of surface-grafted HA particles

Surface Initiator

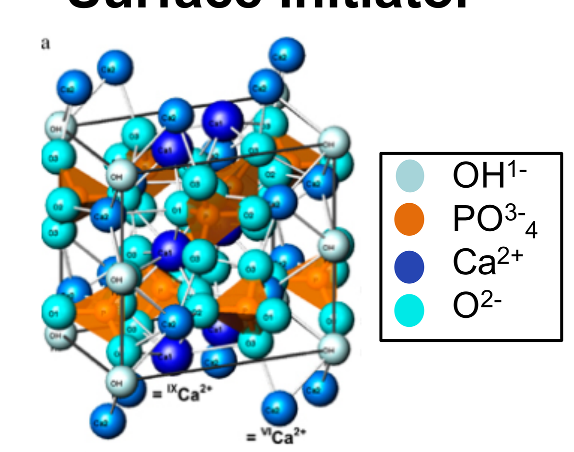


Figure 12. HA Crystalline structure[6]

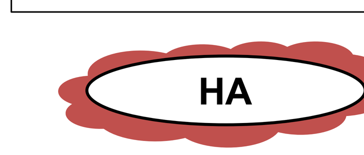


Figure 13. Polymer-coated HA cartoon

Nanoparticle Stability:

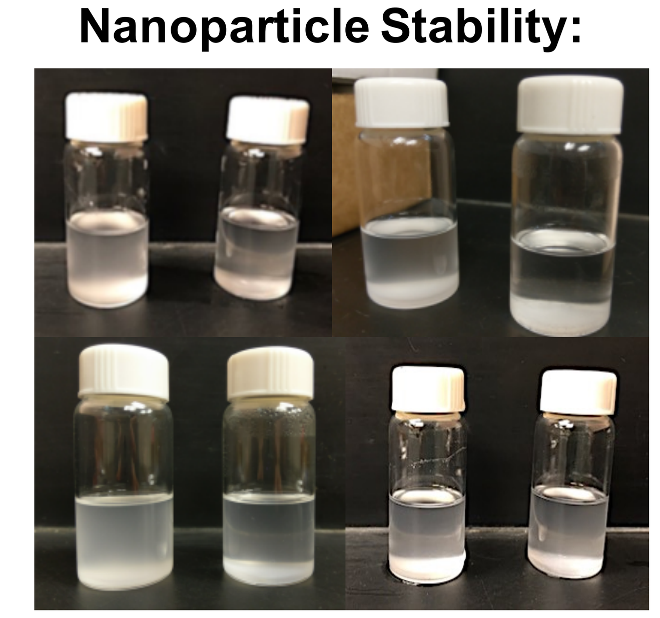


Figure 14. Conducted stability tests with surface-grafted HA nanoparticles(left) and unmodified HA nanoparticles(right) in chloroform solution after 30 minutes

Conclusions

- The increase in concentration correlates with the decrease in nanoparticle size.
- Different sizes of HA were synthesized successfully at 180°C using the hydrothermal method with desired morphology
- The surface modification of HA nanoparticles with lactide was conducted under various conditions and the results were inconclusive.
- The IR data and stability tests showed evidence of polymer, but no coating was visible in the TEM images

Future Work

- Revisit surface modification and investigate new method for successful attachment
- Electrospinning PLA-coated HA nanoparticles with PLA

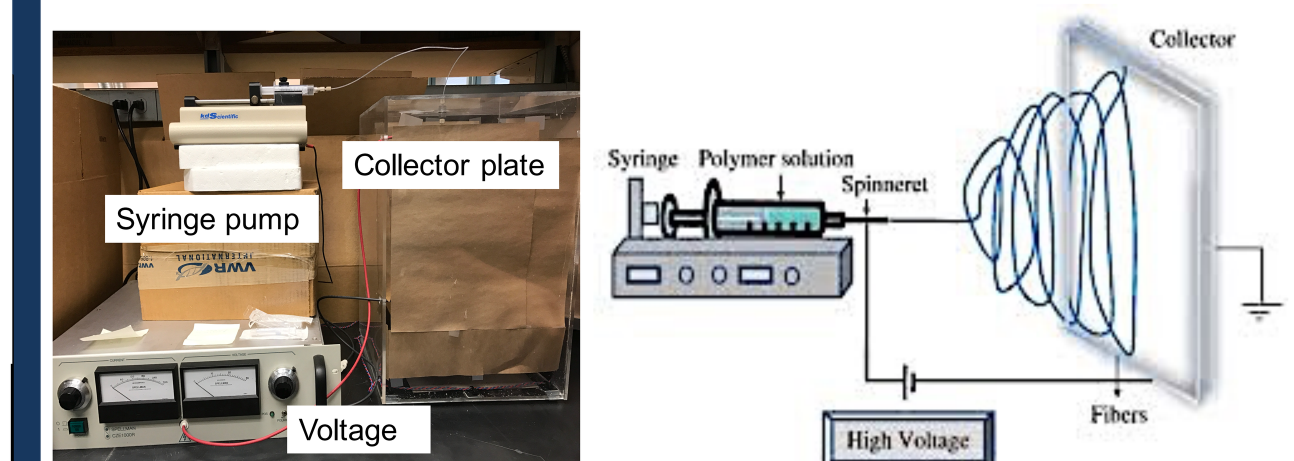


Figure 15. Electrospinning set-up[3]

- Hydrophilicity manipulation with block co-polymers
- Polyethylene glycol (PEG) incorporation will allow for hydrophilicity enhancement
- Successful encapsulation of PEG around hydrophobic, PLA fiber will allow for effective cell adhesion, inducing the body to form new bone
- Will offer vast improvements over the current standard for treating bone defects

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