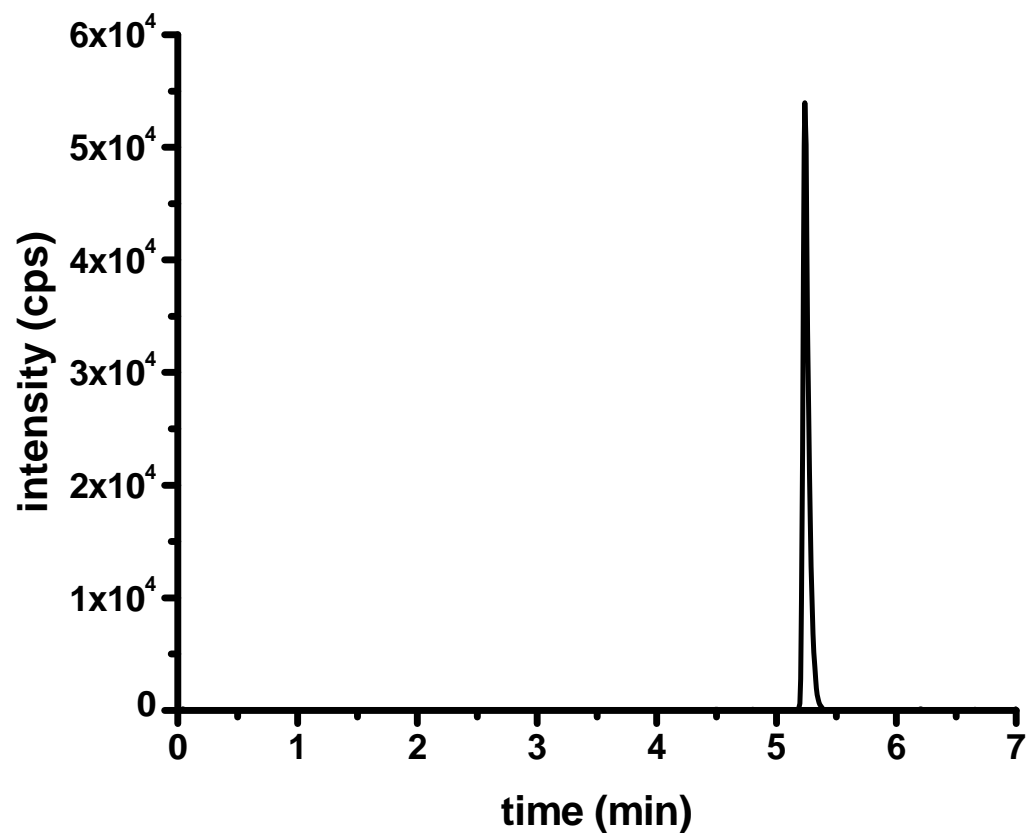
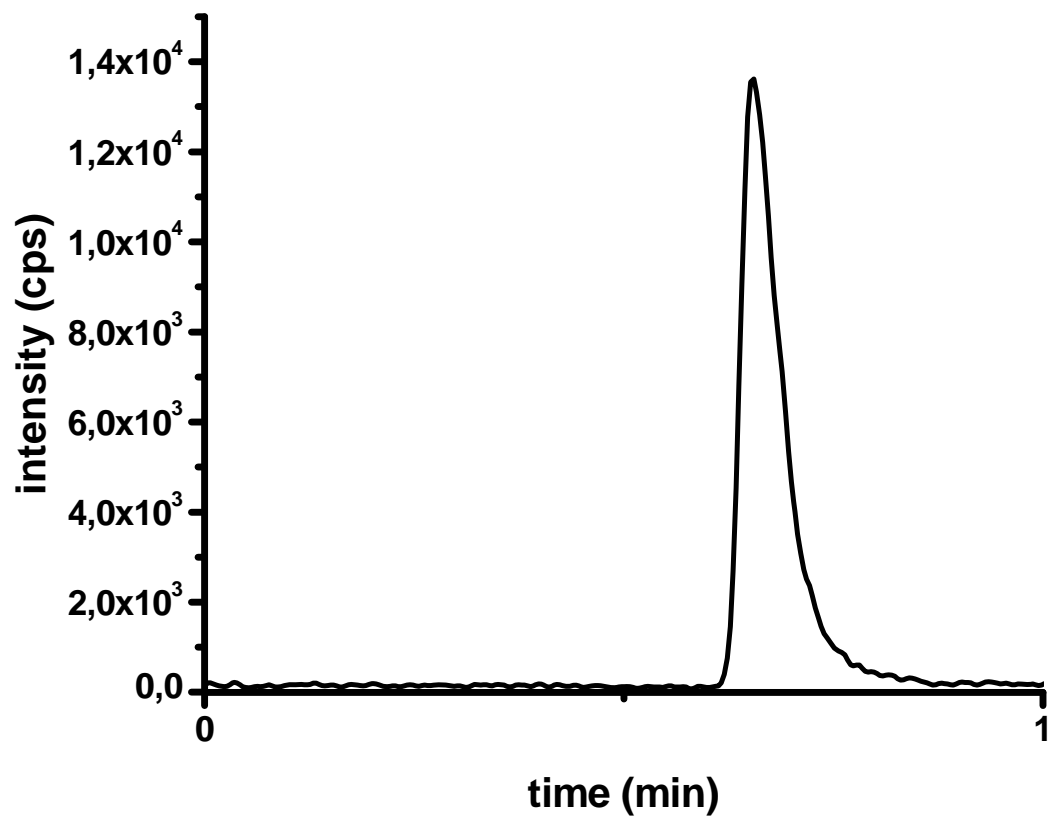


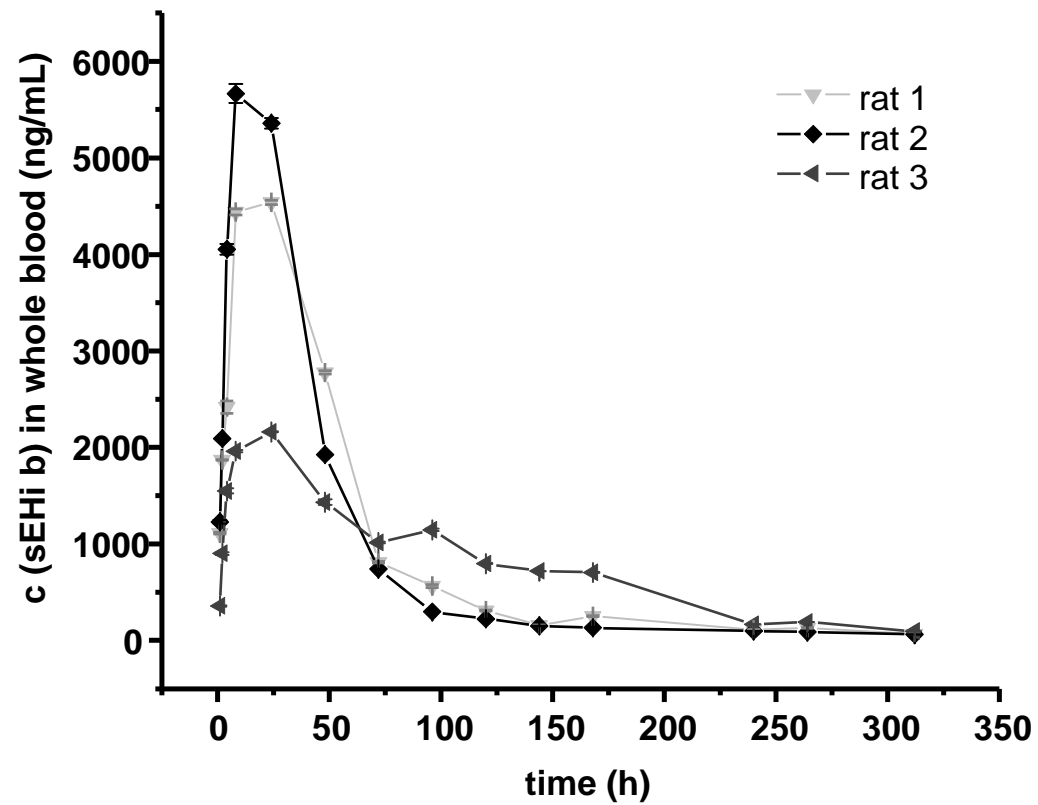
**Supplementary Figure I:** Break through test of the SPE column. 20  $\mu\text{l}$  of 100 nM standard solution ( 25 % ACN, 2.5 % HAc) were injected in the loading flow 1250  $\mu\text{l}/\text{min}$  of 100 % water containing 0.1 % HAc and the eluent of the SPE was monitored by ESI(-)-MS/MS. After 5 minutes the eluent was changed in 0.2 min to 100 % ACN in order to elute the loaded analytes. The SRM signal of DCF is shown.



**Supplementary Figure II:** Elution profile from SPE column. The separation column was removed from the setup (Fig.2) and the eluent of the SPE was directly monitored by ESI(-)-MS/MS. The SRM signal of DCF an injection (20  $\mu$ l) of a 10 nM standard solution is shown.



**Supplementary Figure III:** PK profile of sEHi b in whole blood. The PK profile of sEHi b (Figure 7) as investigated after i.p. dosing (10 mg/kg BW) in three rats. The curves for each individual animal are displayed. Error bars represent SD of three injections.



**Supplementary Table I:** Gradients and flow rates of gradient pump 1 and pump 2 and time points the valve is switched.

<b>time (min)</b>	<b><i>Pump 1</i> flow rate (µL/min)</b>	<b>% B</b>		
0	1250	0		
0.48	1250	0		
0.49	300	0		
0.5	300	0		
0.51	1250	100		
1.5	1250	100		
1.51	1250	0		
2.1	1250	0		
<b>time (min)</b>	<b><i>Pump 2</i> flow rate (µL/min)</b>	<b>% B</b>		
0	300	50		
0.5	300	50		
1.6	300	60		
1.85	300	100		
2.05	300	100		
2.06	300	50		
2.1	300	50		
<b>time (min)</b>	<b><i>Six Port Valve</i> position</b>	<b>SPE column</b>	<b>mode</b>	<b>separation column</b>
0-0.5	A	loading		equilibrating
0.5-1	B	transferring		transferring
1.0-2.1	A	cleaning/ equilibrating		eluting/ cleaning

**Supplementary Table II:** Application of the method on Rofecoxib and several sEHi (Fig. 7 displays the structures of the sEHi a-g). The mean the recovery rate of 3 independent spiked whole blood samples and RSD of the analysis (inter sample variation) is shown. Intra sample variation is represented by the mean of the RSD of three injections of the same sample.

compound	recovery rate (%) /spiked concentration	intra sample RSD (%)	inter sample RSD (%)
ROF	95.11 / 10 nM	12.8	7.58
	97.23 / 30 nM	5.89	8.15
	100.1 / 100 nM	6.63	8.49
sEHi a	99.00 / 10 nM	3.95	3.20
	99.93 / 30 nM	3.11	4.83
	107.9 / 100 nM	1.83	2.72
sEHi c	95.80 / 10 nM	4.16	8.65
	101.2 / 30 nM	11.1	3.79
	105.8 / 100 nM	2.21	3.05
sEHi d	100.5 / 10 nM	6.43	3.69
	100.0 / 30 nM	2.35	5.02
	102.1 / 100 nM	4.09	1.82
sEHi e	96.19 / 10 nM	5.03	6.06
	106.6 / 30 nM	3.54	4.39
	99.60 / 100 nM	6.68	6.88