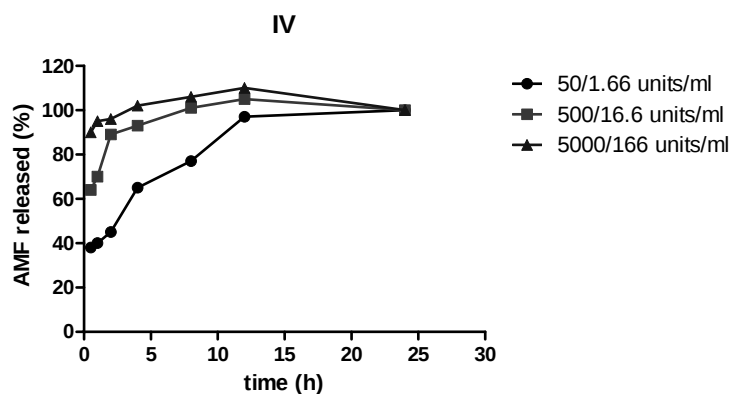


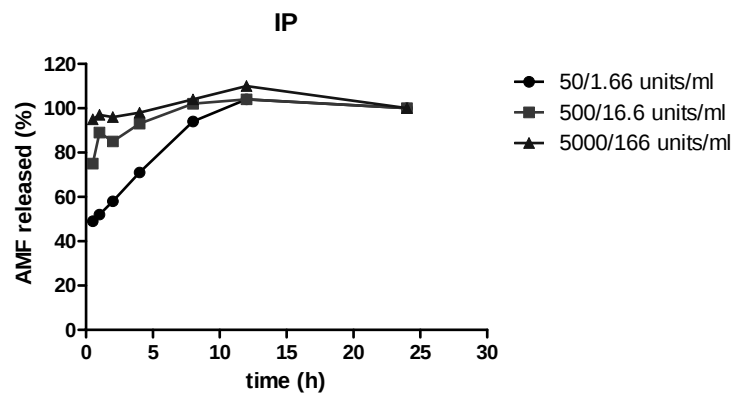
Supporting Information 1

Figure 1. Time-course of AMF release by β -glucuronidase/sulfatase at the indicated concentrations in plasma samples obtained from rats treated with AMF A) IV (2 min after injection), B) IP (at the 1h for AMF conjugates), and C) PO (at the time of 2h for AMF conjugates). The time-course of enzymatic AMF release in the presence of different concentrations of β -glucuronidase/sulfatase (50/1.66 units/mL, 500/16.6 units/mL, and 5000/166 units/mL) in rat plasma samples obtained at $t_{\max}$ after IV, IP, and PO administration. These results showed that complete enzymolysis of AMF could be achieved after 12 h with 5,000/166 units/mL β -glucuronidase/sulfatase in samples obtained after IV or IP administration (Figure 1A and B). In the $t_{\max}$ samples obtained after PO administration, there was no difference in AMF release in the presence of 500/16.6 units/mL and 5,000/166 units/mL β -glucuronidase/sulfatase (Figure 1C). Based on these results, we established the optimal conditions used in the present study, as described in the Methods section (Sample preparation).

A.



B.



C.

