

Supporting Information

**Differential Effects of *Glycyrrhiza* Species on Genotoxic Estrogen Metabolism:
Licochalcone A downregulates P450 1B1, whereas Isoliquiritigenin Stimulates It**

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Figure Legends

Figure S1. Chemical profiles of GG, GU and GI, as measured by UHPLC-UV. Liquiritin (1), liquiritigenin -7-O-apiosylglucoside (2), and Liquiritin apioside (3) are all LigF equivalents, which share the same core aglycone LigF structure. Isoliquiritin (5), isoliquiritin apioside (6), and licuraside (7) are all considered LigC equivalents, which share the same core aglycone LigC structure.

Figure S2. Structures of LigC and LigF equivalents

Figure S3. MS fragmentation pattern of dansyl-4-MeOE₁. Representative positive ESI fragmentation mass spectra for parent ion dansyl-4-MeOE₁ was shown. Parent ion Q1 with m/z of 534.4 was captured and scanned for Q3 product ions formation and the most intensive product ion with m/z of 171.2 was selected to monitor in the LC-MS/MS.

Figure S4. Representative SRM chromatograms with transition 534.4 – 171.2 analyzing 2-MeOE₁ and 4-MeOE₁ metabolites showing improved sensitivity for A) current method compared to B) reference 9. Note enhanced signal to noise for SCIEX 5500 QTRAP and shorter run times than the previous method using the API-3000 mass spectrometer. MCF-10A cells treated with E₂ (1 μM) were collected and analyzed for 2-MeOE₁ and 4-MeOE₁ metabolites as described in A) Material and Methods and B) reference 9.

Figure S5. Cytokines cooperatively induced P450 1B1 mRNA expression in MCF-10A cells. qPCR analysis of P450 1B1 mRNA was performed after MCF-10A cells were incubated with TNF-α (10 ng/mL) or IFN-γ (10 ng/mL) and TNF-α with IFN-γ (10 ng/mL each) for 24 h.

Results are the mean \pm SEM of three independent experiments analyzed by one-way ANOVA with Dunnett's multiple comparison post-test, * $p < 0.001$.

Figure S6. Effect of licorice compounds on XRE-luciferase activity. HepG2 cells were incubated with TCDD (10 nM) or TCDD with LigF/LigC (10 μ M) for 24 h before analysis of XRE-luciferase reporter activity. Results are the mean \pm SEM analyzed by one-way ANOVA with Dunnett's multiple comparison post-test, * $p < 0.001$.

Figures

Figure S1

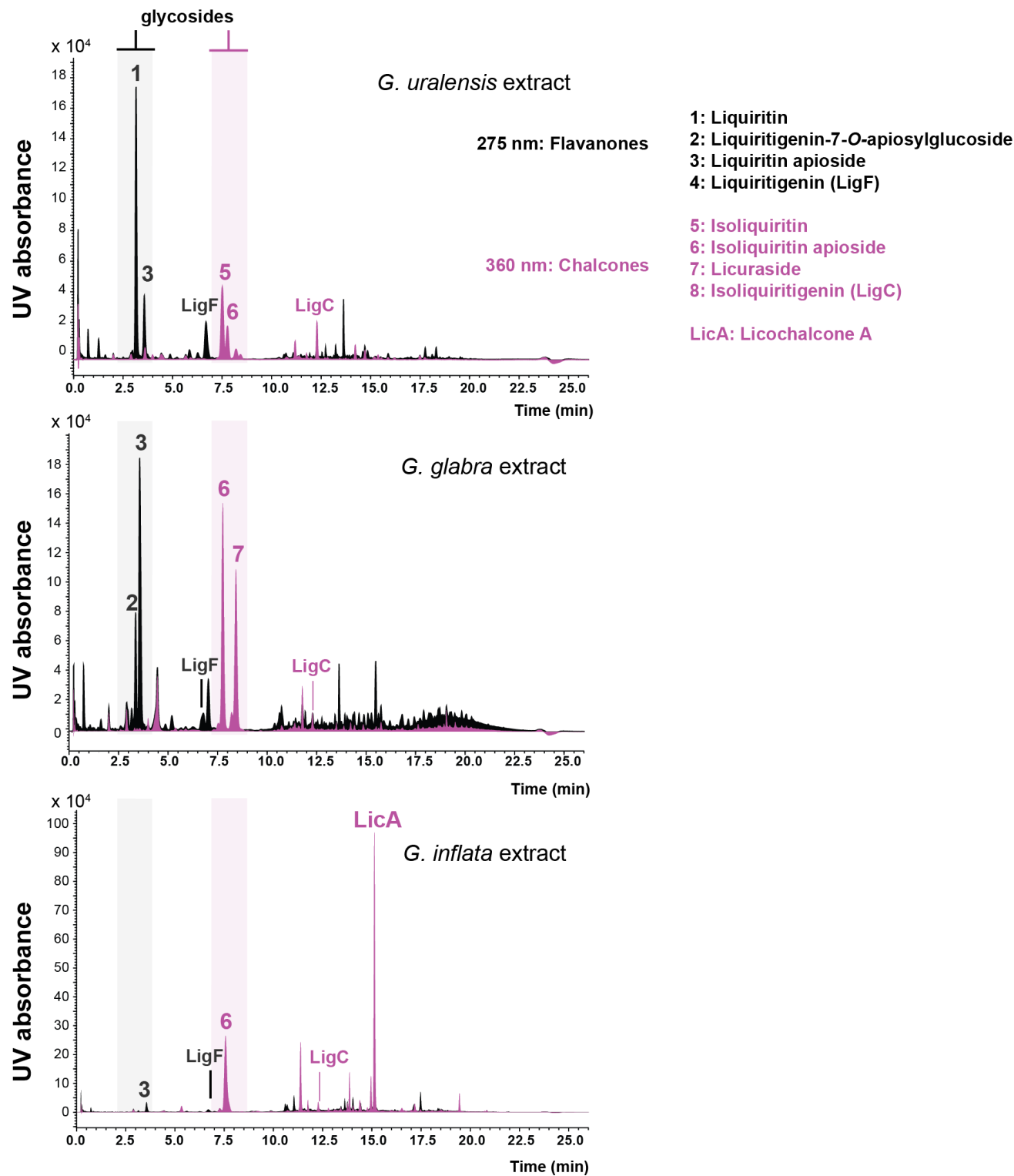
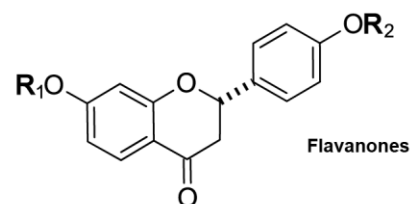


Figure S2

LigF Equivalents

1	Liquiritin	$R_1:H$	$R_2:\beta\text{-Glc}$
3	Liquiritin apioside	$R_1:H$	$R_2:\beta\text{-Api}(1\rightarrow2)\beta\text{-Glc}$
2	Liquiritigenin-7-O-Apiosylglucoside	$R_1:\beta\text{-Api}(1\rightarrow2)\beta\text{-Glc}$	$R_2:H$
4	Liquiritigenin (LigF)	$R_1:H$	$R_2:H$



LigC Equivalents

5	Isoliquiritin	$R_1:H$	$R_2:\beta\text{-Glc}$
6	Isoliquiritin apioside	$R_1:H$	$R_2:\beta\text{-Api}(1\rightarrow2)\beta\text{-Glc}$
7	Licuraside	$R_1:\beta\text{-Api}(1\rightarrow2)\beta\text{-Glc}$	$R_2:H$
8	Isoliquiritigenin (LigC)	$R_1:H$	$R_2:H$

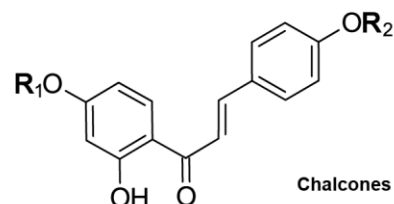


Figure S3

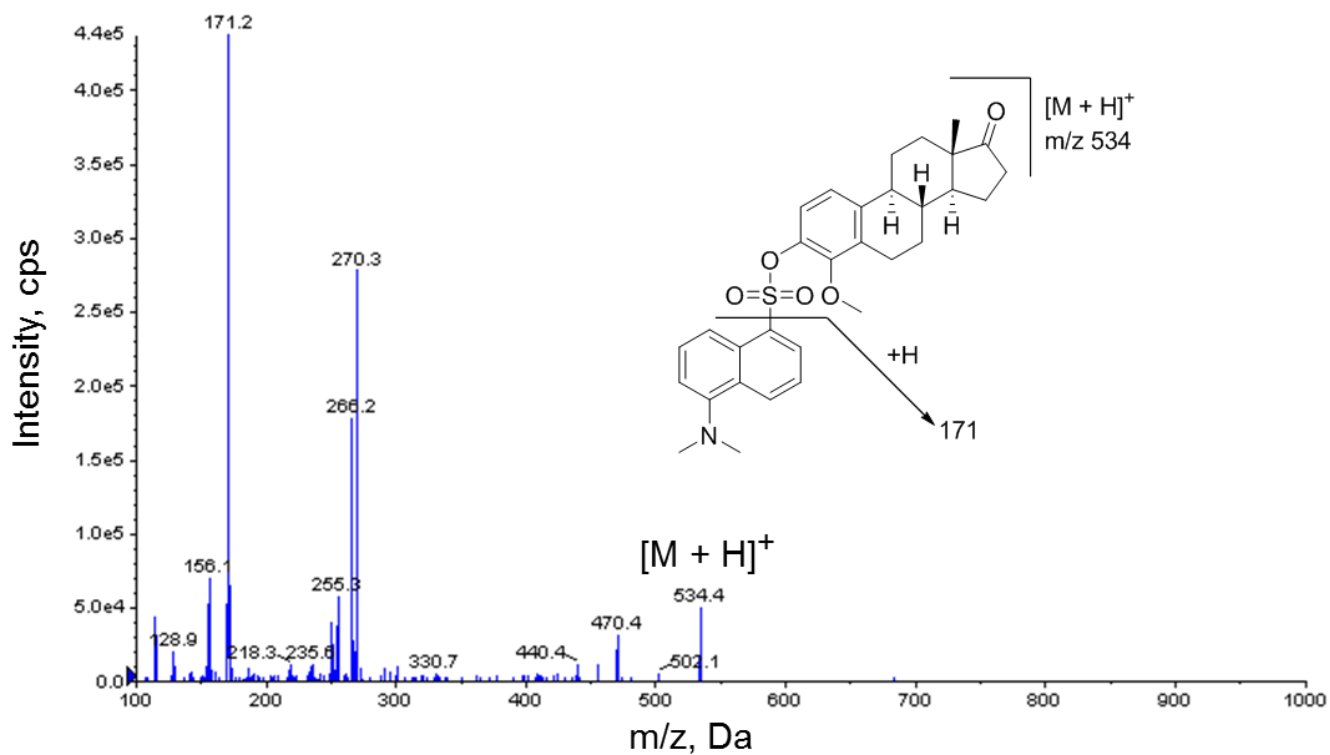


Figure S4

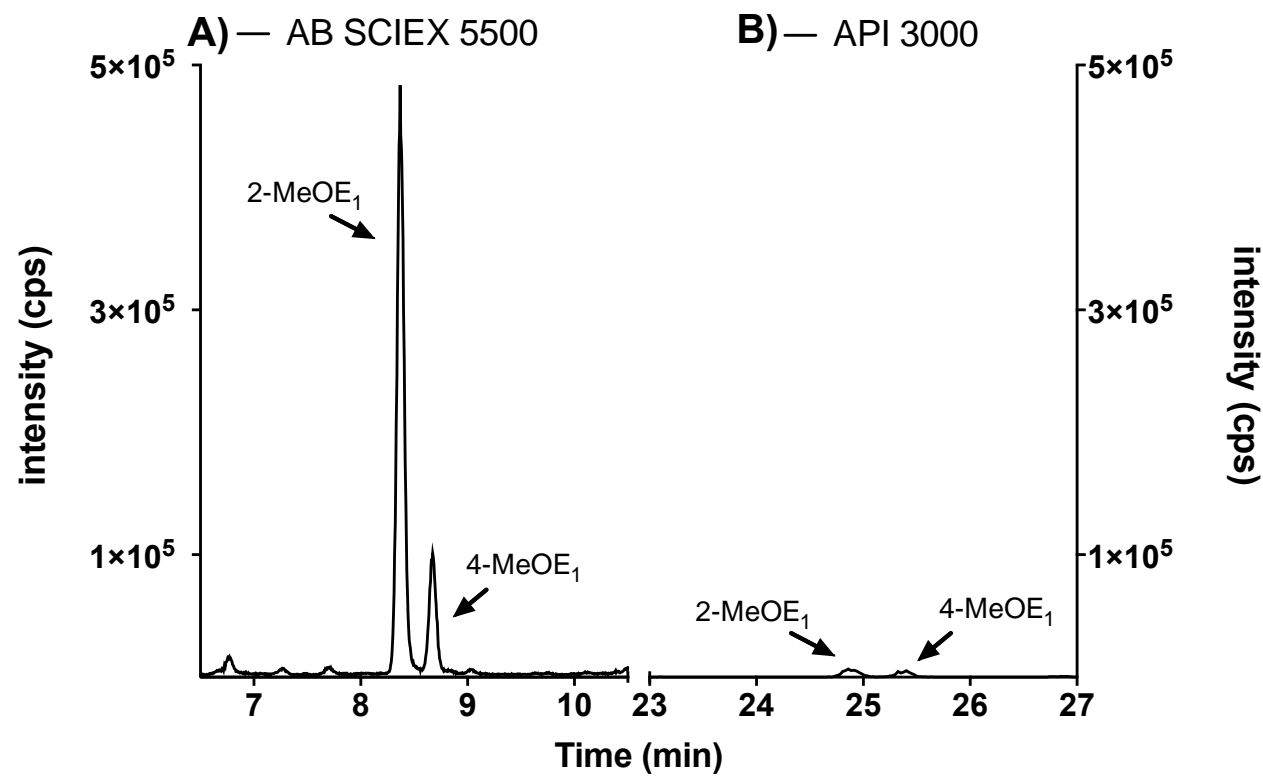


Figure S5

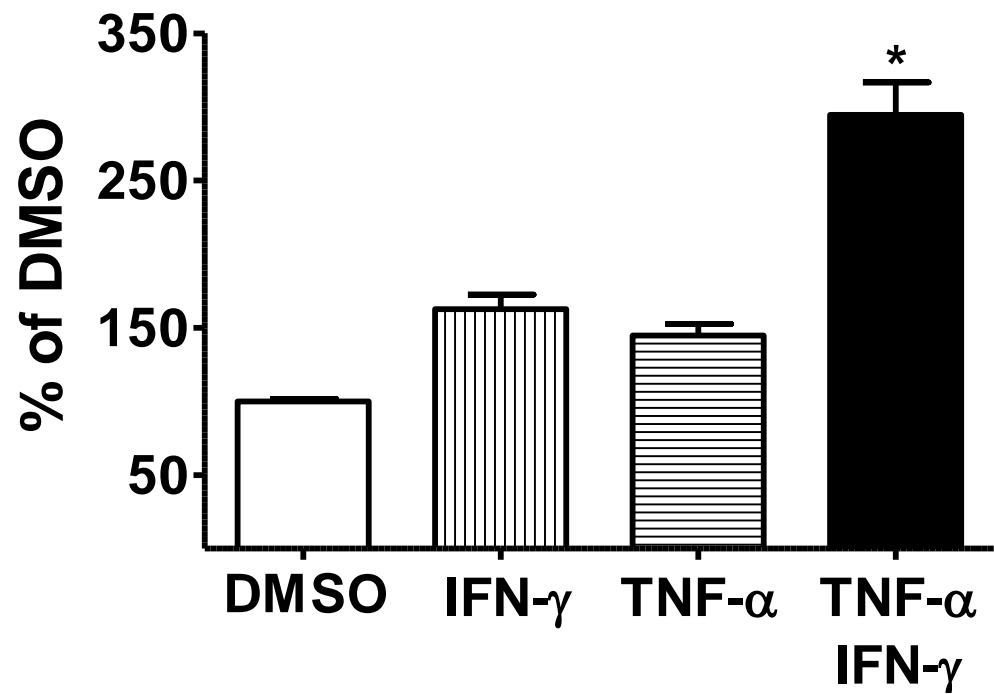


Figure S6

