

Supporting information for:

**Development of CaCO<sub>3</sub> microspheres based composite hydrogel for dual delivery of growth factor and Ca to enhance bone regeneration**

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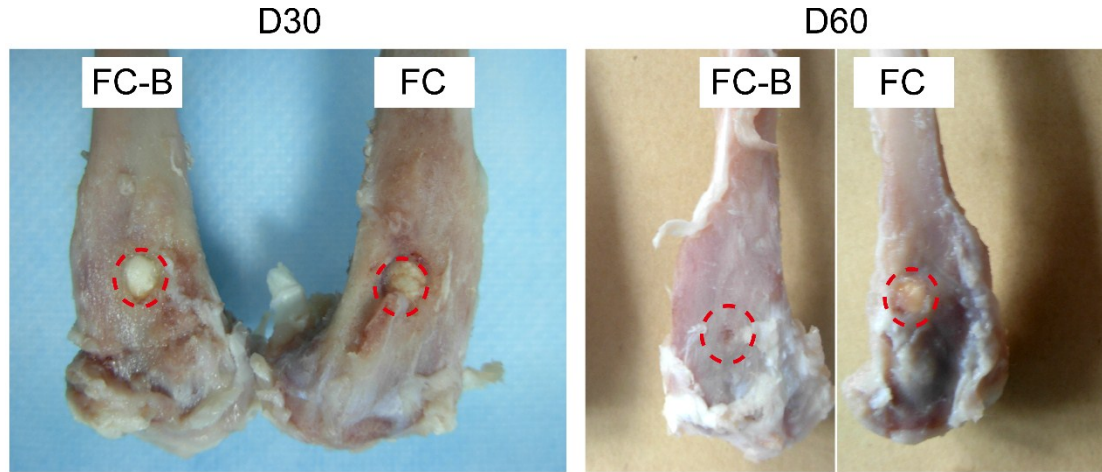


Figure S1. Digital images of tibia bone tissue with created defects after implanting  $\text{CaCO}_3$ /fibrin-glue composite hydrogels for (A) 30 days and (B) 60 days. FC-B was  $\text{CaCO}_3$ /fibrin-glue composite hydrogel with BMP-2 and FC was  $\text{CaCO}_3$ /fibrin-glue composite hydrogel without BMP-2.

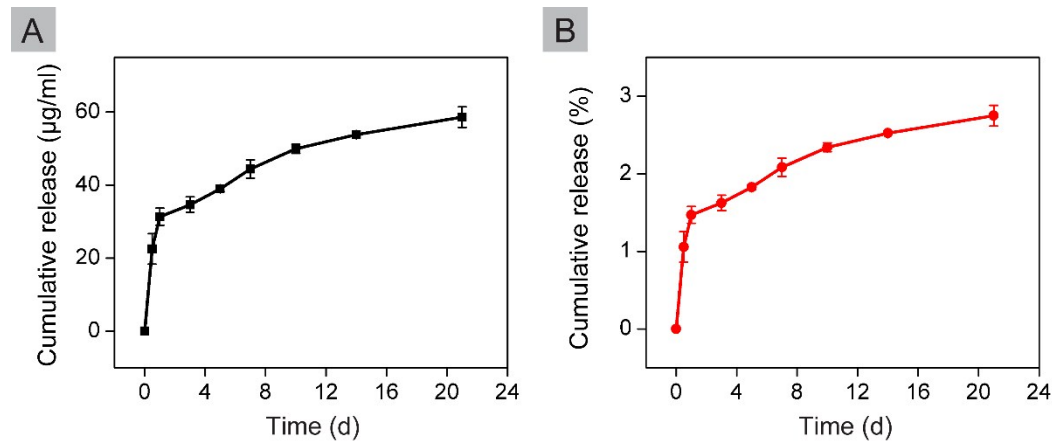


Figure S2. Cumulative release of (A)  $\text{Ca}^{2+}$  and (B)  $\text{CaCO}_3$  from casein and heparin co-functionalized  $\text{CaCO}_3$  microspheres. After sterilization (soaking in 75% ethanol and then UV radiation), 16 mg  $\text{CaCO}_3$  microspheres were suspended in 3 ml PBS solution containing 1% (v/v) penicillin/streptomycin and then incubated in 37°C water bath. At predetermined time points, 1.5 ml solution was taken out and replenished with fresh PBS.  $\text{Ca}^{2+}$  concentration was quantified using a Calcium-O-Cresolphthalein complexone method and the released amount of  $\text{CaCO}_3$  was calculated accordingly by assuming that only  $\text{Ca}^{2+}$  and  $\text{CO}_3^{2-}$  ions were released from microspheres. Three replicates were prepared. Data = mean  $\pm$  SD.