

Appendix A. Supplementary Data

In the article's main text, the amplitude percentage of the ultrasound horn as the input setting on the sonicator was reported (i.e., 20%, 40%, and 80% ultrasonic amplitudes) to aid in experimental reproduction. In order to provide a better understanding of what ultrasonic powers were delivered, the *ideal* ultrasound intensities were measured at 20%, 40%, and 80% (Fig. S1 A). These values were calculated by recording the power delivered by the ultrasonic transducer under experimental conditions (Fig. S1 B, 5 mL of PBS in a 50 mL conical tube with the ultrasound horn axially centered suspended 2 cm above the samples) minus the power reading in air, divided by the cross-sectional ultrasound horn's area.

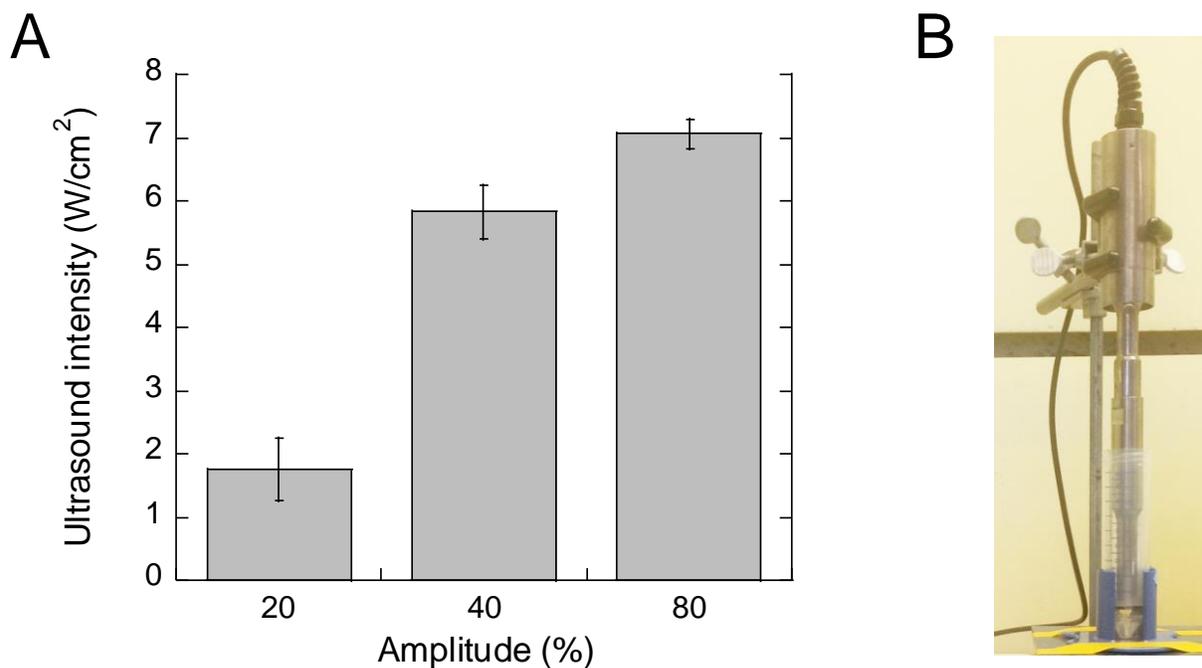


Fig. S1. (A) Measured ideal ultrasound intensities associated with 20%, 40%, and 80% amplitude. (B) Photograph of the experimental setup. The ultrasonic horn is submerged in 5 mL of PBS in a 50 mL conical tube, centered with the conical tube, and suspended 2 cm above the sample.

As previously described in early sonophoresis work [S1], the actual power output for the system is less than the idealized value displayed on the device. Thus, the values provided in Fig. S1 are likely overestimates of the actual ultrasonic power. Directly recording this intensity is complex due to reflections and variations in the physical arrangement of the experimental setup from experiment to experiment. However, as a point of reference, the ultrasound intensity for this experimental configuration was previously measured to be 120 mW/cm² at 20% amplitude [S2]. The ultrasound intensities and settings used here are also within the range of other studies where ultrasound is used to trigger release [S2-S4].

Supplementary Data References

- [S1] Mitragotri S, Blankschtein D, Langer R. Ultrasound-mediated transdermal protein delivery. *Science* 1995;269:850-3.
- [S2] Huebsch N, Kearney CJ, Zhao X, Kim J, Cezar C, Suo Z, Mooney DJ. Ultrasound-triggered disruption and self-healing of reversibly cross-linked hydrogels for drug delivery and enhanced chemotherapy. *Proc Natl Acad Sci USA* 2014;111(27):9762-7.
- [S3] Kearney CJ, Skaat H, Kennedy SM, Hu J, Darnell M, Raimondo TM, Mooney DJ. Switchable release of entrapped nanoparticles from alginate hydrogels. *Adv Healthc Mater* 2015;4(11):1634-9.
- [S4] Park D, Park H, Seo J, Lee S. Sonophoresis in transdermal drug deliveries. *Ultrasonics* 2014;54(1):56-65.