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Supporting Information

## **Tunable Antibiotic Delivery From Gellan Hydrogels**

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**Figure S1.** Schematic of hydrogel swelling studies. (A) Rehydration ratio setup. The rehydration ratio was evaluated using eq (1). (B) Equilibrium swelling ratio ( $Q_s$ ) and "swollen-initial mass" setup.  $Q_s$  and "swollen-initial mass" were evaluated using eq. (2) and subtracting post fabrication hydrogel mass ( $W_i$ ) from swollen hydrogel mass ( $W_s$ ), respectively.



**Figure S2**: Viscosity versus shear rate for ointment hydrogels with and without vancomycin and vancomycin loaded CNPs measured over a shear rate of 0.1 to 10 Hz.



**Figure S3.** Storage (G') and loss (G'') moduli of non-drug loaded ointment and sheet hydrogels over a frequency sweep of 10 to 600 Hz. Data are shown as mean  $\pm$  standard deviation; significance was calculated using a two-tailed t-test indicating that \*\*\*p < 0.001 for G' and G'' between sheet and ointment hydrogels (n = 5).



**Figure S4:** QCM-D analysis of vancomycin-gellan interaction; frequency change ( $\Delta F$ ) and dissipation change ( $\Delta D$ ) over time are shown for a representative test (n = 3). Data for odd overtones 3, 5, 7, 9, and 11 is shown. Key: 1 = water baseline, 2 = BPEI, 3 = water rinse, 4 = gellan, 5 = water rinse, 6 = vancomycin, 7 = water rinse.



**Figure S5.** Equilibrium swelling ratio in water,  $1 \times PBS$ , and 1 mM and 7 mM CaCl<sub>2</sub> solutions at 37°C for (A) vancomycin-loaded sheet hydrogels without CNPs, (B) composite sheet hydrogels, (C) vancomycin-loaded ointment hydrogels without CNPs, and (D) composite ointment hydrogels. Data are shown as mean ± standard deviation; significance was calculated using one-way ANOVA with Tukey's post-hoc analysis indicating that \**p* < 0.05 between each test condition for a given hydrogel formulation (*n* = 3).



**Figure S6.** Vancomycin loading and release from CNPs. (A) Percent of available vancomycin loaded in CNPs and ratio of mg of vancomycin loaded per mg of CNPs for different loading times (2:1 w/w vancomycin:CNP in 1× PBS at 23°C). (B) Daily release of vancomycin from CNPs (loaded with vancomycin for 24 hours) in 1× PBS at 37°C. Data are shown as mean  $\pm$  standard deviation; significance was calculated using one-way ANOVA with Tukey's post-hoc analysis indicating that \**p* < 0.05 for mg vancomycin loaded and percent vancomycin loaded between 10 minutes and 3 and 24 hours. (*n* = 3).



**Figure S7**: Storage (G') and loss (G'') moduli of all of hydrogels examined (with and without vancomycin and CNPs) over a frequency sweep of 10 to 600 Hz. Data are shown as mean  $\pm$  standard deviation; significance between sheet and ointment hydrogel formulations was calculated using a two-tailed t-test indicating that \*\*\*p < 0.001 between G' and G'' for all sheet and ointment hydrogels (n = 5).



**Figure S8:** Stress-strain analysis of vancomycin loaded sheet hydrogels with and without vancomycin loaded CNPs. Young's moduli values were derived from the slope of the linear region of the curves. Data are shown as mean  $\pm$  standard deviation; significance was calculated using a two-tailed t-test indicating that \*\*p < 0.05 between vancomycin loaded sheet and composite sheet hydrogels at all strain values (n = 3).



**Figure S9:** (A) Vancomycin release from vancomycin loaded sheet and ointment hydrogels containing non-drug loaded CNPs in 1× PBS at 37°C. (B) Vancomycin release from hydrogels containing vancomycin loaded only within CNPs (no free vancomycin) in 1× PBS at 37°C. Data is shown as a percent cumulative release normalized to the total vancomycin loaded in the hydrogel and an absolute cumulative release ( $\mu$ g). Data are shown as mean ± standard deviation; significance was calculated using two-way ANOVA with Tukey's post-hoc analysis indicating that \**p* < 0.05 between cumulative release of sheet and ointment gels for each subsequent day over 6 days for (A) and from days 4 through 9 for (B) (*n* = 3).



**Figure S10.** Hydrogel stability over time as measured by a change in wet hydrogel mass for (A) vancomycin loaded sheet hydrogels and (B) composite sheet hydrogels in  $1 \times$  PBS and water at 20°C and 37°C. Data are shown as mean ± standard deviation; significance was calculated using two-way ANOVA with Tukey's post-hoc analysis indicating that \**p* < 0.05 between the samples indicated for each day examined (*n* = 3).