

## **Supplementary Information**

### **Incomplete hydrolysis of curcumin conjugates by $\beta$ -glucuronidase. Detection of complex conjugates in plasma**

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**SI Table 1. Molecular and fragment ions used for SRM analyses of curcumin conjugates in positive ion mode.** Transitions in blue font in the calculated/predicted ion pairs resulted in successful detection of a conjugate from both unlabeled and d<sub>6</sub>-curcumin.

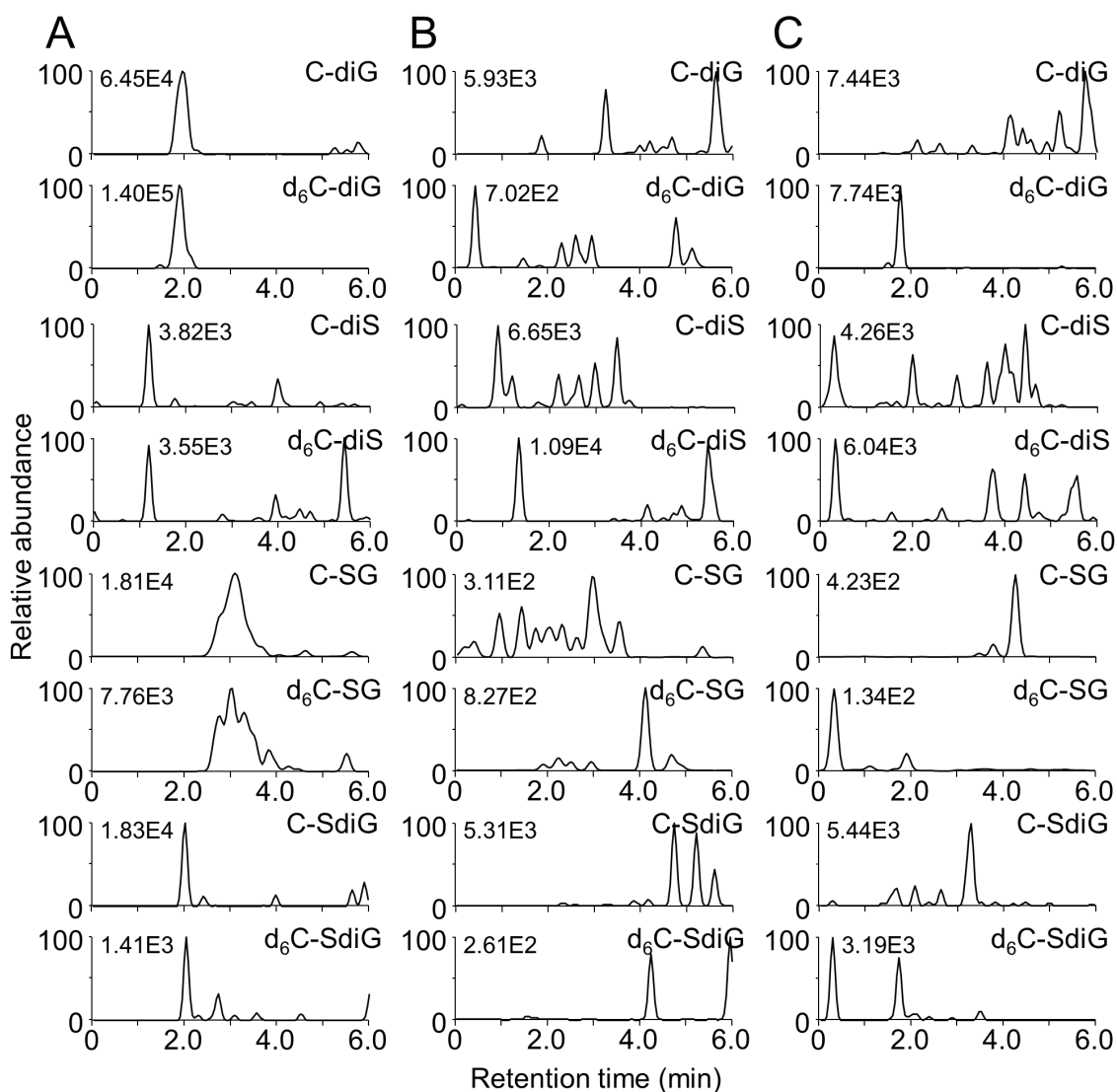
Conjugate	curcumin			CID (eV)	d <sub>6</sub> -curcumin	
	[M+H] <sup>+</sup> ( <i>m/z</i> )	fragment ( <i>m/z</i> )	loss		[M+H] <sup>+</sup> ( <i>m/z</i> )	fragment ( <i>m/z</i> )
Experimentally determined ion pairs:						
curcumin	369.0	177.0	192 (cleave)	20	375.3	180.2
C-G	545.2	369.2	176 (G)	15	551.4	375.2
C-S	449.4	285.4	164 (cleave)	20	455.4	291.0
Calculated/predicted ion pairs:						
C-diG	721.6	369.2	352 (2G)	15	727.6	375.2
	721.6	545.2	176 (G)	15	727.6	551.4
C-diS	529.5	369.2	160 (2S)	15	535.5	375.2
	529.5	449.4	80 (S)	15	535.5	455.4
	529.5	285.4	244 (cleave)	20	535.5	291.0
C-SG	625.6	369.2	256 (GS)	15	631.6	375.2
	625.6	545.2	80 (S)	15	631.6	551.4
	625.6	449.4	176 (G)	15	631.6	455.4
	625.6	285.4	340 (cleave)	20	631.6	291.0
C-SdiG	801.7	369.2	423 (SdiG)	15	807.7	375.2
	801.7	721.6	80 (S)	15	807.7	727.6
	801.7	449.4	352 (diG)	15	807.7	455.4
	801.7	285.4	516 (cleave)	20	807.7	291.0
C-GdiS	705.6	369.2	336 (GdiS)	15	711.6	375.2
	705.6	529.5	176 (G)	15	711.6	535.2
	705.6	449.4	256 (GS)	15	711.6	455.4
	705.6	285.4	420 (cleave)	20	711.6	291.0

C, curcumin; G, glucuronide; S, sulfate.

**SI Table 2. Molecular and fragment ions used for SRM analyses of curcumin conjugates in negative ion mode.** Transitions in blue font in the calculated/predicted ion pairs resulted in successful detection of a conjugate from both unlabeled and d<sub>6</sub>-curcumin.

Conjugate	curcumin			CID (eV)	d <sub>6</sub> -curcumin	
	[M-H] <sup>-</sup> (m/z)	fragment (m/z)	loss		[M-H] <sup>-</sup> (m/z)	fragment (m/z)
Experimentally determined ion pairs:						
curcumin	367.4	217.0	150 (cleave)	10	373.1	220.0
C-G	543.4	217.0	326 (cleave)	20	549.4	220.0
C-S	447.2	217.0	230 (cleave)	15	453.2	220.0
Calculated/predicted ion pairs:						
C-diG	719.6	217.0	502 (cleave)	20	725.6	220.4
	719.6	543.4	176 (G)	15	725.6	549.4
C-diS	527.5	217.0	310 (cleave)	15, 20	533.5	220.4
	527.5	447.2	80 (S)	15	533.5	453.2
C-SG	623.6	217.0	406 (cleave)	15, 20	629.6	220.4
	623.6	543.4	80 (S)	15	629.6	549.4
	623.6	447.2	176 (G)	15	629.6	453.2
C-SdiG	799.7	217.0	582 (cleave)	15, 20	805.7	220.4
	799.7	719.6	80 (S)	15	805.7	725.6
	799.7	447.2	352 (diG)	15	805.7	453.2
C-GdiS	703.6	217.0	486 (cleave)	15, 20	709.6	220.4
	703.6	527.5	176 (G)	15	709.6	533.5
	703.6	447.2	256 (GS)	15	709.6	453.2

C, curcumin; G, glucuronide; S, sulfate.



**SI Fig. 1. Analysis of complex conjugates in plasma of mice treated with a 1:1 mixture of curcumin and d<sub>6</sub>-curcumin with and without hydrolysis.** (A) Untreated plasma, (B) plasma treated with β-glucuronidase, (C) plasma treated with sulfatase. Panel (A) shows the same chromatograms as Figure 5 in the main text. Ion trace chromatograms were acquired using analytical conditions listed in Table 1 in the main text. The numbers indicate the highest ion intensity in each trace.