Supplemental data Figure legend:

Figure 1: Combined negative ion electrospray LC-MS-MS SRM chromatogram of 8-PN, 6-PN, IX, XH, and their respective glucuronides in rat liver homogenates from a rat that was treated with XH subcutaneously (**A**). LC-MS-MS SRM chromatograms of 8-PN/6-PN SRM transitions (**B**), and of 8-PN/6-PN glucuronides SRM transitions (**C**) of the same sample. SRM transitions: XH/IX: *m/z* 353-119; 8-PN/6-PN: *m/z* 339-219. XH GlcA/IX GlcA: *m/z* 529-353; 8-PN GlcA/6-PN GlcA: *m/z* 515-339.

Figure 2: Negative ion electrospray LC-MS-MS SRM chromatogram of XH GlcAs (**A**), of 8-PN GlcAs (**B**) and of 6-PN GlcA (**C**) after rat microsomal incubations with pure XH (**A**), 8-PN (**B**), and 6-PN (**C**). SRM transitions: XH GlcA/IX GlcA: m/z 529-353 (**A**); 8-PN GlcA/6-PN GlcA: m/z 515-339 (**B** and **C**). To generate glucuronide conjugates of prenylated flavonoids (10 μM), rat liver microsomes (0.5 mg/ml) were preincubated on ice with alamethicin (25 μg/ml) in a 50 mM Tris-HCl buffer, pH 7.5, supplemented with 10 mM magnesium chloride. The reaction was started by adding uridine diphospho glucuronic acid (2 mM) and incubations were carried out for 30 min at 37 °C. The reaction was stopped by adding acetonitrile. After centrifugation, an aliquot of the supernatant was directly analyzed by LC-MS-MS.

Figure 3: Combined negative ion electrospray LC-MS-MS SRM chromatogram of 8-PN, 6-PN, IX, XH, and their respective glucuronides in rat mammary gland homogenate from a rat that was treated with XH subcutaneously (**A**). LC-MS-MS SRM chromatogram of 8-PN/6-PN glucuronides (**B**). SRM transitions: XH/IX: *m/z* 353-119;

8-PN/6-PN: *m/z* 339-219. XH GlcA/IX GlcA: *m/z* 529-353; 8-PN GlcA/6-PN GlcA: *m/z* 515-339.

Figure 4: LC-MS-MS chromatograms of XH and its metabolites in plasma from a rat dosed with XH subcutaneously. SRM was carried out with negative ion electrospray and collision-induced dissociation. The precursor and product ion transition for each measurement are indicated above each chromatogram.

Figure 5: Densiometric analysis of western blots demonstrating Nrf2 nuclear accumulation by hops. HepG2 cells were treated with DMSO (0.2%), positive control BF (1.7 μM), XH (8 μM), and hop extract (20 μg/mL) for 6 hrs and Nrf2 protein was visualized by western blot analysis. Imaging and analysis was performed using FluoroChem software (Cell Biosciences). Each protein band density was normalized to the respective histone 3 band density and was represented as the fold induction of Nrf2 nuclear accumulation in relation to the DMSO control. Three independent experiments were performed to obtain the average ± SD. *: $p<0.05$ BF significantly induced Nrf2 nuclear accumulation (ANOVA with Dunnett's post test).

Figure 1

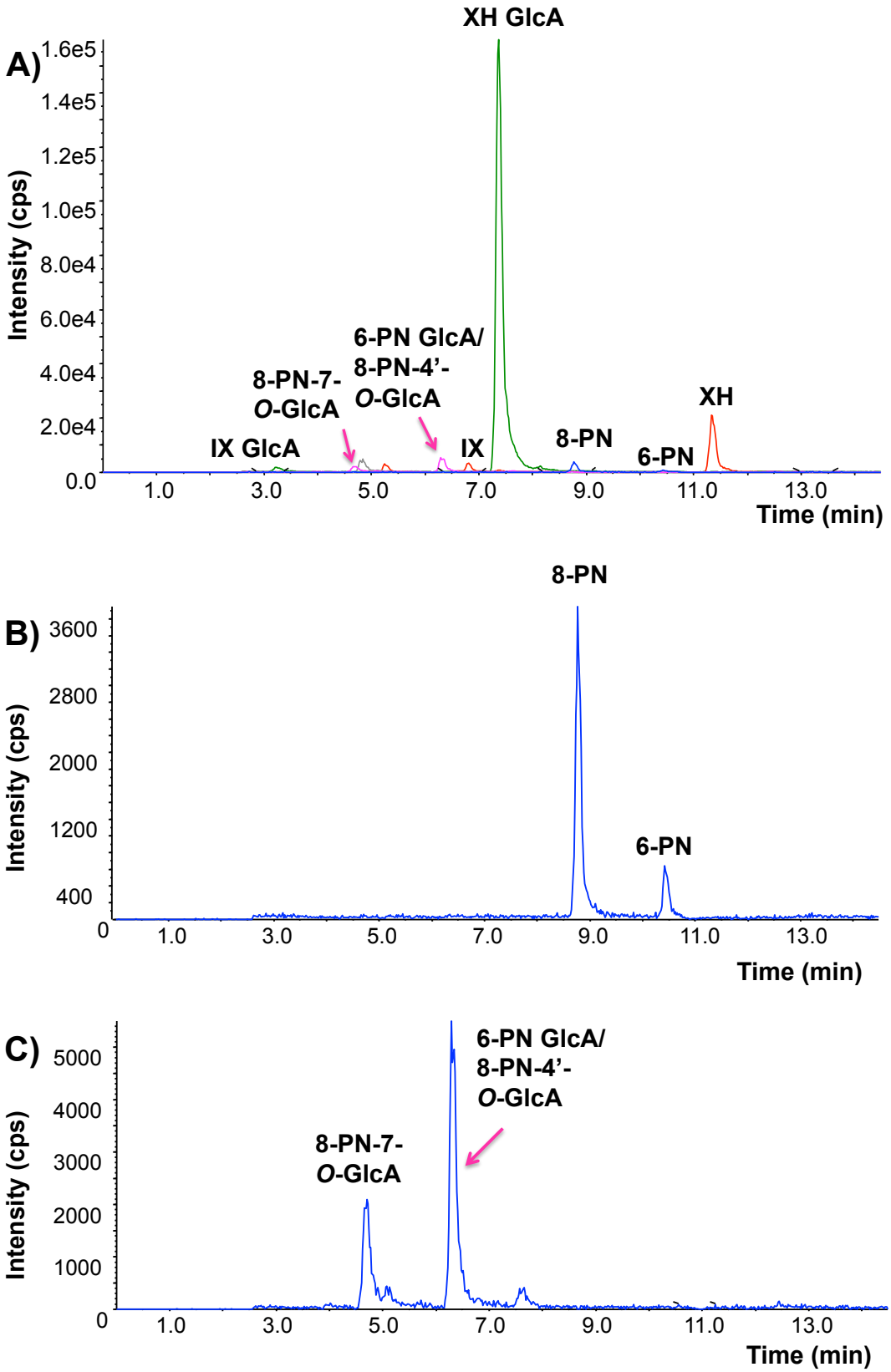
A)
XH GlcA
Intensity (cps)
1.6e5
1.4e5
1.2e5
1.0e5
8.0e4
6.0e4
4.0e4
2.0e4
0.0
6-PN GlcA/
8-PN-4'-
O-GlcA
8-PN-7-
O-GlcA
IX GlcA
IX
8-PN
6-PN
XH
1.0
3.0
5.0
7.0
9.0
11.0
13.0
Time (min)
B)
8-PN
Intensity (cps)
3600
2800
2000
1200
400
0
6-PN
1.0
3.0
5.0
7.0
9.0
11.0
13.0
Time (min)
C)
6-PN GlcA/
8-PN-4'-
O-GlcA
Intensity (cps)
5000
4000
3000
2000
1000
0
8-PN-7-
O-GlcA
1.0
3.0
5.0
7.0
9.0
11.0
13.0
Time (min)

Figure 2

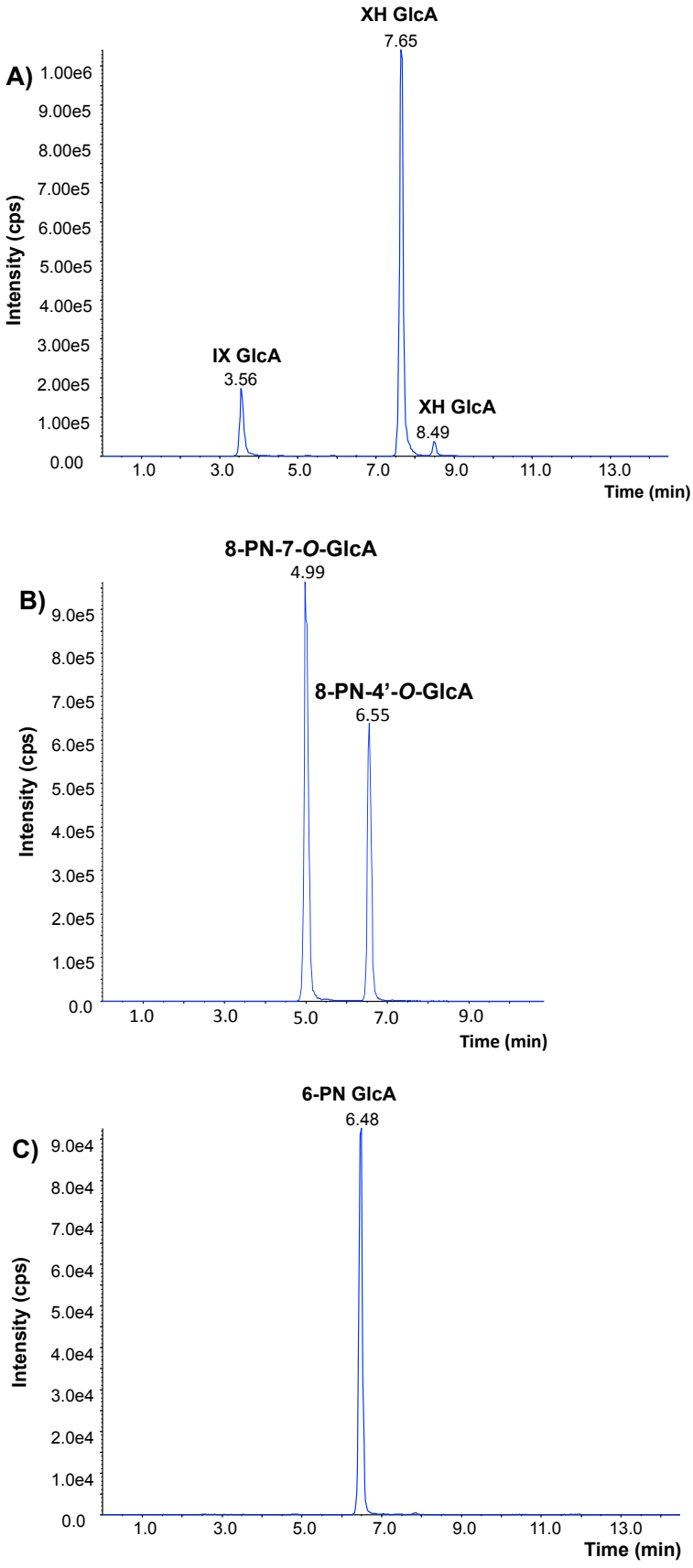
A)
XH GlcA
7.65
IX GlcA
3.56
XH GlcA
8.49
Intensity (cps)
Time (min)
B)
8-PN-7-O-GlcA
4.99
8-PN-4'-O-GlcA
6.55
Intensity (cps)
Time (min)
C)
6-PN GlcA
6.48
Intensity (cps)
Time (min)

Figure 3

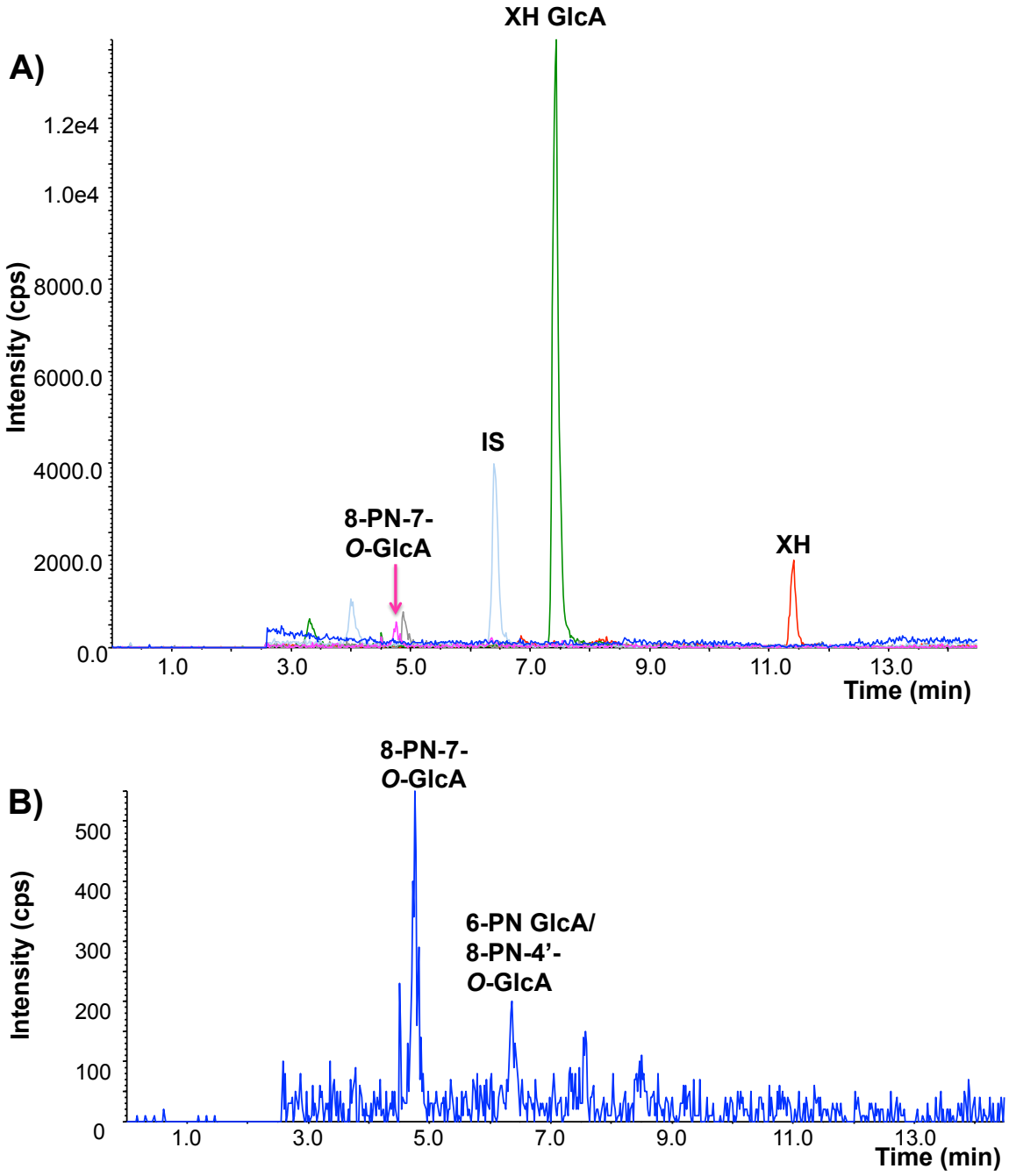
A)
XH GlcA
IS
8-PN-7-
O-GlcA
XH
Intensity (cps)
1.2e4
1.0e4
8000.0
6000.0
4000.0
2000.0
0.0
1.0
3.0
5.0
7.0
9.0
11.0
13.0
Time (min)
B)
8-PN-7-
O-GlcA
6-PN GlcA/
8-PN-4'-
O-GlcA
Intensity (cps)
500
400
300
200
100
0
1.0
3.0
5.0
7.0
9.0
11.0
13.0
Time (min)

Figure 4

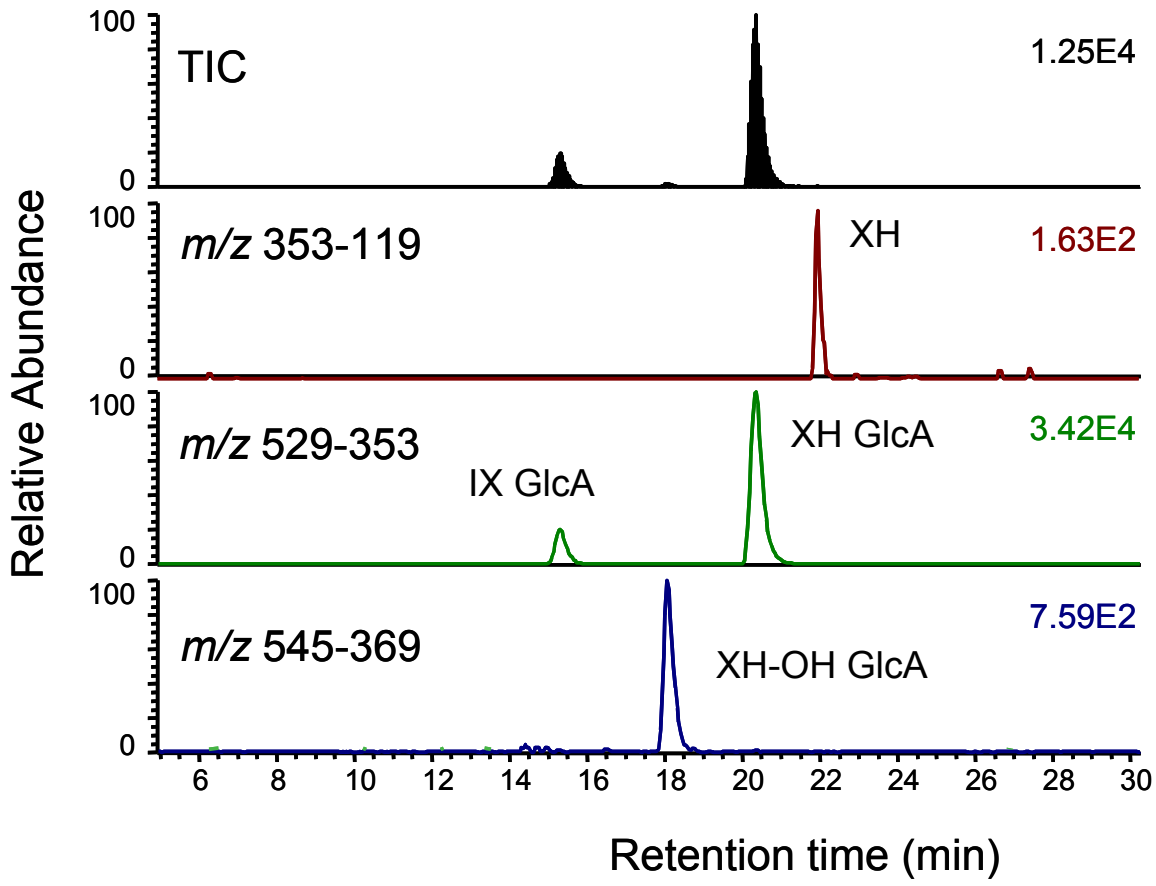
100
TIC
1.25E4
0
100
m/z 353-119
XH
1.63E2
0
100
m/z 529-353
XH GlcA
3.42E4
IX GlcA
0
100
m/z 545-369
7.59E2
XH-OH GlcA
0
Relative Abundance
6
8
10
12
14
16
18
20
22
24
26
28
30
Retention time (min)

Figure 5