Supporting Information

In vitro and *in vivo* studies of metabolic activation of emodin

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Content

Table S1. Apparent kinetic values for the metabolism of EM to M1 by P450s 2C19 and 1A2

P450	K_m (μM)	k_{cat} (s^{-1})	k_{cat}/K_m [($s \cdot \mu M)^{-1}$]
2C19	36±10	1.5±5.9×10^{-2}	4.0×10^{-2}
1A2	1.5×10^3±90	4.2±2.3×10^{-1}	2.7×10^{-3}

Values are means±SD determined from non-linear regression analysis fitting to Michaelis-Menten curves from triplicate experiments in a range of concentrations of EM.
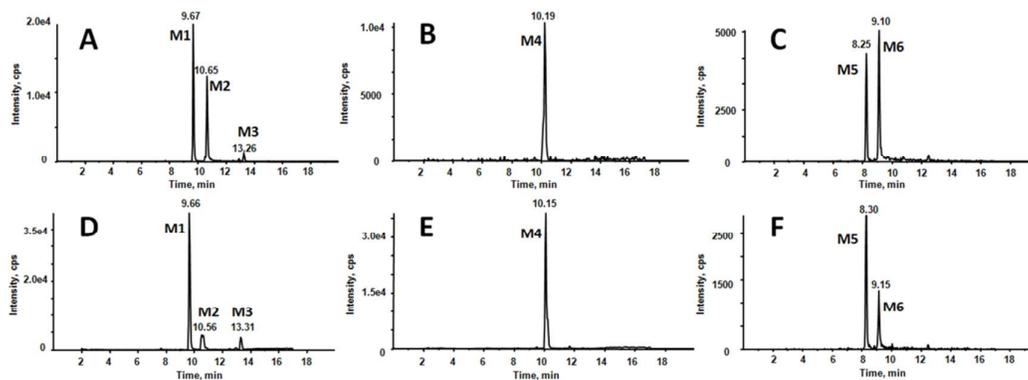
Figure S1. Extracted ion (m/z 287→139 for M1, M2, and M3) chromatograms obtained from LC-Q-Trap MS analysis of human (A) or rat (D) liver microsomal incubations containing EM in the presence of NADPH. Extracted ion (m/z 432→301 for M4) chromatograms obtained from LC-Q-Tra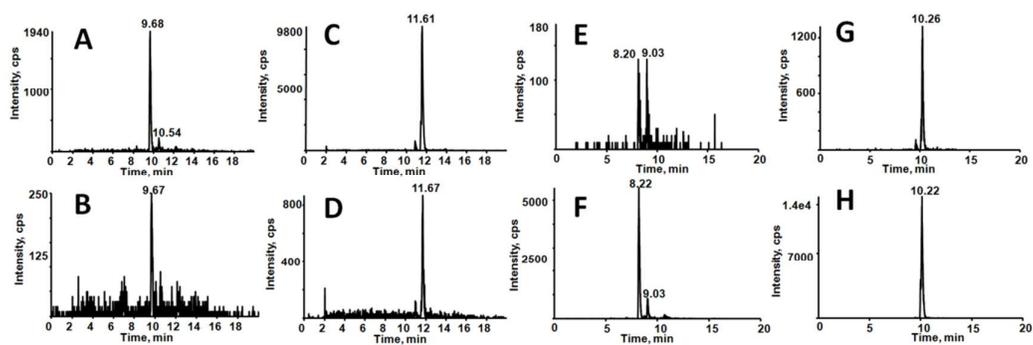p MS analysis of human (B) or rat (E) microsomal incubations containing EM and NAC in the absence of NADPH. Extracted ion (m/z 448→317 for M5 and M6) chromatograms obtained from LC-Q-Trap MS analysis of human (C) or rat (F) microsomal incubations containing EM and NAC in the presence of NADPH.
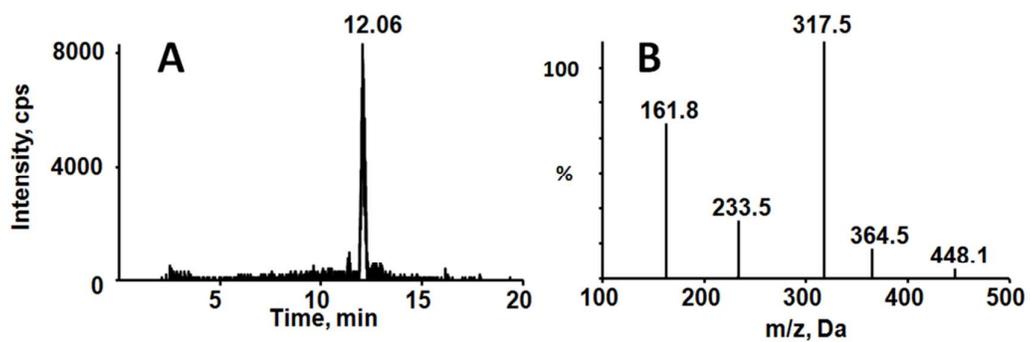
Figure S2. A: Extracted ion (*m/z* 448→317) chromatograms obtained from LC-Q-Trap MS analysis of the NAC conjugate derived from 5-hydroxyemodin from emodin.   B: MS/MS spectrum of NAC conjugate derived from 5-hydroxyemodin.

Figure S3. Extracted ion (*m/z* 434→303 for **1** and *m/z* 450→319 for **2** and **3**) chromatograms obtained from LC-Q-Trap MS analysis of rat liver microsomal incubations EM and NAC in the presence (A) or absence (C) of NADPH under nitrogen. Extracted ion (*m/z* 434→303 for **1** and *m/z* 450→319 for **2** and **3**) chromatograms obtained from LC-Q-Trap MS analysis of rat liver microsomal incubations with EM and NAC in the presence (B) or absence (D) of NADPH in the air. Extracted ion (*m/z* 432→301 for M4 and *m/z* 448→317 for M5 and M6) chromatograms obtained from LC-Q-Trap MS analysis of rat liver microsomal incubations EM and NAC in the presence (E) or absence (G) of NADPH under nitrogen. Extracted ion (*m/z* 432→301 for M4, *m/z* 448→317 for M5, M6) chromatograms obtained from LC-Q-Trap MS analysis of rat liver microsomal incubations with EM and NAC in the presence (F) or absence (H) of NADPH in the air.
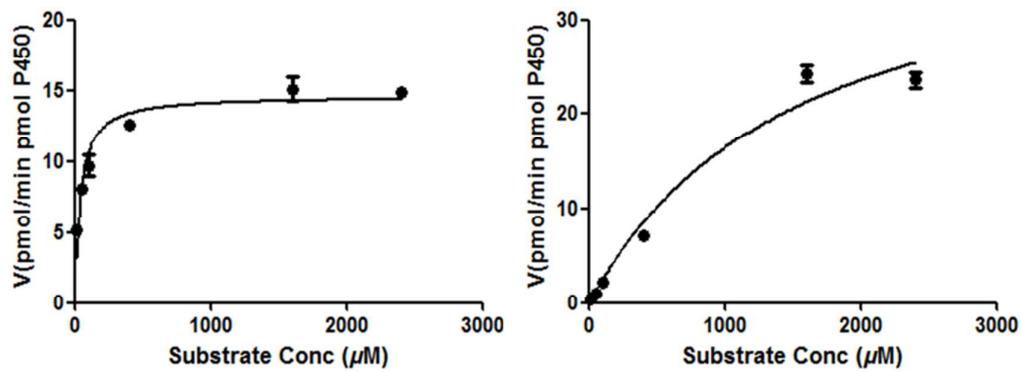
Figure S4. Kinetic data for biotransformation of emodin to M1 by P450s 2C19 (A) and 1A2 (B).   Experiments were performed in triplicate at each concentration points.