

Test parameter	0.9 % DMSO	Negative Control
Cell Count (x 1.000) n=3	730 (605 - 1020)	555 (435 – 610)
Vitality [%] n=3	80 (80 – 89)	84 (79 – 89)
LDH [U/l] n=5	71 (44 – 81)	25 (21 – 30)
XTT (OD) n=15	1.8 (1.8 – 2.8)	1.3 (1.2 – 1.5)
CYP1A2- activity: resorufin [pmol/l], n=8	3.7 (2.9 – 4.8)	5.5 (2.6 – 5.7)

**Supplementary Table S1:** Test results for HepG2/C3A cells after exposure to 0.9 % DMSO (dimethyl sulfoxide) compared with pure cell culture medium after 3 days incubation. Values represent as median and min/max. LDH: lactate dehydrogenase

	pH		
	C <sub>max</sub>	C <sub>5x</sub>	C <sub>10x</sub>
<b>Midazolam</b> (300 ng/ml   1500 ng/ml   3000 ng/ml)	7,71 7,71 / 7,75	7,71 7,69 / 7,73	7,82 7,78 / 7,82
<b>Propofol</b> (2 µg/ml   10 µg/ml   20 µg/ml)	7,69 7,69 / 7,71	7,73 7,73 / 7,75	7,69 7,67 / 7,69
<b>S-Ketamine</b> (1 µg/ml   5 µg/ml   10 µg/ml)	7,70 7,70 / 7,71	7,79 7,78 / 7,80	7,81 7,80 / 7,82
<b>Thiopental</b> (1 mg/ml   5 mg/ml   10 mg/ml)	7,75 7,75 / 7,77	7,79 7,79 / 7,83	8,01 * 7,92 / 8,01
<b>Fentanyl</b> (10 ng/ml   50 ng/ml   100 ng/ml)	7,74 7,72 / 7,76	7,68 7,66 / 7,70	7,68 7,68 / 7,68
<b>Remifentanyl</b> (15 ng/ml   75 ng/ml   150 ng/ml)	7,66 7,65 / 7,66	7,62 7,60 / 7,65	7,62 7,62 /
<b>Sufentanyl</b> (1 ng/ml   5 ng/ml   10 ng/ml)	7,66 7,65 / 7,68	7,75 7,73 / 7,78	7,71 7,70 / 7,72
<b>Negative control</b>	7,75 7,71 / 7,85		

**Supplementary Table S2:** pH for HepG2/C3A cells in medium after exposure to sedatives and opioids in concentrations C<sub>max</sub>, C<sub>5x</sub> and C<sub>10x</sub>. Values represent as median and 25th/75th percentile. Significance between negative control and exposure groups is indicated by \* p < 0.05.

	pH		
	C <sub>max</sub>	C <sub>5x</sub>	C <sub>10x</sub>
<b>Midazolam</b> (300 ng/ml   1500 ng/ml   3000 ng/ml)	7,63 7,61 / 7,65	7,88 * 7,79 / 7,89	7,74 7,71 / 7,74
<b>Propofol</b> (2 µg/ml   10 µg/ml   20 µg/ml)	7,64 7,63 / 7,65	7,68 7,67 / 7,69	7,68 7,64 / 7,68
<b>S-Ketamine</b> (1 µg/ml   5 µg/ml   10 µg/ml)	7,64 7,64 / 7,65	7,74 * 7,72 / 7,74	7,73 * 7,71 / 7,74
<b>Thiopental</b> (1 mg/ml   5 mg/ml   10 mg/ml)	7,71 * 7,70 / 7,71	7,95 * 7,84 / 7,97	7,76 * 7,74 / 7,77
<b>Fentanyl</b> (10 ng/ml   50 ng/ml   100 ng/ml)	7,67 7,66 / 7,67	7,65 7,64 / 7,65	7,64 7,63 / 7,68
<b>Remifentanil</b> (15 ng/ml   75 ng/ml   150 ng/ml)	7,58 7,58 / 7,59	7,64 7,61 / 7,76	7,58 7,56 / 7,58
<b>Sufentanil</b> (1 ng/ml   5 ng/ml   10 ng/ml)	7,63 7,60 / 7,64	7,64 7,63 / 7,64	7,63 7,60 / 7,67
<b>Negativkontrolle</b>	7,66 7,60 / 7,69		

**Supplementary Table S3:** pH for HepG2/C3A cells in plasma after exposure to sedatives and opioids in concentrations C<sub>max</sub>, C<sub>5x</sub> and C<sub>10x</sub>. Values represent as median and 25th/75th percentile.

Significance between negative control and exposure groups is indicated by \* p < 0.05