Supporting Information

Nanoindentation for monitoring time-variant mechanical strength of drug-loaded collagen hydrogel regulated by hydroxyapatite nanoparticles

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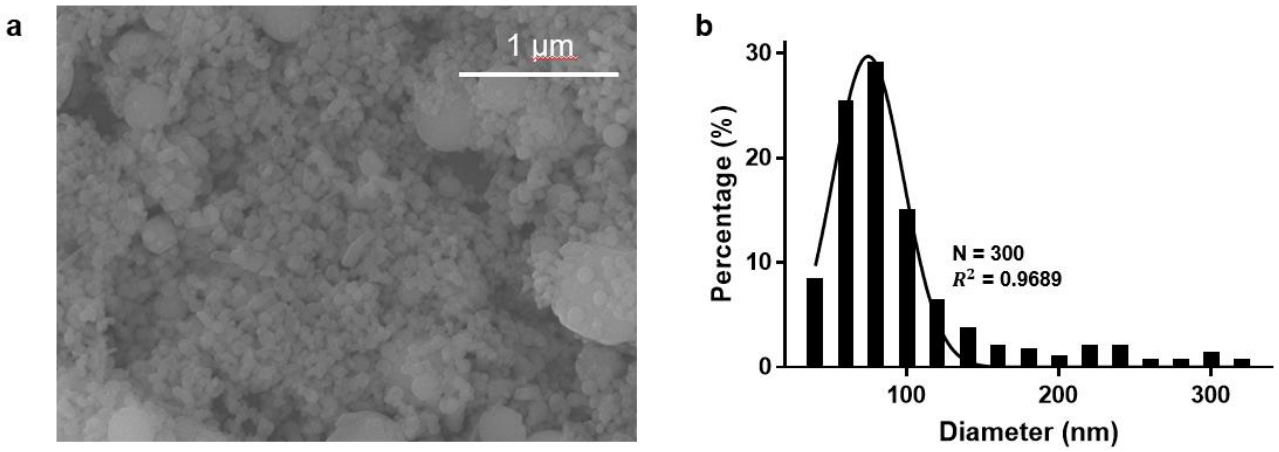

Figure S1. SEM image and size distribution of hydroxyapatite nanoparticles (HAPs). (a) SEM image showed the morphology of HAPs adapted to fabricate the HAP/Col hydrogels. (b) Histogram and single Gaussian model of the HAPs size distribution were extracted from the left SEM image.

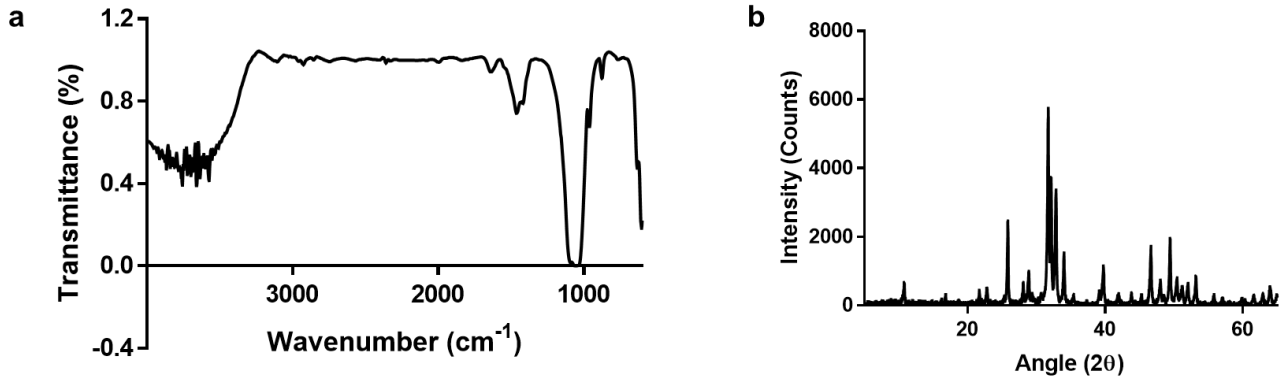

Figure S2. FTIR and XRD analysis of HAP. (a) FTIR spectra, and (b) X-ray diffraction pattern of the HAP.

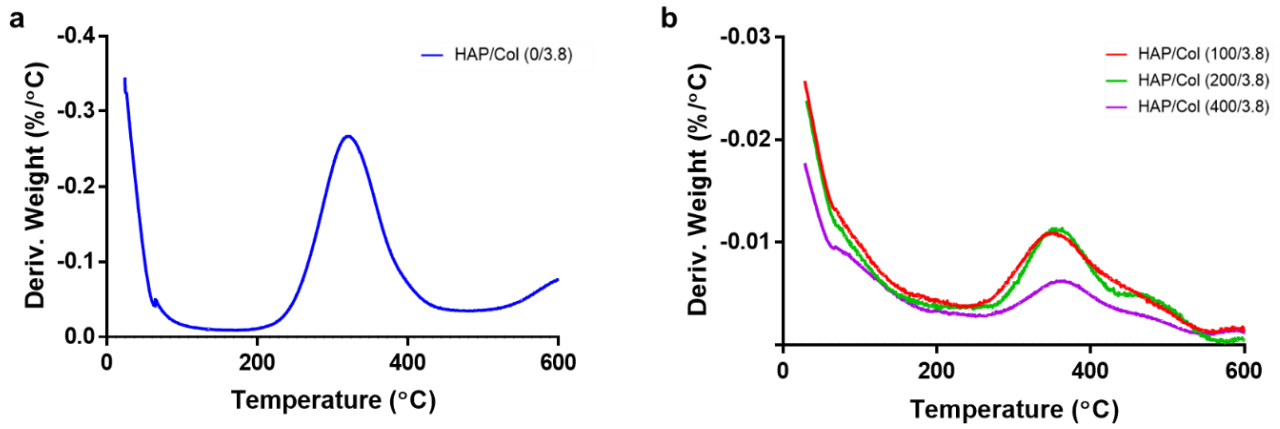

Figure S3. DTG curves of the HAP/Col hydrogels. DTG curves of (a) the HAP/Col (0/3.8) hydrogel, and (b) the HAP/Col hydrogels (100/3,8, 200/3.8, and 400/ 3.8). Data showed that the HAP/Col (400/3.8) hydrogel intensity exhibited relatively lower than the other HAP/Col hydrogels (i.e., 100/3.8 and 200/3.8).

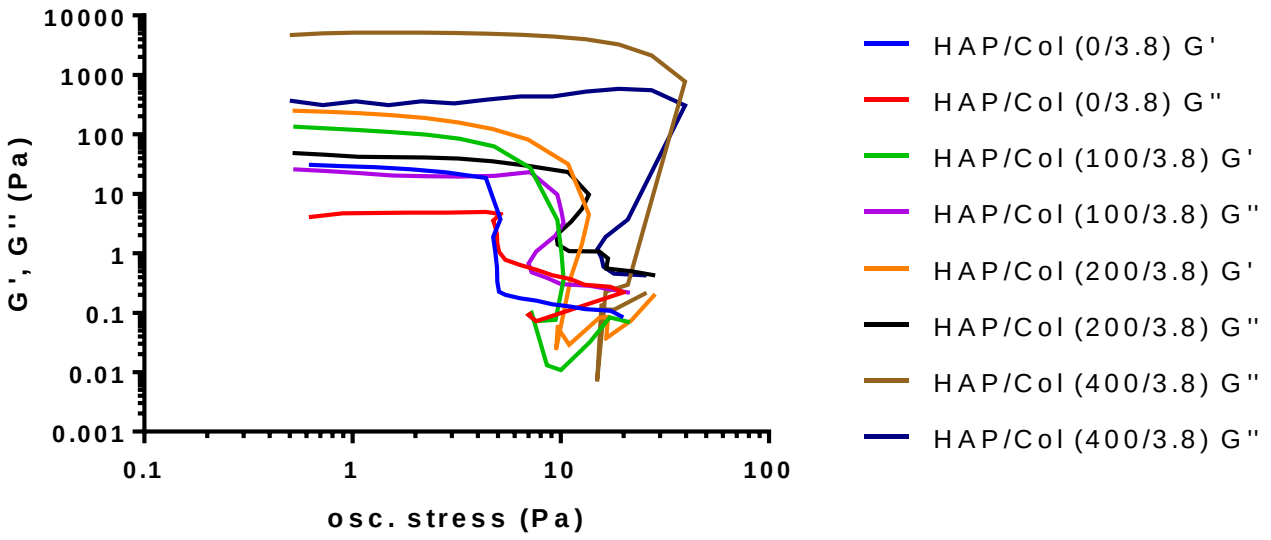

Figure S4. Oscillation stress sweep of the HAP/Col hydrogels. Stress sweep tests were performed on each HAP/Col hydrogel using a rheometer. The results exhibited the G' and G'' values versus oscillation stress for each HAP/Col hydrogel.

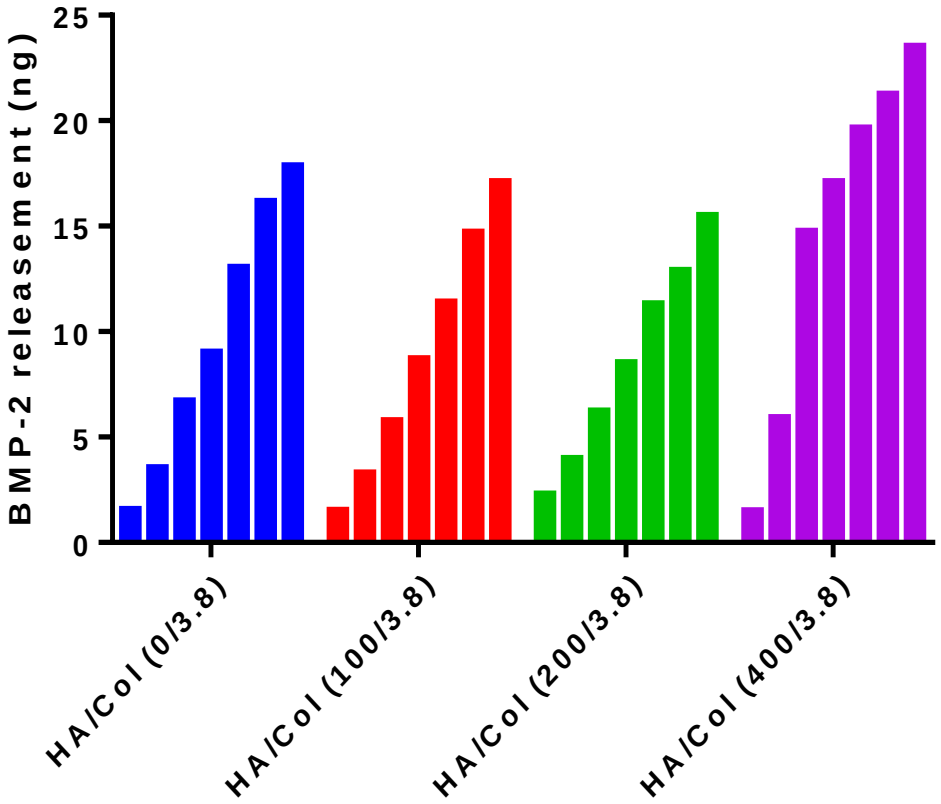

Figure S5. Cumulative BMP-2 release of each HAP/Col hydrogel for 28 days. The amount of BMP-2 release was measured by using rhBMP-2 ELISA kit. Each bar of HAP/Col hydrogel sequentially represented the cumulative drug release at 1 day, 3 days, 5 days, 7 days, 14 days, 21 days, and 28 days.

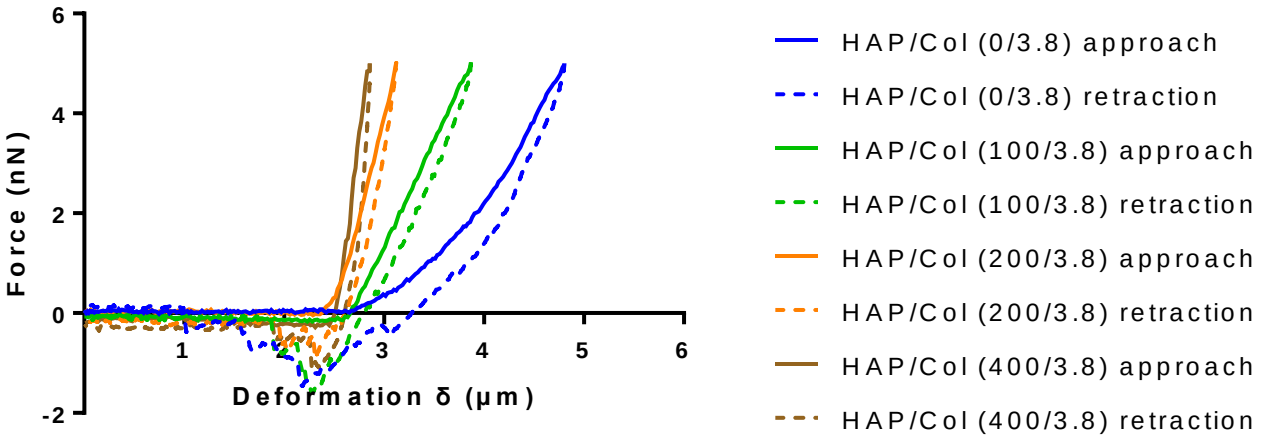

Figure S6. Force-Distance (F-D) curves of the HAP/Col hydrogels. The F-D curves showed a full cycle containing an approach curve and a retract curve. This mode measured the cantilever deflection versus the tip sample distance. The cantilever scanned towards the surface, while the cantilever was moving further into the sample, and it started to bend with an increasing loading force. Once the cantilever reached the maximum predefined loading force, the cantilever became to retract from the sample. Due to the adhesion force between the sample and the cantilever, the tip may delay leaving the surface of sample.

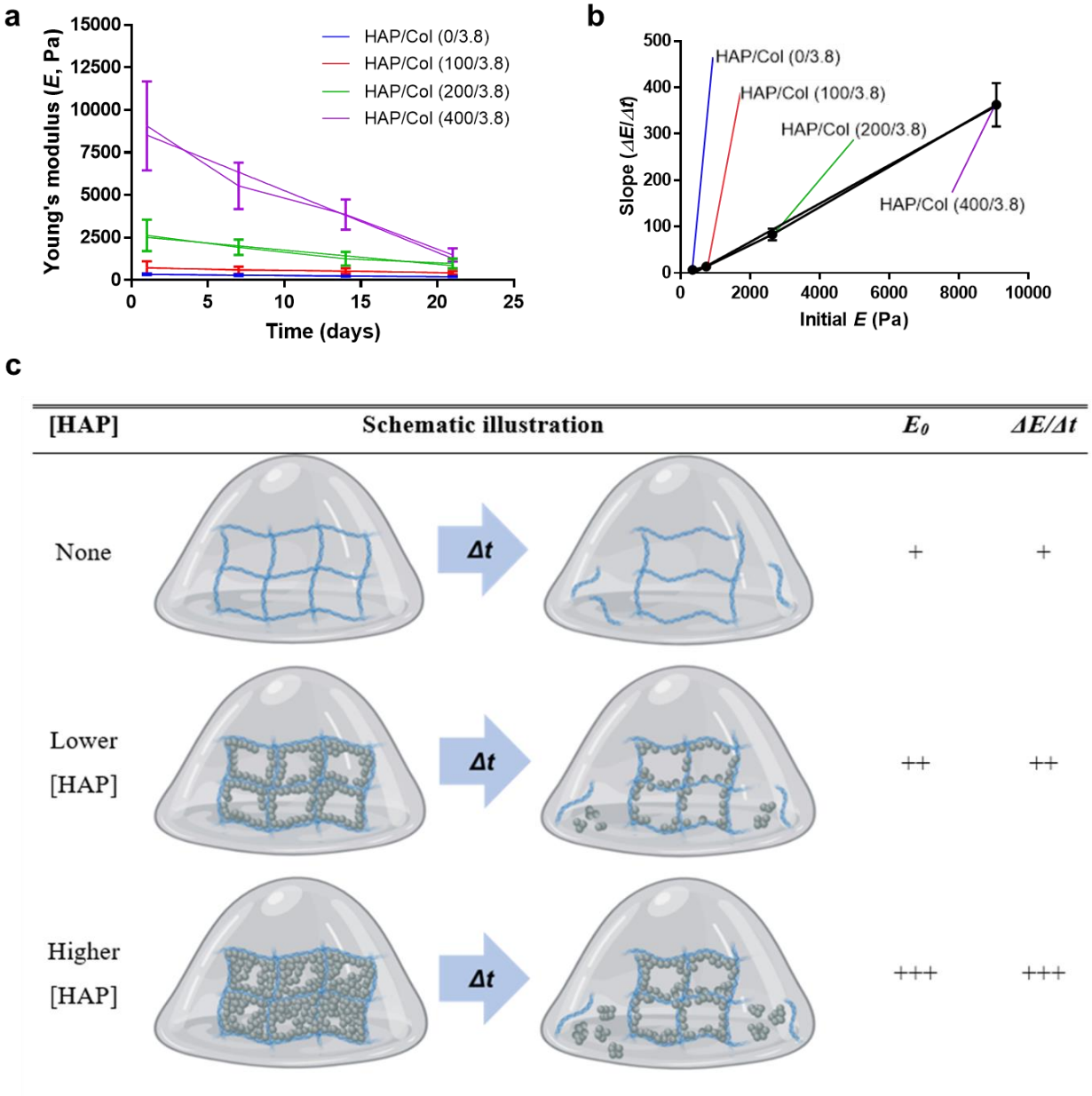

Figure S7. The time variant *E* changes of the HAP/Col hydrogels for 21 days. (a) The *E* changes of the HAP/Col hydrogels for 21 days. The line was fitted by linear regression ($R^2 > 0.998$). (b) The lines exhibited the sloped of each HAP/Col hydrogel. (c) The schematic illustrated a degradation of the HAP/Col hydrogels depending on HAP concentration. [HAP], HAP concentration; E_0, initial *E*; $\Delta E/\Delta t$, degradation rate.

Table S1. Maximum swelling ratio of the HAP/Col hydrogels.

HAP/Col hydrogel	Maximum swelling ratio (%)
HAP/Col (0/3.8)	583 ± 71.6
HAP/Col (100/3.8)	458 ± 12.8
HAP/Col (200/3.8)	387.3 ± 10.9
HAP/Col (400/3.8)	339.8 ± 28.6