SUPPORTING INFORMATION

I. Supplementary Methods

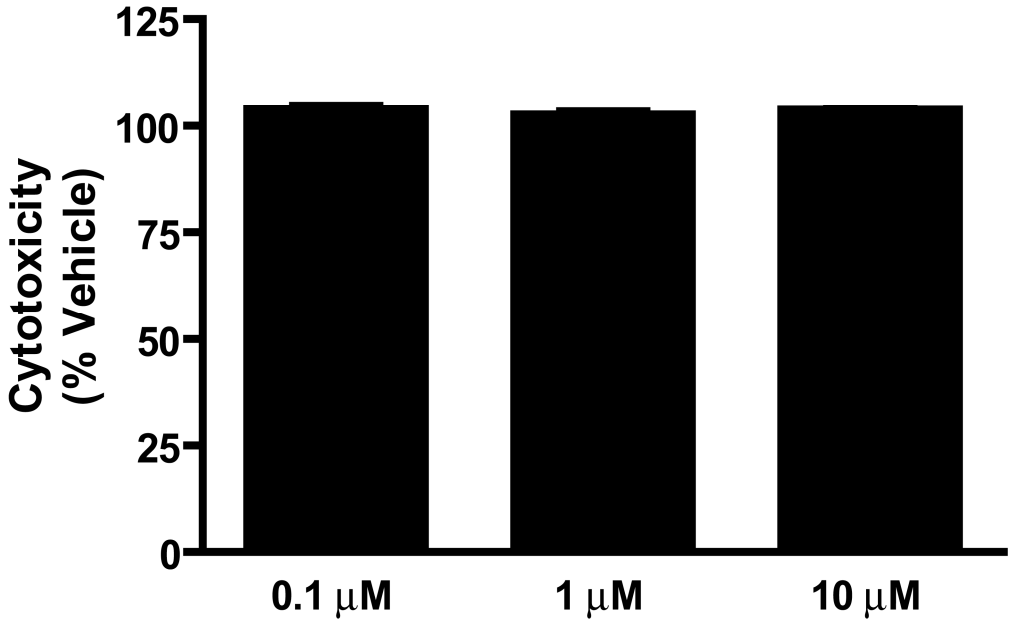
I3S purity assessment. The purity of the compound was determined by HPLC using a Waters LC system with a Beckmann Ultrasphere C18 column (250mm x 4.6 mm, 5µm) equipped with PDA detector. The mobile phase consisted of 5 mmol of tetrabutyl ammonium phosphate in methanol/water (30/70) with flow rate of 1.0 ml/min. A UV spectrum at 279 nm was extracted from the PDA data during HPLC analysis. ^{1}H-NMR and ^{13}C-NMR spectra were measured on a Bruker Avance II 500 MHz or 600 MHz instrument at 300°K. Chemical shifts were reported in parts per million (δ) relative to the internal standard of tetramethylsilane (TMS). The signals observed were described as follows: s (singlet), d (doublet), t (triplet).
The indoxyl sulfate was determined to be pure based on the single peak observed at R_t=21.7 min. by HPLC analysis. No other peaks were detected. The ^{1}H-NMR (CD_3OD) δ 7.01 (t, 1H, J=7.49Hz, H_5), 7.09 (t, 1H, J=7.59Hz, H_6), 7.20 (s, 1H, H_2), 7.30 (d, 1H, J=8.18Hz, H_7), 7.67 (d, 1H, J=7.95Hz, H_4). The ^{13}C-NMR (150 MHz, CD_3OD) δ 110.92 (C-7), 114.23 (C-2), 117.52 (C-4), 118.50 (C-5), 121.11 (C-4a), 121.27 (C-6), 131.17 (C-3), 133.74 (C-7a). The spectra data confirm the compound as indoxyl sulfate with more than 99.9% purity.

Cytotoxicity assays. Huh7 cells were seeded into 96-well plates at $2x10^3$ cell/well. Following overnight culture, cells were incubated with either vehicle (DMSO) or increasing concentrations of indoxyl-3-sulphate for 48 h. Cytotoxicity was assessed using the lactate dehydrogenase-based TOX-7 kit (Promega, Madison, WI) following the manufacturer's instructions. Cytotoxicity was determined by calculating the ratio of released LDH activity/total (cellular and released) LDH activity.

II. Supplementary Table S1

Table S1. Primers for Real-Time PCR

Gene	Forward (5'→3')	Reverse (5'→3')
CYP1A1	TCTTCCTTCGTCCCCTTCAC	TGGTTGATCTGCCACTGGTT
CYP1A2	GGGCACTTCGACCCTTACAA	GCACATGGCACCAATGACG
CYP1B1	TGCCTGTCACTATTCCTCATGCCA	ATCAAAGTTCTCCGGGTTAGGCCA
UGT1A1	AACTTTCTGTGCGACGTGGTT	GTCACCTCTCTCTGAAGGAATTCTG
UGT1A6	AGCCCAGACCCTGTGTCCTA	CCACTCGTTGGGAAAAAGTCA
IL-6	AAATTCGGTACATCCTCGACGGCA	AGTGCCTCTTTGCTGCTTTCACAC
SAA1	AGGCTCAGACAAATACTTCCATGC	TCTCTGGCATCGCTGATCACTTCT
L13a	CCTGGAGGAGAAGAGGAAAGAGA	GAGGACCTCTGTGTATTTGTCAA



Supporting Figure S1. Indoxyl-3-sulphate is not cytotoxic to hepatoma cells. Huh7 cells were incubated for 48 h with increasing concentrations of indoxyl-3-sulphate, as indicated. Cytotoxicity was assessed by measuring LDH release. Data represents percentage cytotoxicity ± SEM relative to vehicle-treated.