IDENTIFICATION OF INTESTINAL UDP-GLUCURONOSYLTRANSFERASE INHIBITORS IN GREEN TEA (*CAMELLIA SINENSIS*) USING A BIOCHEMOMETRIC APPROACH: APPLICATION TO RALOXIFENE AS A TEST DRUG VIA IN VITRO TO IN VIVO EXTRAPOLATION

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DRUG METABOLISM AND DISPOSITION

SUPPLEMENTARY INFORMATION

Fig. S1. Concentration-dependent inhibition of intestinal microsomal UGT activity (4-MU glucuronidation) by purified catechins. Methanol (2%, v/v) served as vehicle control. Nicardipine (400 μM) and silybin B (100 μM) served as positive control UGT inhibitors (Gufford, 2014). All catechins were tested at 100 μM. Bars and error bars denote mean ± SD, respectively, of triplicate incubations.

Fig. S2. Dixon plots showing inhibition of raloxifene-4'-glucuronide (R4G; left) or raloxifene-6-glucuronide (R6G; right) formation by ECG (upper) and EGCG (lower). Symbols denote individual data points of duplicate incubations.

Fig. S3. Concentration-dependent inhibition of intestinal microsomal UGT activity (raloxifene glucuronidation) by purified catechins. Methanol (2%, v/v) served as vehicle control. Nicardipine (400 μM) and silybin B (100 μM) served as positive control UGT inhibitors (Gufford et al., 2014). All catechins were tested at 10 and 100 μM. Bars and error bars denote mean ± SD, respectively, of triplicate incubations. R4G, raloxifene 4'-glucuronide; R6G, raloxifene 6-glucuronide.

Supplementary Reference

Gufford BT, Chen G, Lazarus P, Graf TN, Oberlies NH and Paine MF (2014) Identification of diet-derived constituents as potent inhibitors of intestinal glucuronidation. Drug Metab Dispos 42:1675-1683

Fig. S1

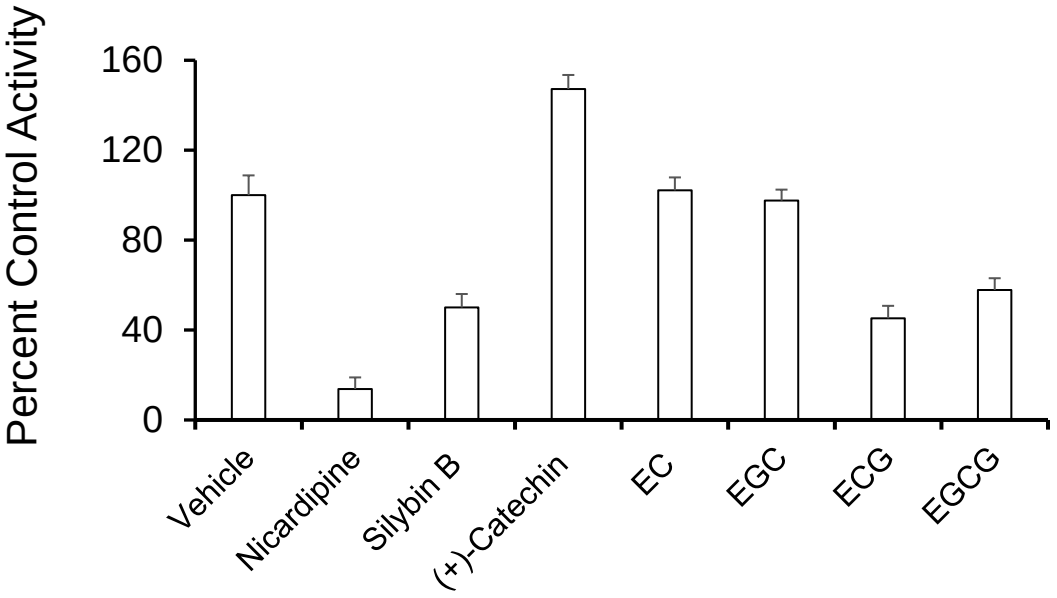

Percent Control Activity
160
120
80
40
0
Vehicle
Nicardipine
Silybin B
(+)-Catechin
EC
EGC
ECG
EGCG

Fig. S2

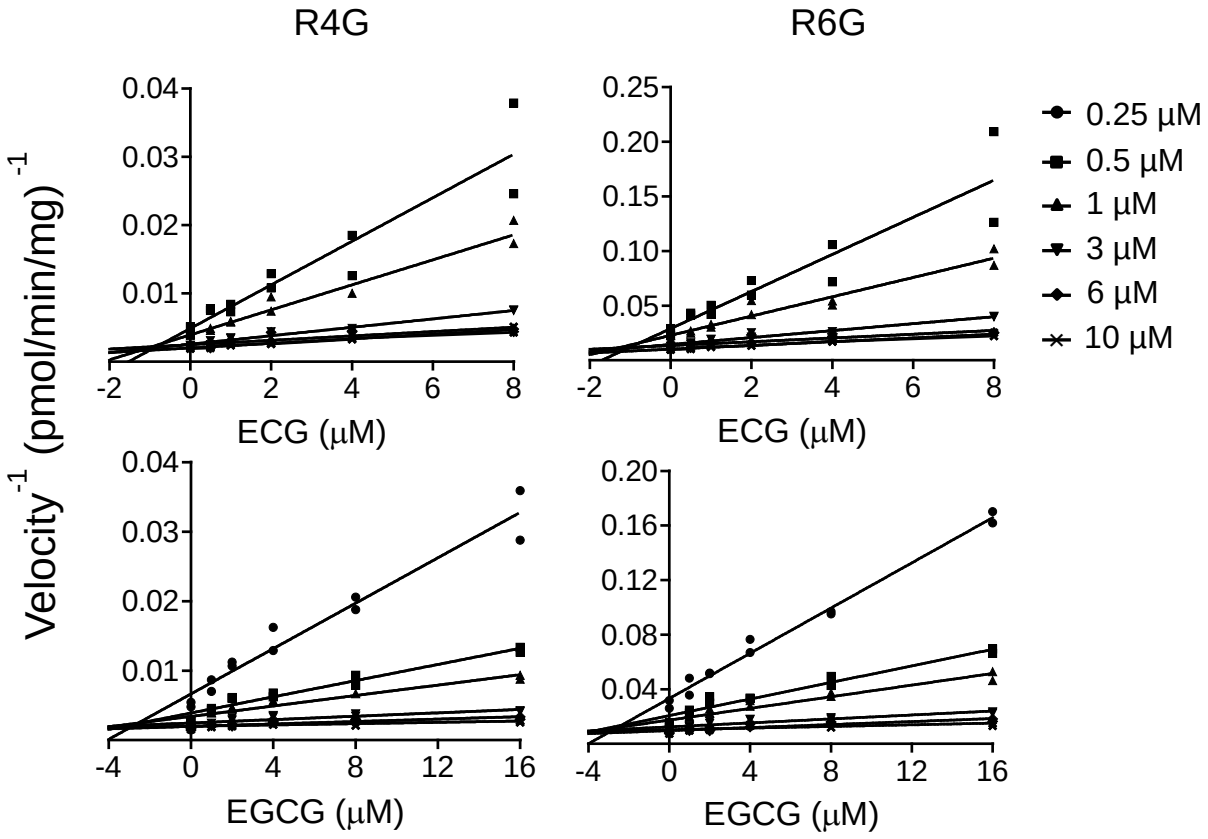
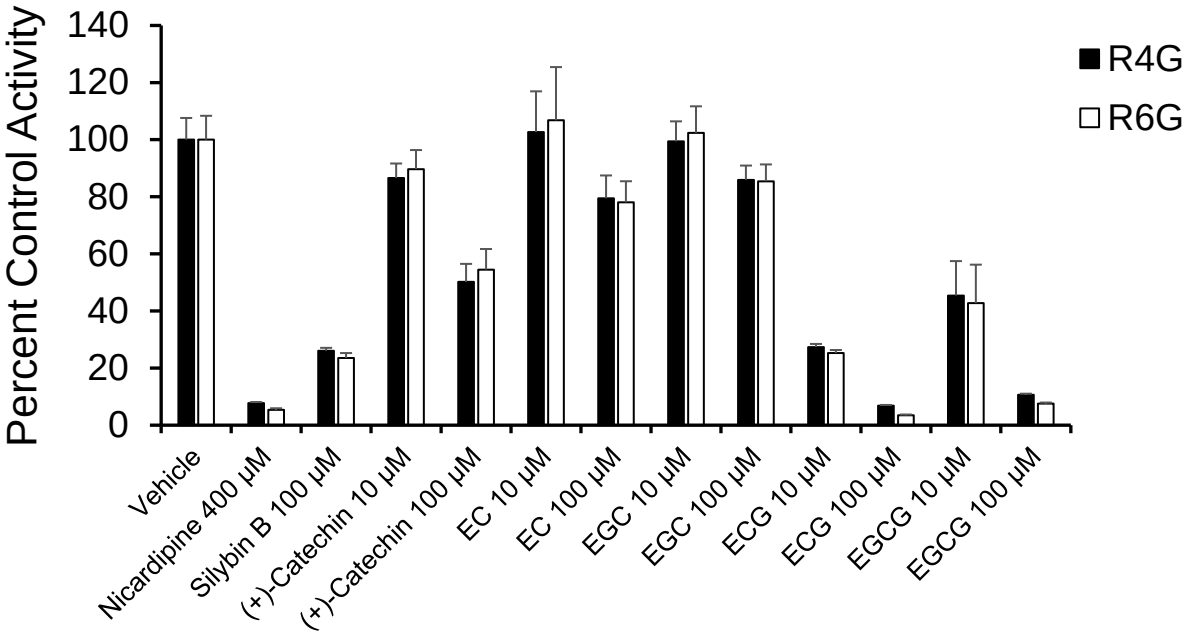

R4G
R6G
Velocity-1 (pmol/min/mg)-1
ECG (μM)
EGCG (μM)
0.25 μM
0.5 μM
1 μM
3 μM
6 μM
10 μM

Fig. S3


Percent Control Activity
140
120
100
80
60
40
20
0
R4G
R6G
Vehicle
Nicardipine 400 μM
Silybin B 100 μM
(+)-Catechin 10 μM
(+)-Catechin 100 μM
EC 10 μM
EC 100 μM
EGC 10 μM
EGC 100 μM
ECG 10 μM
ECG 100 μM
EGCG 10 μM
EGCG 100 μM