## **Supporting Information**

## Extracts from the aerial portions of goldenseal (*Hydrastis canadensis* L.) synergistically enhance the antibacterial activity of berberine via efflux pump inhibition

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Figure 2. Comparison of base peak LC-MS chromatograms for an equimolar mixture of the standard alkaloids berberine, hydrastine and canadine at 1  $\mu$ M (A) and a 100-fold dilution of a ethanolic extract from the pooled aerial portions of goldenseal (*H. canadensis*) (B). The numbers above the peaks indicate the m/z value of the ion detected, which was consistent with M<sup>+</sup> for berberine (monoisotopic mass of 336.12 g/mole), and MH<sup>+</sup> for hydrastine and canadine (monoisotopic masses of 384.14 and 340.15 g/mole, respectively). CID fragments of the M<sup>+</sup> ion for berberine (C), the MH<sup>+</sup> ion for hydrastine (E), and the MH<sup>+</sup> ion for canadine (G), matched those obtained for the corresponding ions in the extract (D, F, and H). Alkaloids were identified in all other extracts using the same type of chromatographic and spectroscopic data shown here.



Figure 6. Percent fluorescence over time for *S. aureus* (NCTC 8325-4) loaded with ethidium bromide and treated with various compounds and controls. Treatments included the known efflux pump inhibitor CCCP (positive control), and purified standards of the alkaloids berberine, hydrastine and canadine. All extracts and CCCP were dissolved in Müeller Hinton broth containing 2% DMSO. Data points represent the average of three separate experiments (using 3 different pellets of *S. aureus*). Error bars are +/- standard error.