



Supplementary Figure legend

Fig. S1. Representative total ion chromatograms (TIC) of (a) reserpine standard (33 nM) and (b) a 1:1 mixture of reserpine (33 nM) and protein. The multiple reaction monitoring (MRM) spectra obtained from each chromatographic peak in (a) and (b) are shown as insets. The average retention time for (a) was 1.68 ± 0.01 min and for (b) was 1.88 ± 0.01 min ($n=6$ replicate injections, alternating between (a) and (b)). The reproducible increase in retention time and decrease in relative abundance (nearly 3-fold) of the peak in (b) suggest the formation of a complex between reserpine and the protein. This complex is thought to partially dissociate during the electrospray process as demonstrated by the decrease in relative abundance of the released reserpine peak compared to (a).

Supplementary Materials and Methods

S.1. LC-MS analysis

A Thermo Surveyor MS Liquid Chromatograph (San Jose, CA) equipped with a Phenomenex (Torrance, CA) Gemini-NX 5 μm , 2.1 x 150 mm C_{18} HPLC column with isocratic elution using 35% mobile phase A, 0.1% v/v formic acid in water, and 65% mobile phase B was 0.1% v/v formic acid in methanol (MeOH) was used for separation of the reserpine and the suspect reserpine protein adduct. The column temperature was 30°C and the autosampler tray was set at 4°C. The mobile phase flow rate was 300 $\mu\text{L}/\text{min}$ with 10 minutes equilibration time. The detection of reserpine and adduct was achieved using a Thermo TSQ Quantum Ultra (San Jose, CA) triple-quadrupole mass spectrometer. The HPLC effluent flowed directly into the electrospray interface of the mass spectrometer. The interface was operated in the positive ion mode with a spray voltage of 3.5 kV. The ion transfer tube (heated capillary) was set at 325°C. Multiple reaction monitoring (MRM) of the transitions of m/z 609.32 \rightarrow 194.8 and m/z 609.32 \rightarrow 397.07 was observed and recorded as a reproduced total ion chromatogram (TIC) for 10 minutes following a 2 mL full loop injection.