Hyperforin induced activation of the Pregnane X Receptor is influenced by the Organic Anion Transporting Polypeptide 2B1 (OATP2B1)

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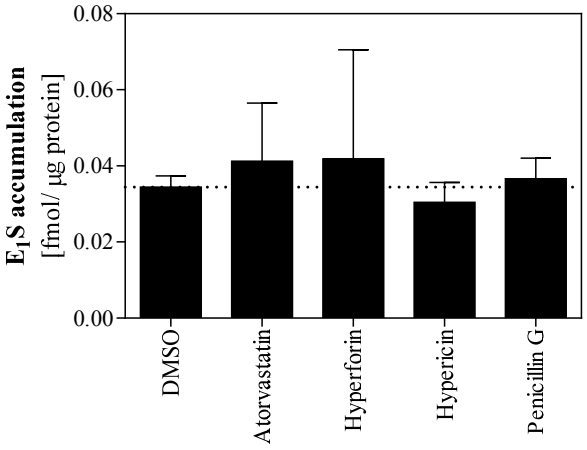
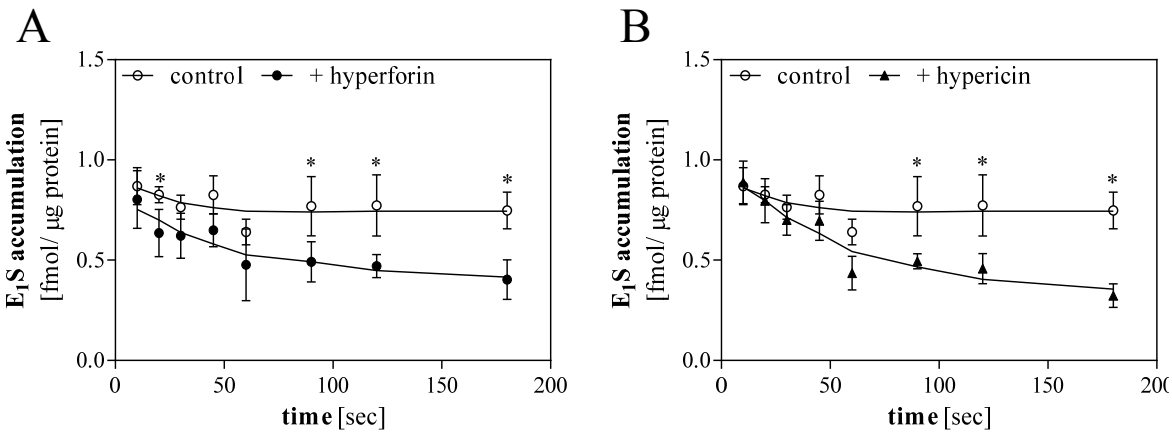
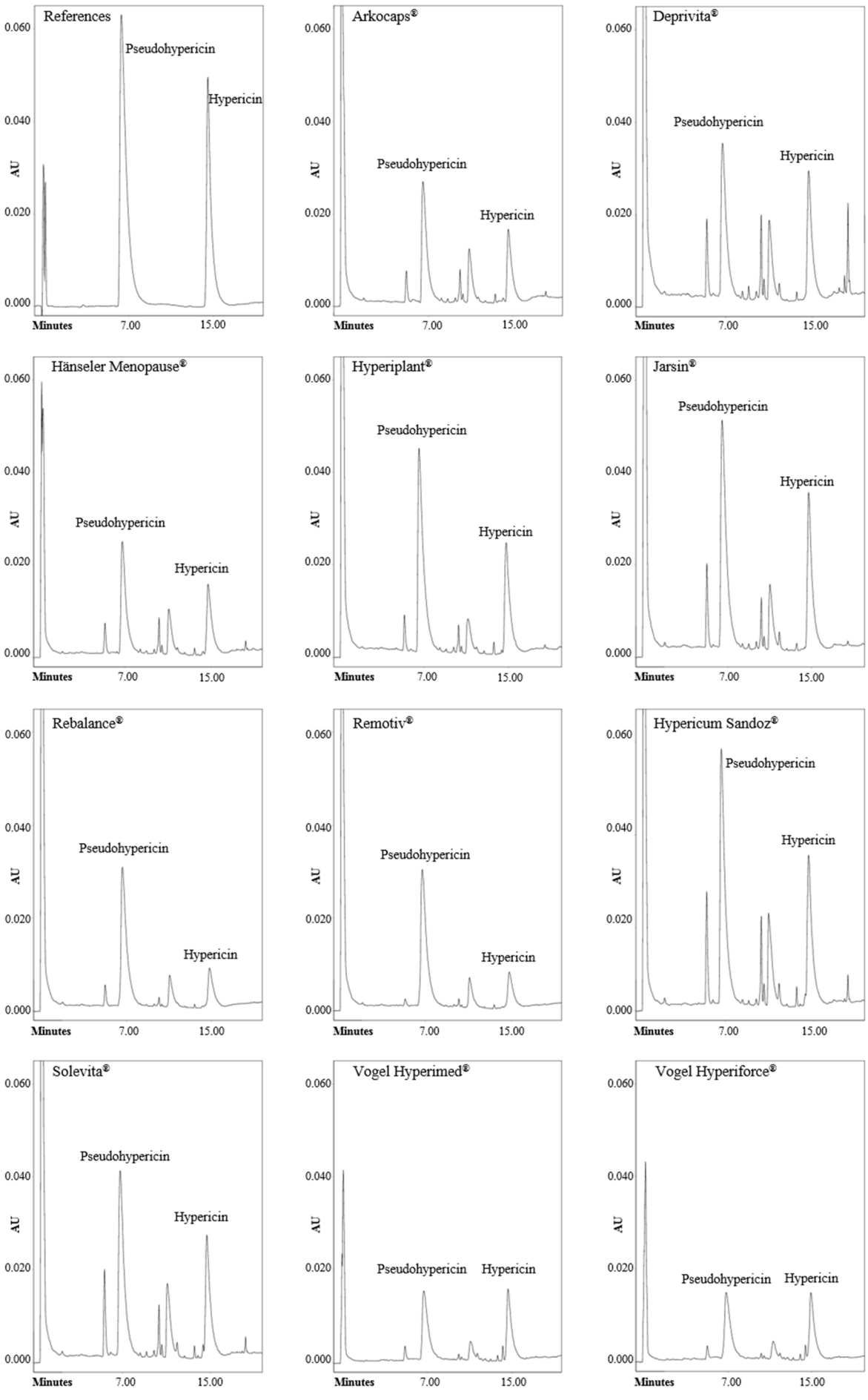
- Supplemental Data -



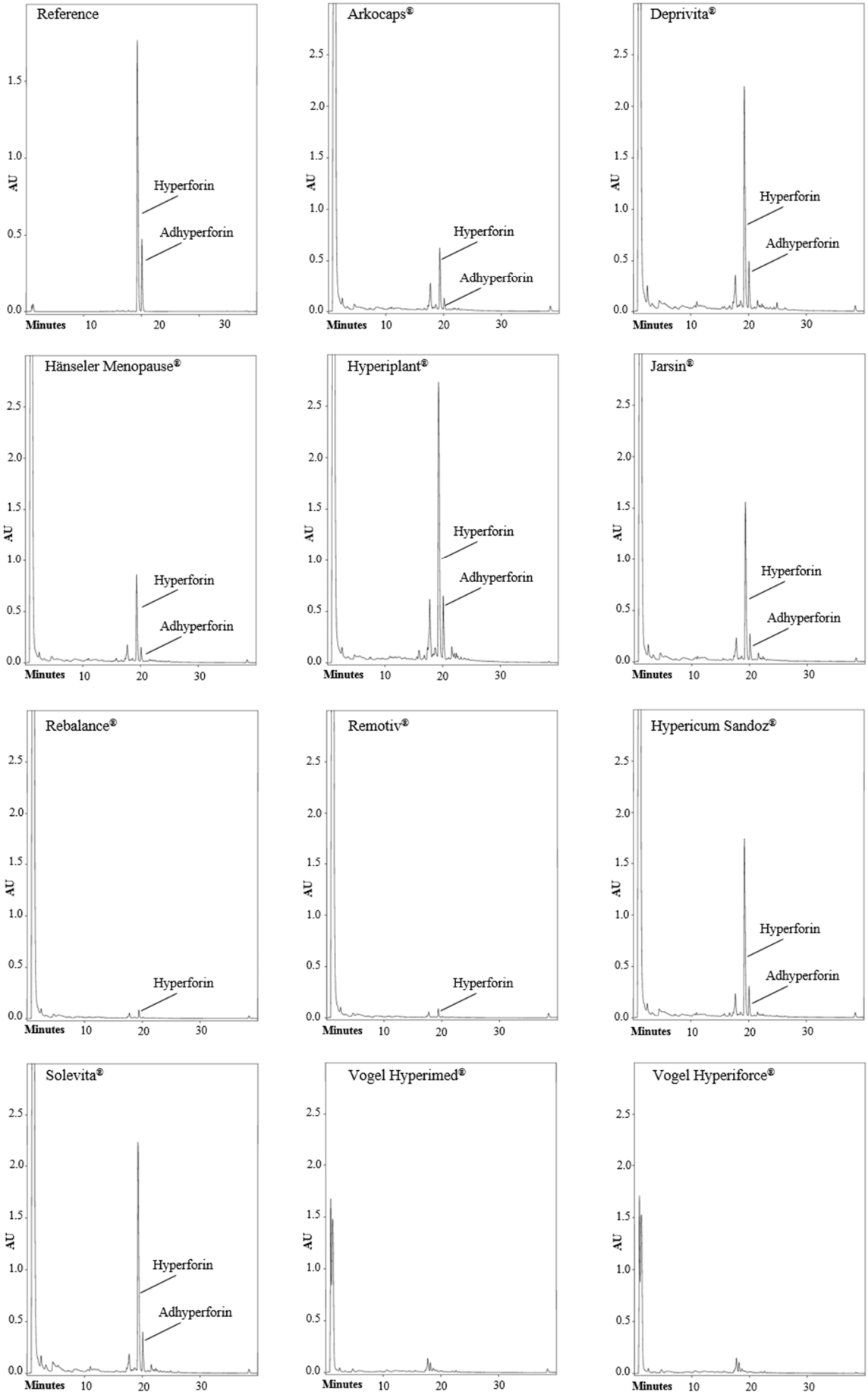
Supplemental Figure 1. Counterflow experiments performed in MDCKII cells. Cells were exposed to [^{3}H]-E_1S for 30 min. After reaching the steady state the supernatant was replaced by [^{3}H]-E_1S supplemented with DMSO or the respective test compound. Atorvastatin was used as positive control, penicillin G served as negative control, DMSO was the solvent control. Data are presented as mean ± SD of n=3 independent experiments each performed in biological triplicates. For statistical analysis one-way ANOVA was used corrected for multiple comparisons (Dunnett's test).



Supplemental Figure 2. Competitive counterflow experiment with hyperforin (A) or hypericin (B). MDCKII-OATP2B1 cells were treated with [^{3}H]-E_1S for 30 min to reach steady state. Then the supernatant was removed and cells were exposed to either the same amount of [^{3}H]-E_1S (control) or the same amount of [^{3}H]-E_1S supplemented with either hyperforin (0.5 µM, A) or hypericin (100 µM, B). Cellular accumulation of the radiolabel was quantified at the respective time points by liquid scintillation counting. Data are presented as mean ± SD, of n=3 independent experiments performed in biological duplicates followed by nonlinear curve fitting with Savistsky-Golay smoothing. *$p \leq 0.05$, two-way ANOVA with Sidak's multiple comparisons test.


References
Pseudohypericin
Hypericin
Arkocaps®
Pseudohypericin
Hypericin
Deprivita®
Pseudohypericin
Hypericin
Hänseler Menopause®
Pseudohypericin
Hypericin
Hyperiplant®
Pseudohypericin
Hypericin
Jarsin®
Pseudohypericin
Hypericin
Rebalance®
Pseudohypericin
Hypericin
Remotiv®
Pseudohypericin
Hypericin
Hypericum Sandoz®
Pseudohypericin
Hypericin
Solevita®
Pseudohypericin
Hypericin
Vogel Hyperimed®
Pseudohypericin
Hypericin
Vogel Hyperiforce®
Pseudohypericin
Hypericin
AU
0.060
0.040
0.020
0.000
Minutes
7.00
15.00

Supplemental Figure 3. Chromatograms of a mixture of the references hypericin (TOCRIS) and pseudohypericin (Sigma-Aldrich), and of the 11 in Switzerland marketed St. John's wort formulations. Detection was at 588 nm. Experiments were performed n=3 with three independent experiments, one representative chromatogram is shown.


Reference
Hyperforin
Adhyperforin
Arkocaps®
Hyperforin
Adhyperforin
Deprivita®
Hyperforin
Adhyperforin
Hänseler Menopause®
Hyperforin
Adhyperforin
Hyperiplant®
Hyperforin
Adhyperforin
Jarsin®
Hyperforin
Adhyperforin
Rebalance®
Hyperforin
Remotiv®
Hyperforin
Hypericum Sandoz®
Hyperforin
Adhyperforin
Solevita®
Hyperforin
Adhyperforin
Vogel Hyperimed®
Vogel Hyperiforce®
AU
Minutes
0.0
0.5
1.0
1.5
2.0
2.5
10
20
30

Supplemental Figure 4. Chromatograms of the reference hyperforin (Sigma-Aldrich) and of the 11 in Switzerland marketed St. John's wort formulations. Detection was at 272 nm. Experiments were performed n=3 with three independent experiments, one representative chromatogram is shown.