

## Supporting Information

A pre-column derivatization method allowing quantitative metabolite profiling of carboxyl and phenolic hydroxyl group containing pharmaceuticals in human plasma via liquid chromatography-inductively coupled plasma-tandem mass spectrometry (LC-ICP-MS/MS)

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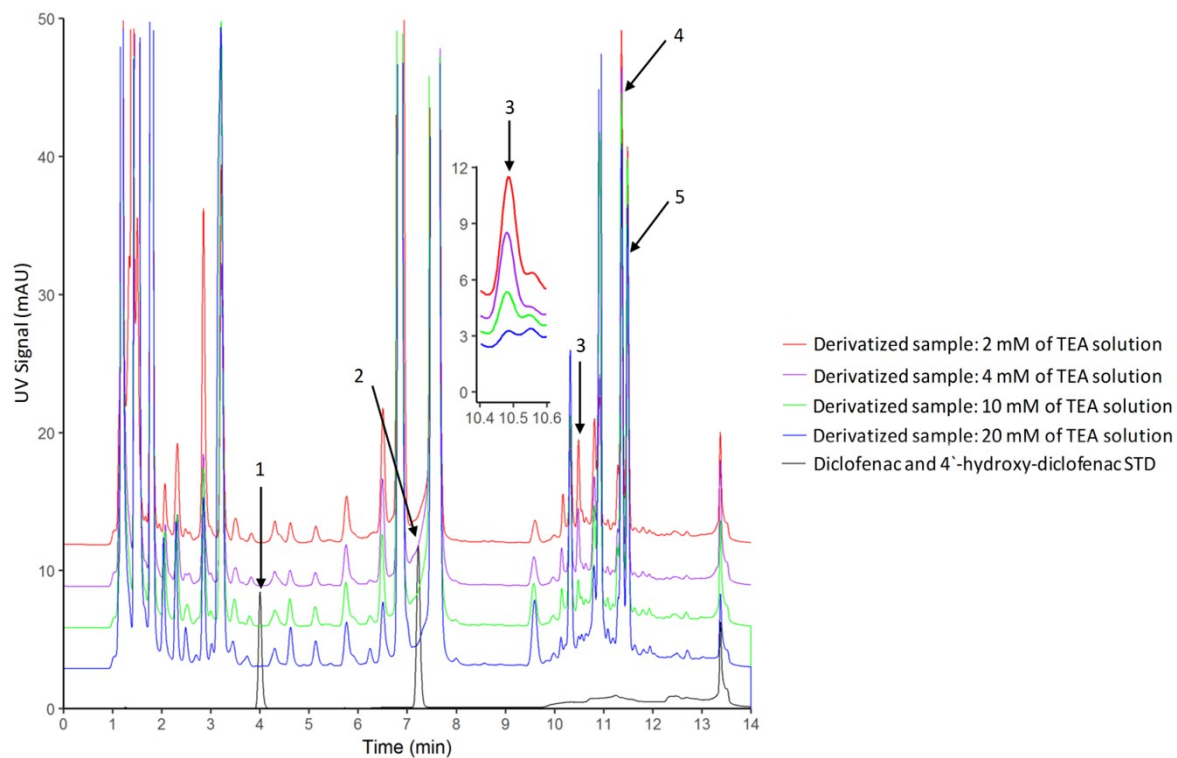
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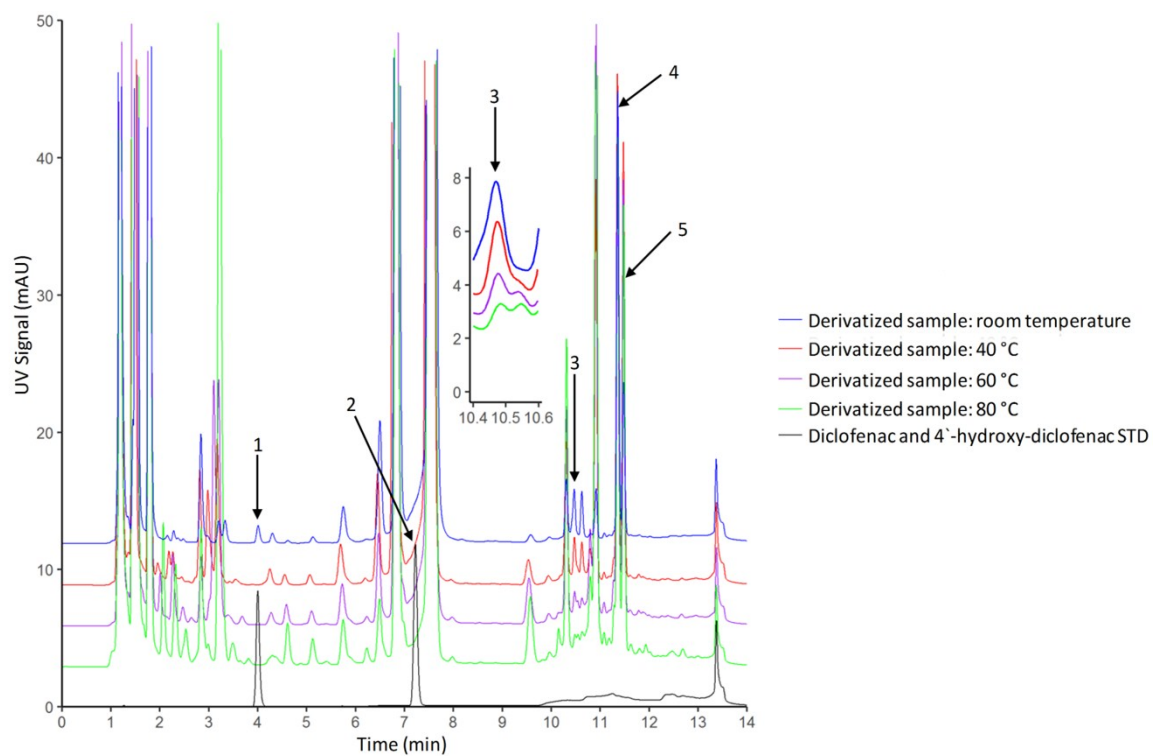
**Figure S-1. Investigation of the effect of the TEA concentration: HPLC-UV chromatograms of diclofenac and 4'-hydroxy-diclofenac standard and derivatized spiked plasma samples with 2, 4, 10 and 20 mM of TEA**

**Peaks: 1: 4'-hydroxy-diclofenac; 2: diclofenac; 3: primary derivative of 4'-hydroxy-diclofenac; 4: derivative of diclofenac; 5: secondary derivative of 4'-hydroxy-diclofenac**

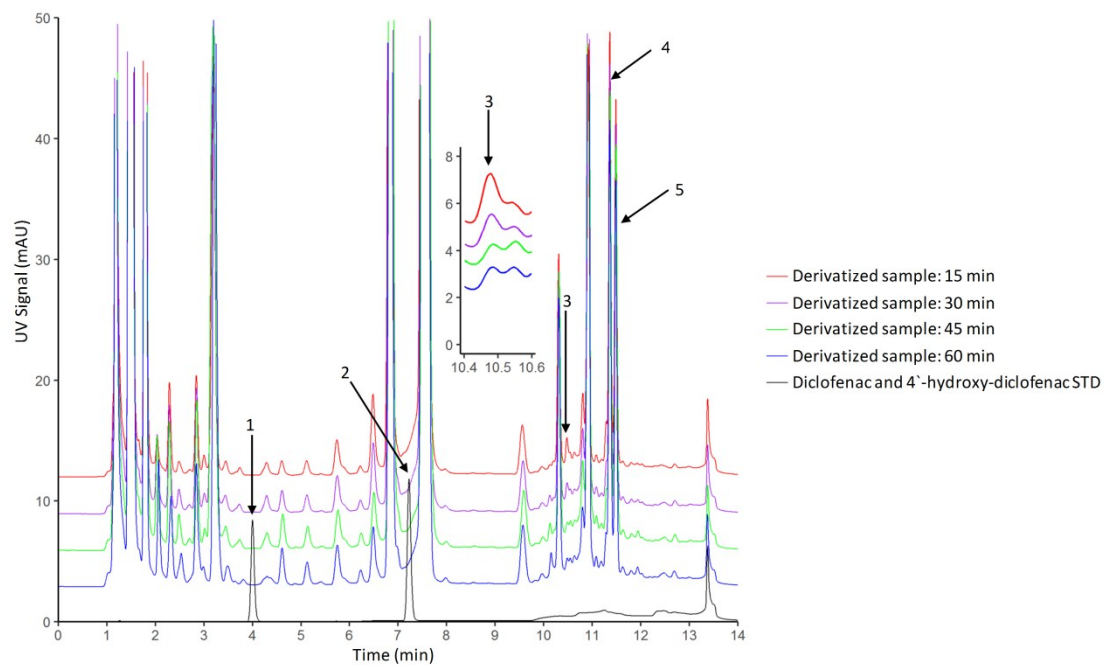


**Figure S-2. Investigation of the effect of the reaction temperature: HPLC-UV chromatograms of diclofenac and 4'-hydroxy-diclofenac standard and derivatized spiked plasma samples at room temperature, 40 °C, 60 °C and 80 °C**

**Peaks: 1: 4'-hydroxy-diclofenac; 2: diclofenac; 3: primary derivative of 4'-hydroxy-diclofenac; 4: derivative of diclofenac; 5: secondary derivative of 4'-hydroxy-diclofenac**



**Figure S-3. Investigation of the effect of the reaction time: HPLC-UV chromatograms of diclofenac and 4'-hydroxy-diclofenac standard and derivatized spiked plasma samples at 80 °C with 15 min, 30 min, 45 min and 60 min reaction time**  
**Peaks: 1: 4'-hydroxy-diclofenac; 2: diclofenac; 3: primary derivative of 4'-hydroxy-diclofenac; 4: derivative of diclofenac; 5: secondary derivative of 4'-hydroxy-diclofenac**



**Figure S-4. Investigation of the effect of the *p*-BPB concentration: HPLC-UV chromatograms of diclofenac and 4'-hydroxy-diclofenac standard and derivatized spiked plasma samples with 4, 8, 20 and 40 mM of *p*-BPB**

**Peaks: 1: 4'-hydroxy-diclofenac; 2: diclofenac; 3: primary derivative of 4'-hydroxy-diclofenac; 4: derivative of diclofenac; 5: secondary derivative of 4'-hydroxy-diclofenac**

