

## Intranasal delivery of phenytoin-loaded nanoparticles to the brain suppresses pentylenetetrazol-induced generalized tonic clonic seizures in epilepsy mouse model

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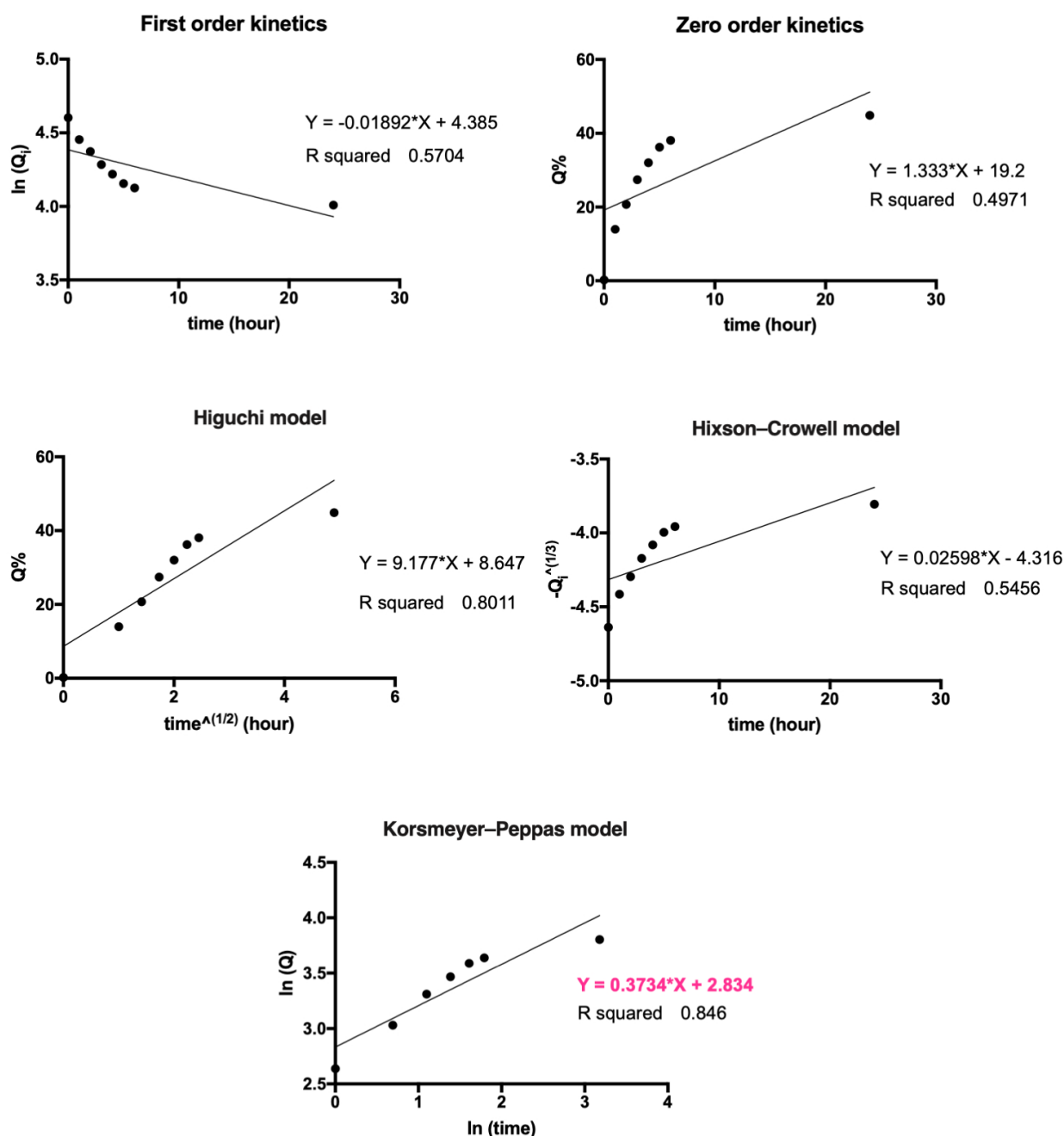
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**Figure S1. Drug release kinetics of L<sub>10</sub>Ci<sup>+</sup>.** Best fitted models for L<sub>10</sub>Ci according to the highest correlation (R<sup>2</sup>) value were Higuchi (R<sup>2</sup> = 0.811) and Korsmeyer-Peppas model (R<sup>2</sup> = 0.846) with release exponent (n) = 0.373.

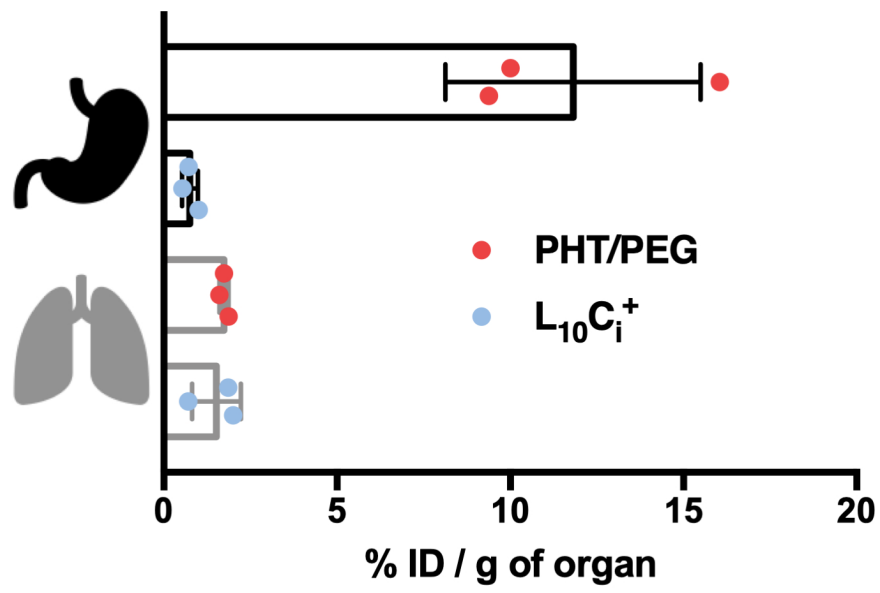
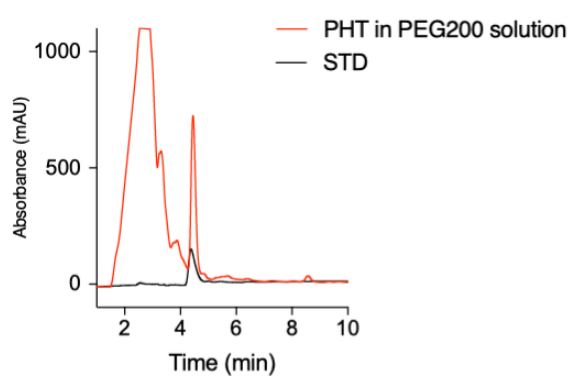
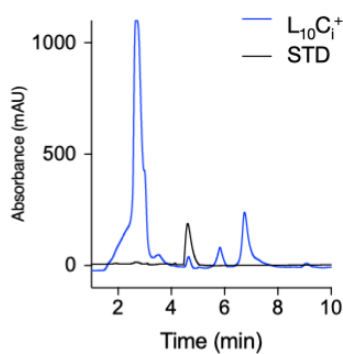


Figure S2. Dosing efficiency of  $L_{10}C_i^+$ . Negligible amounts of PHT were detected in the

# Stomach



# Lungs

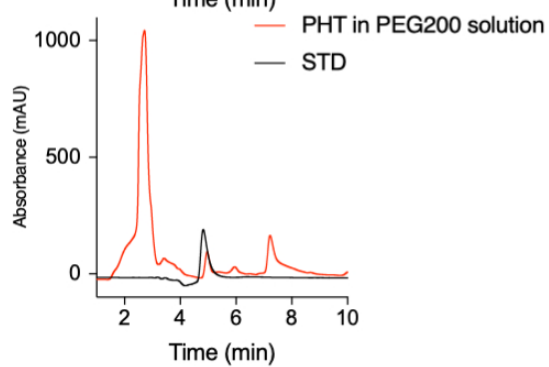
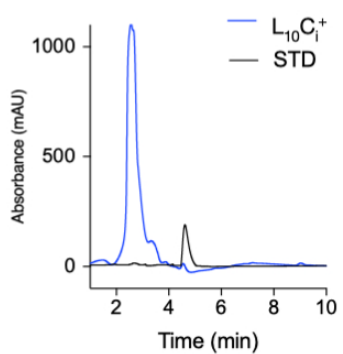
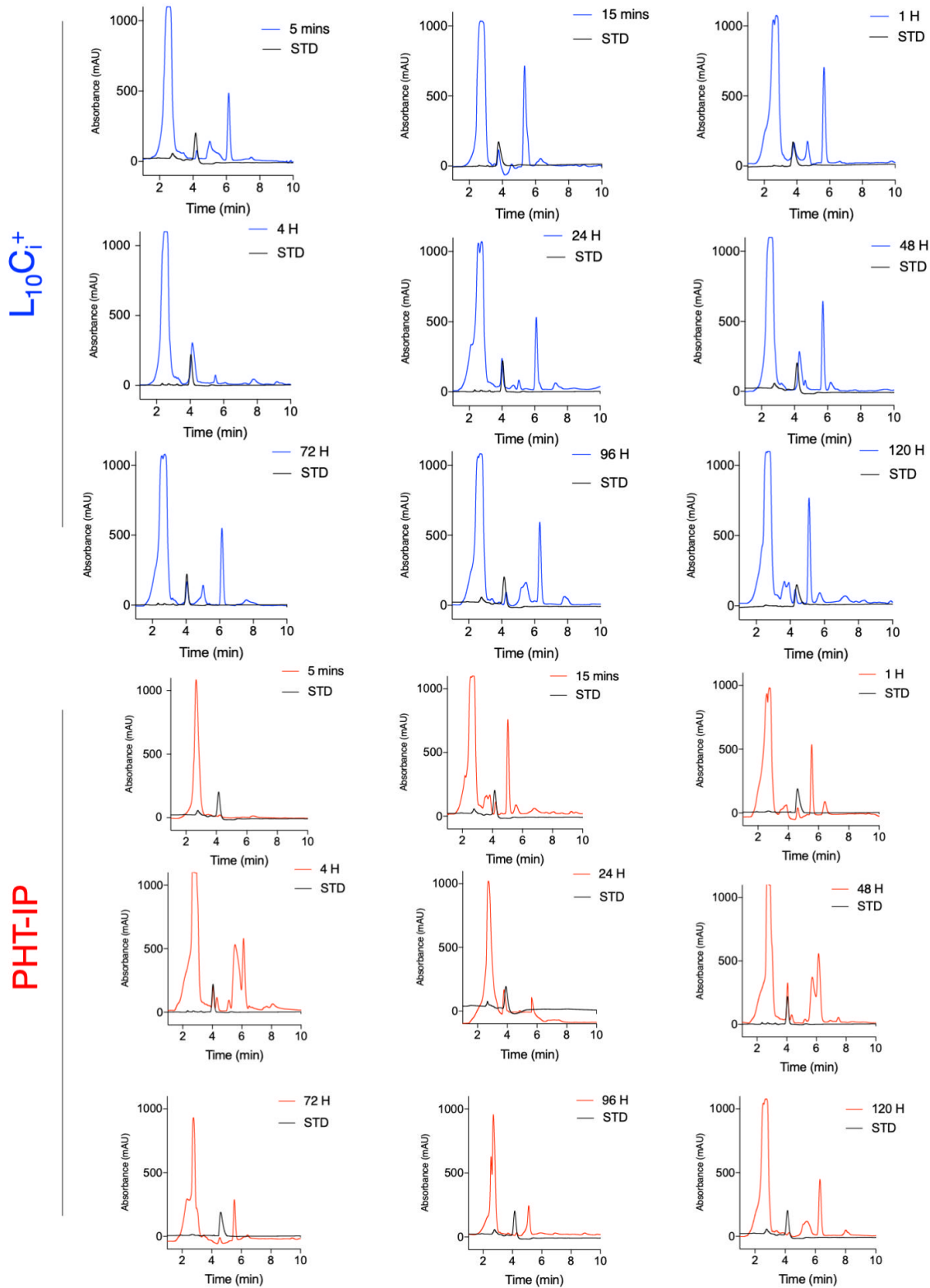


Figure S3. HPLC chromatograms of accumulated amounts of PHT in stomach and lungs following 5 min of  $L_{10}C_i^+$  and PHT/PEG administration at certain time points. PHT peaks in stomach and lungs were interrupted with the standard peak of PHT (50  $\mu\text{g}/\text{ml}$ ), identified as a well defined peak by this method, and quantified as Area.

# Brain

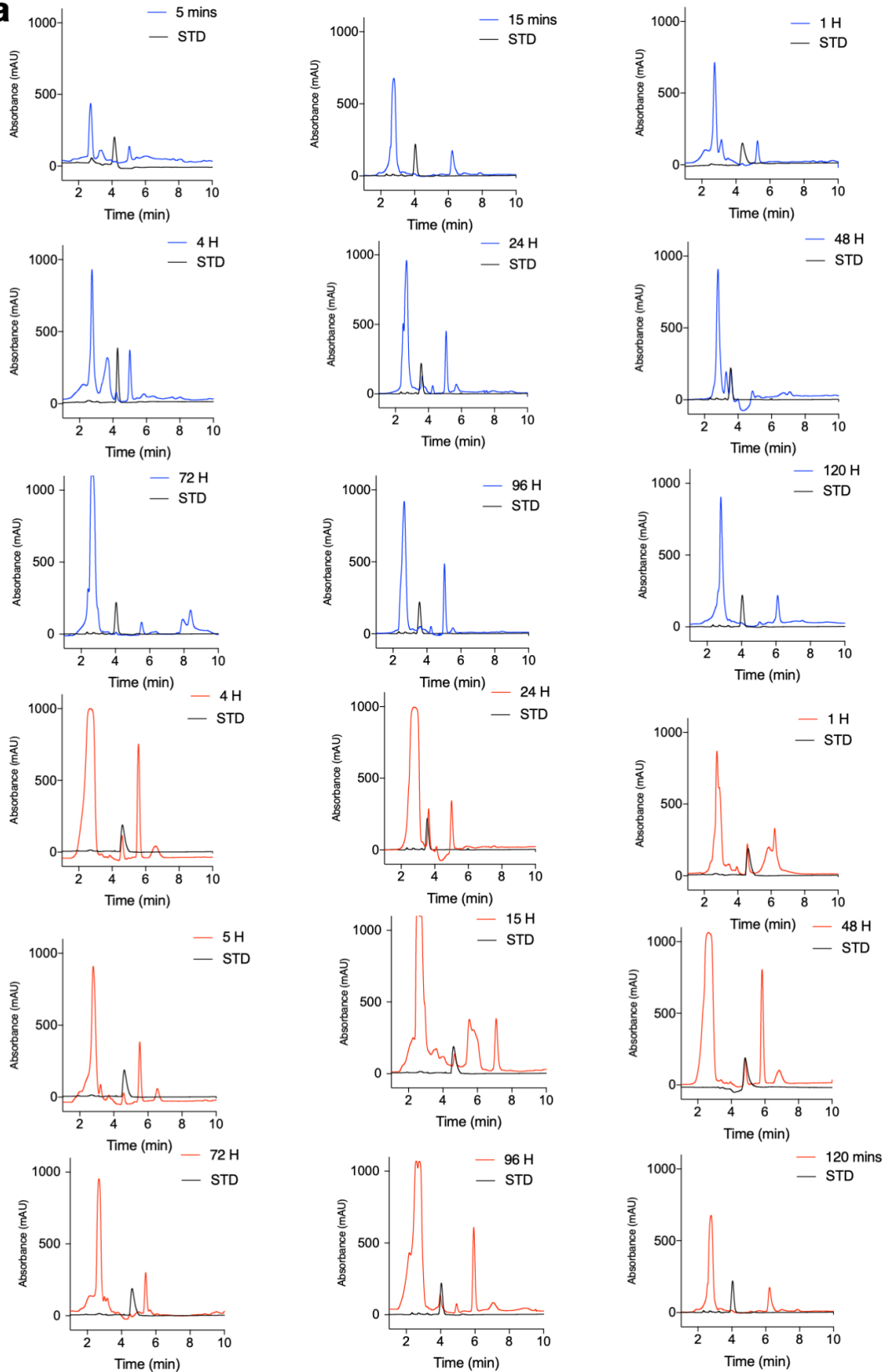


**Figure S4. HPLC chromatograms of accumulated amounts of PHT in brain following L<sub>10</sub>Ci<sup>+</sup> and PHT-IP administration at certain time points.** PHT peaks in brain were interrupted with the standard peak of PHT (50 µg/ ml), identified as a well defined peak by this method, and quantified as Area.

# Plasma

$L_{10}C_i^+$

PHT-IP

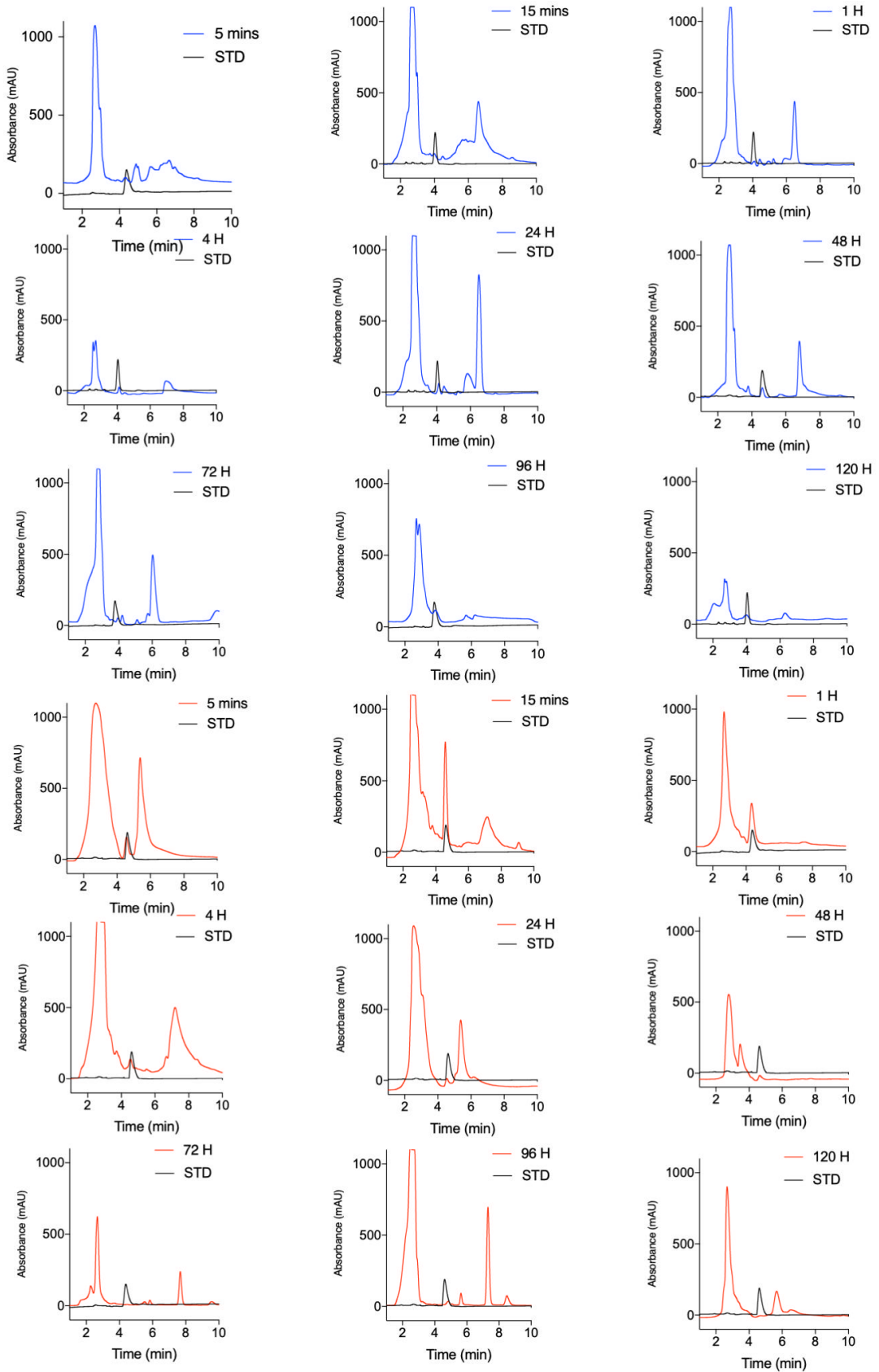


**Figure S5. HPLC chromatograms of accumulated amounts of PHT in plasma following  $L_{10}C_i^+$  and PHT-IP administration at certain time points. PHT peaks in plasma were interrupted with the standard peak of PHT (50  $\mu\text{g}/\text{ml}$ ), identified as a well defined peak by this method, and quantified as Area.**

# Liver

$L_{10}C_i^+$

PHT-IP

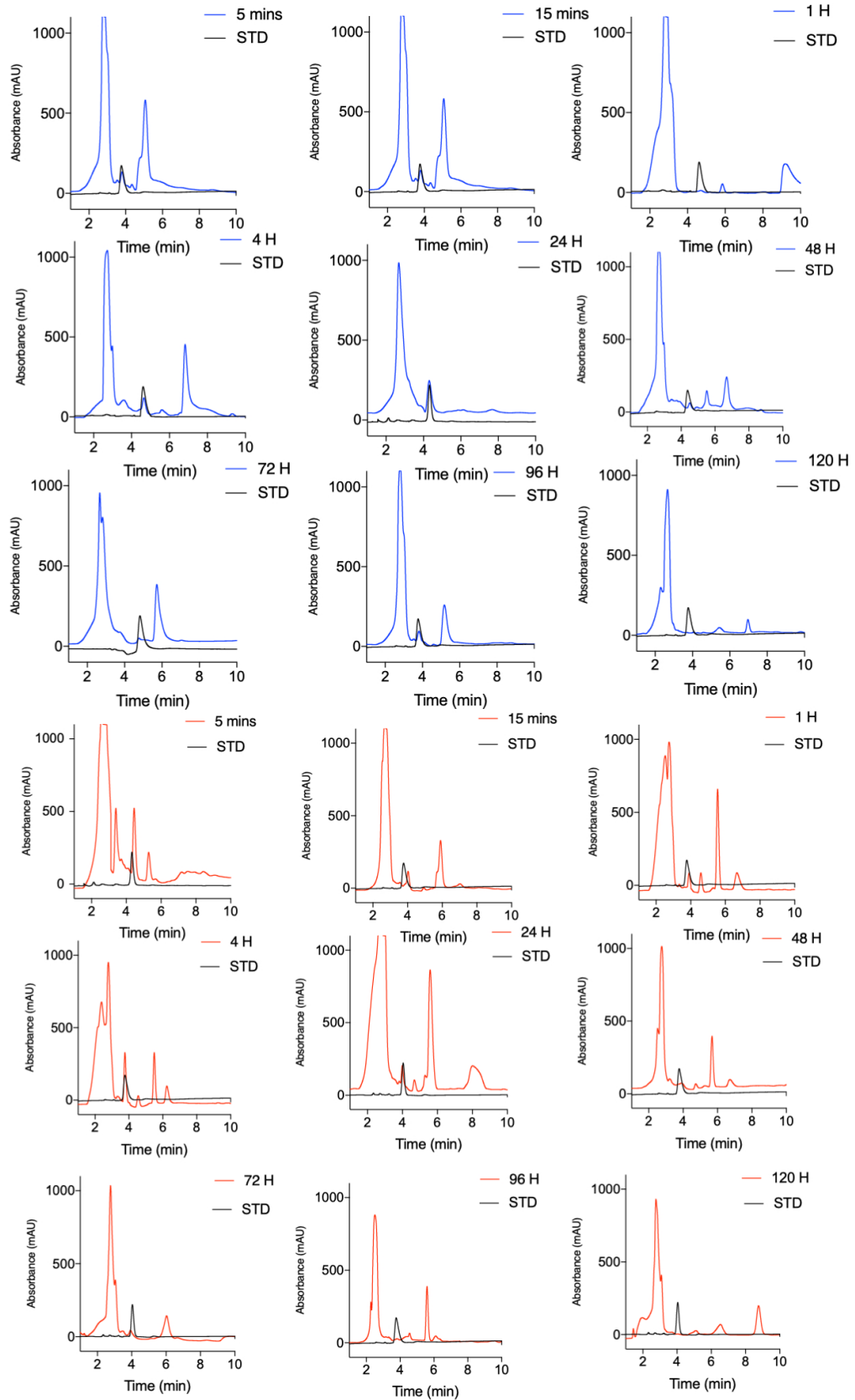


**Figure S6. HPLC chromatograms of accumulated amounts of PHT in liver following  $L_{10}C_i^+$  and PHT-IP administration at certain time points.** PHT peaks in liver were interrupted with the standard peak of PHT (50  $\mu\text{g}/\text{ml}$ ), identified as a well defined peak by this method, and quantified as Area.

# Spleen

$L_{10}C_i^+$

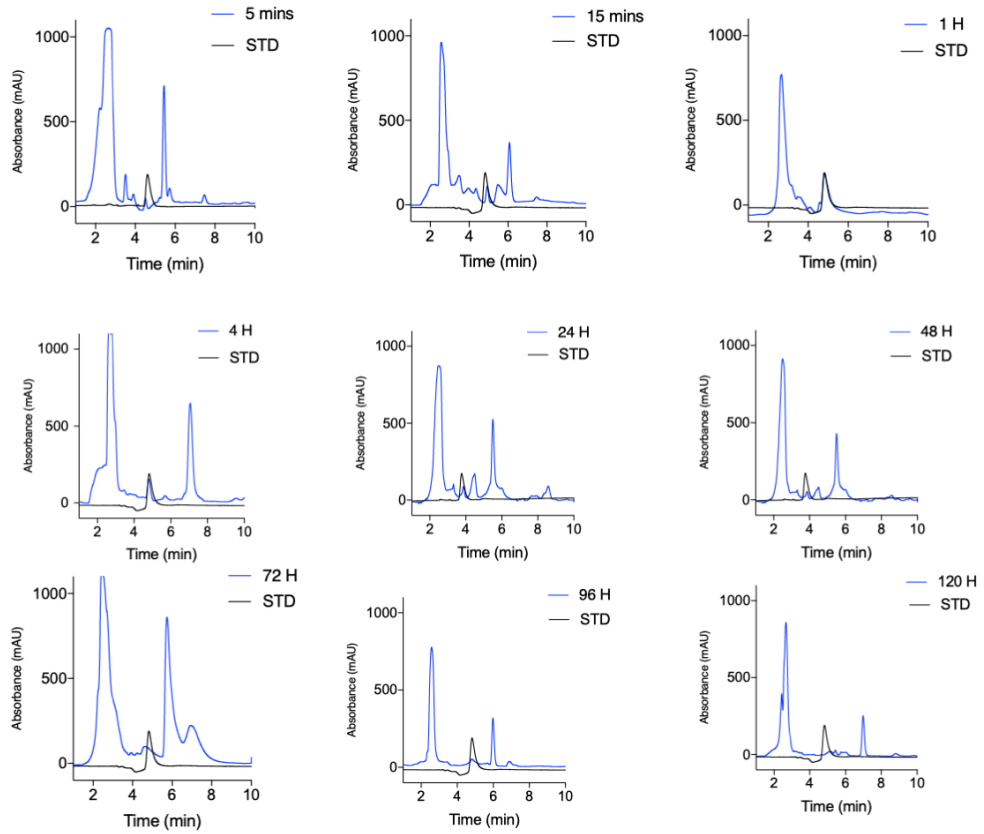
PHT-IP



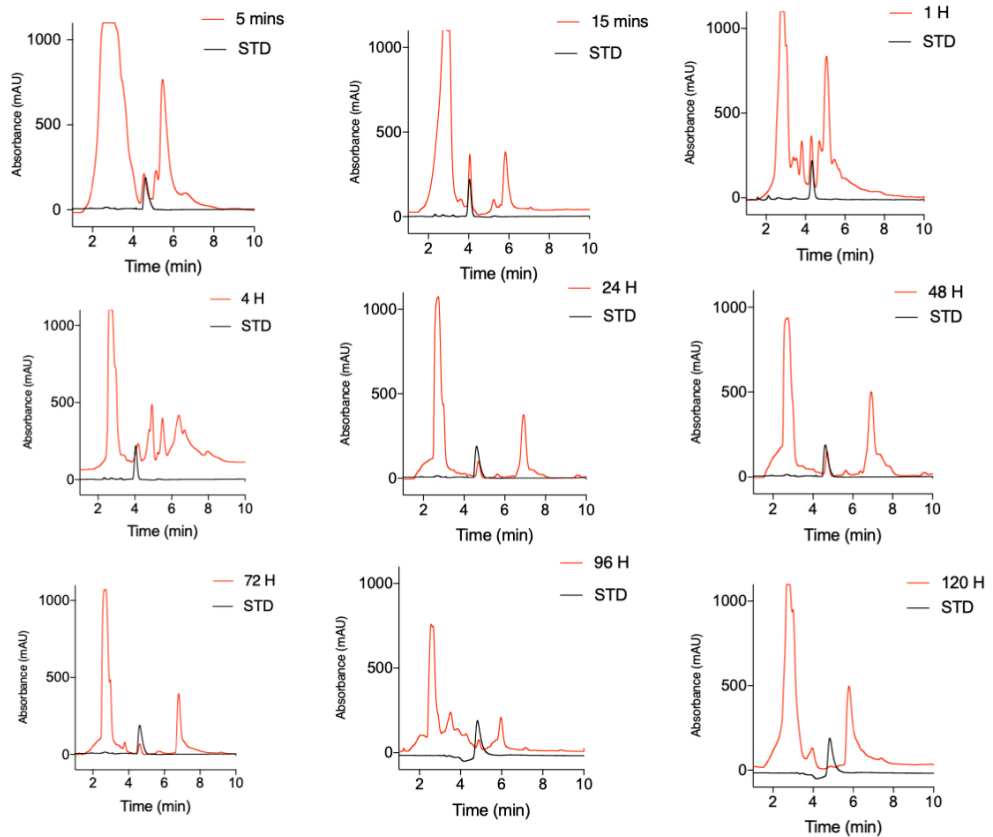
**Figure S7. HPLC chromatograms of accumulated amounts of PHT in spleen following  $L_{10}C_i^+$  and PHT-IP administration at certain time points. PHT peaks in spleen were interrupted with the standard peak of PHT (50  $\mu$ g/ml), identified as a well defined peak by this method, and quantified as Area.**

# Kidneys

$L_{10}C_i^+$

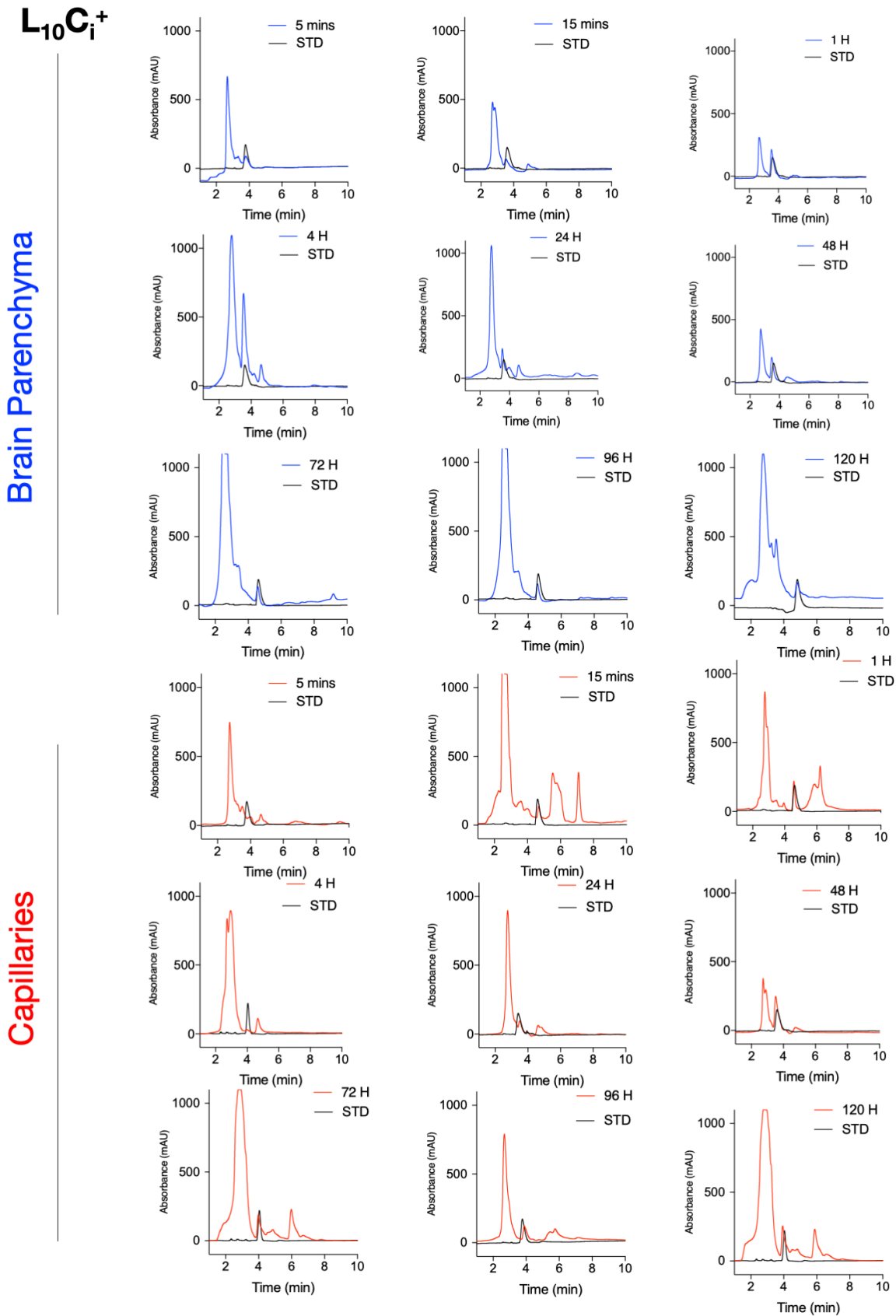


PHT-IP



**Figure S8.** HPLC chromatograms of accumulated amounts of PHT in kidneys following  $L_{10}C_i^+$  and PHT-IP administration at certain time points. PHT peaks in kidneys were interrupted with the standard peak of PHT (50  $\mu$ g/ml), identified as a well defined peak by this method, and quantified as Area.

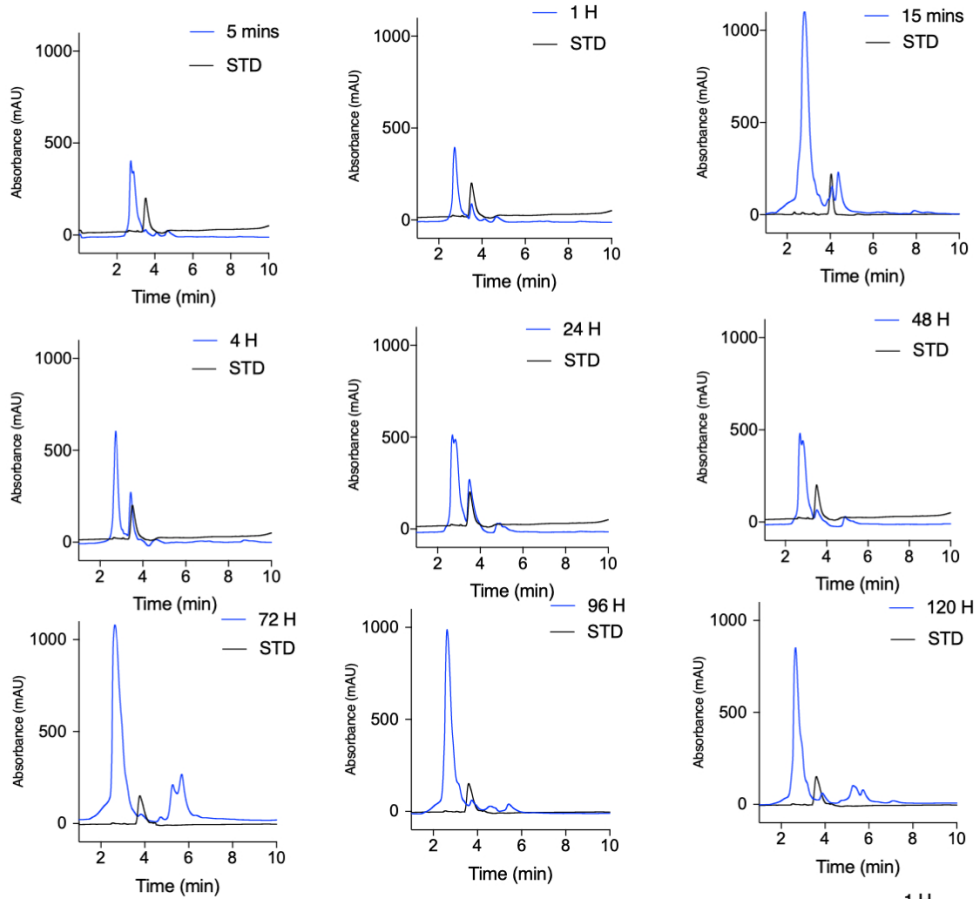




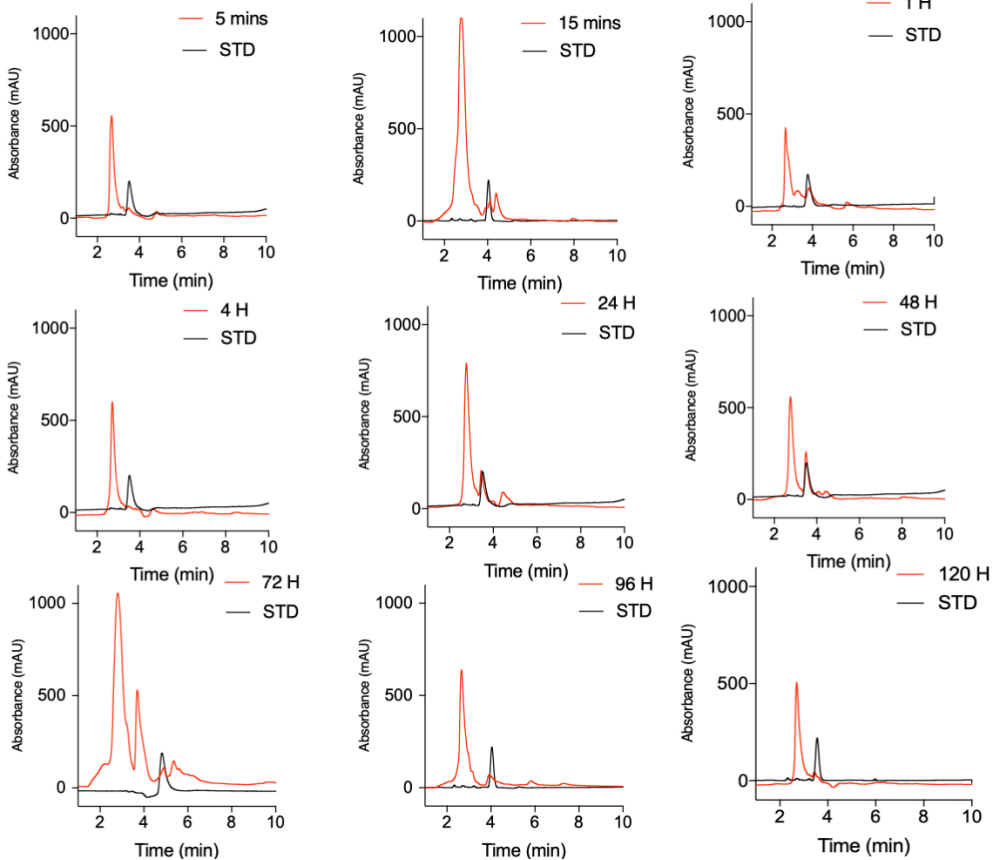
**Figure S9. HPLC chromatograms of accumulated amounts of PHT in brain parenchyma and capillaries following following 4 h of L<sub>10</sub>C<sub>i</sub><sup>+</sup> administration.** PHT peaks in brain parenchyma and capillaries were interrupted with the standard peak of PHT (50 µg/ ml), identified as a well defined peak by this method, and quantified as Area.

# PHT-IP

## Brain Parenchyma

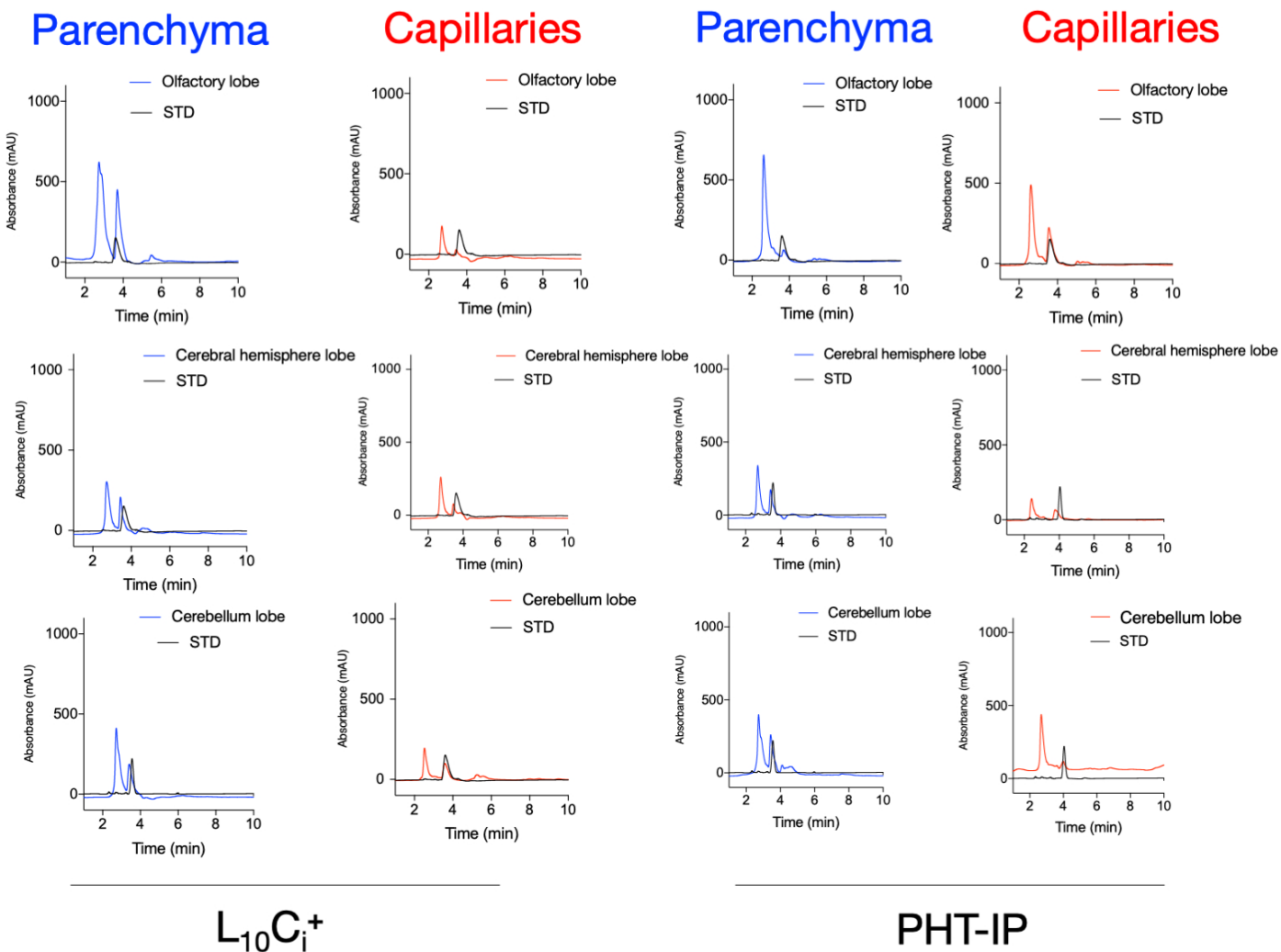


## Capillaries



**Figure S10. HPLC chromatograms of accumulated amounts of PHT in brain parenchyma and capillaries following 4 h of PHT-IP administration.** PHT peaks in brain parenchyma and capillaries were interrupted with the standard peak of PHT (50 µg/ml), identified as a well defined peak by this method, and quantified as Area.

## Brain sections



**Figure S11.** HPLC chromatograms of accumulated amounts of PHT in brain parenchyma and capillaries in brain sections following 4 h of  $L_{10}C_i^+$  and PHT-IP administration. PHT peaks in brain parenchyma and capillaries were interrupted with the standard peak of PHT (50  $\mu\text{g/ml}$ ), identified as a well defined peak by this method, and quantified as Area.