Developing PLA/CDHA Bionanocomposites for Drug Delivery Applications

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Statement of Purpose: The objective of this work is to fabricate PLA (poly-lactic acid)/CDHA (carbonated calcium deficient hydroxyapatite) biocomposites for tissue engineering applications and drug delivery. PLA is acknowledged to be a resorbable polymer with degradation products causing local pH drop leading to cell necrosis [1]. This problem can be solved by incorporating HA (hydroxyapatite) into the matrix [2]. However, HA does not have good resorbability. The novel aspect of this paper is to mix CDHA with its higher resorbability into the PLA matrix. Additionally, CDHA is more close to bone mineral composition as compared to HA [3]. Yet another interesting aspect of this paper is the use of nano CDHA particles synthesized by a low temperature biomimetic process to retain the HCO_3^- ions in the lattice. The electrospun fibers can be controlled at micro- or nano-scale with porous and non-porous morphologies. Finally, such PLA/CDHA electrospun matrix can also be used as delivery system for gentamicin sulfate.

Methods: Two different SBF (simulated body fluids) solutions previously developed by our group were used for CDHA precipitations, one was 5X rapid coating SBF solution [4], and the other was 1.5X t-SBF [5]. CDHA precipitates from these two solutions were named CDHAr and CDHAt respectively. Both CDHA were separately electrospun with PLA in chloroform/DMF mixed solvents to form uniform composites fibers. Different electrospinning parameters were studied to investigate their effect on fiber morphology. As fabricated electrospun fibers were characterized using XRD and SEM and their biocompatibility was tested *in vitro*. Gentamicin sulfate was loaded to electrospun fibers and release behavior will also be studied in future.

Results: The X-ray study showed that the CDHAt and CDHAr were formed as a pure phase. However, they have different morphology as seen in Figure 1.

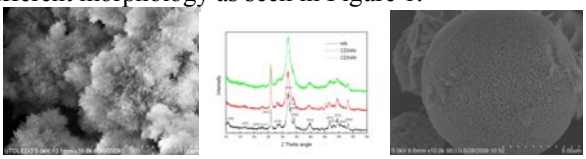

Figure 1. SEM images of CDHAt (left) and CDHAr (right); XRD data of CDHAt, CDHAr and pure HA (center).

Compared to CDHAt, CDHAr can not be used as PLA fibers filler for buffering pH caused by PLA degradation. Where, in PBS solution, the pH values were decreased more in the presence of CDHAr (Fig.2).

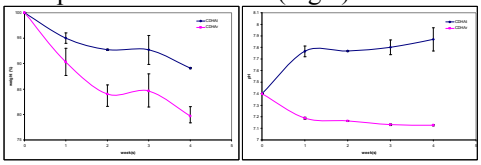

Figure 2. Weight loss and pH variation of CDHAt and CDHAr in PBS buffer for 4 weeks.

Figure 3 showed that the CDHAt and CDHAr were successfully dispersed in PLA electrospun fibers.

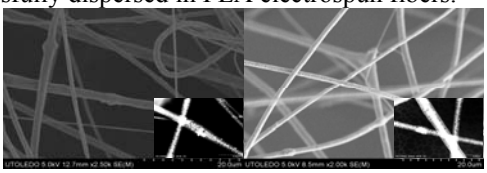

Figure 3. SEM and TEM images of PLA/CDHAt=3:1 (left), and PLA/CDHAr=3:1 electrospun fibers (right)

PLA/CDHA electrospun fibers showed improvements in biocompatibility compared to PLA fibers. A uniform bone-like apatite coating layer was formed on the fibers surface after 7 days of soaking in 1.5X t-SBF (Fig. 4).

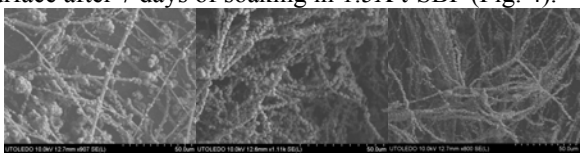

Figure 4. SEM images of PLA, PLA/CDHAt=3:1, and PLA/CDHAr=3:1 electrospun fibers after 7 days soaking in SBF solution (from left to right)

Gentamicin sulfate was loaded to PLA/CDHAt fibers. Figure 5 shows the effect of the porous surface structure on the morphology of electrospun fibers. (Fig.5). It is expected that the presence of porous structure will enhance the release behavior of the loaded antibiotics.

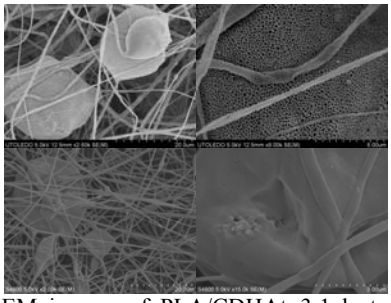

Figure 5. SEM images of PLA/CDHAt=3:1electrospun fibers loaded with Gentamicin sulfate with two different morphologies (top: PLA shell surface with pores; bottom: PLA shell surface without pores)

Conclusions: CDHA nanocrystallite particles be synthesized in a biomimetic process using SBF. The morphology and crystal structure of CDHA depend on the chemical constituents in SBF. CDHA can work as filler for PLA electrospun matrix to improve biocompatibility. The morphology of electrospun fibers is controllable. PLA/CDHA electrospun fibers also show potential applications in drug delivery system development.

References:

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