**Table S1.** IC50 values for displacement of bound [3H]-DAMGO (4 nM) by fentanyl and NFEPP in different tissues.

|  |  |  |
| --- | --- | --- |
| **pH** | **IC50 fentanyl (nM)** | **IC50 NFEPP (nM)** |
| Membranes from HEK 293 cells\* | | |
| **5.5** | 2.4 ± 0.7 (7) | 19.1 ± 6.8 (7) |
| **6.5** | 6.9 ± 1.1 (6) | 18.3 ± 3.3 (6) |
| **7.4** | 4.8 ± 0.7 (7) | 81.9 ± 22.1 (8) |
| Membranes from rat DRG | | |
| **5.5** | 5.8 ± 1.9 (8) | 8.9 ± 3.2 (8) |
| **6.5** | 5.4 ± 1.1 (8) | 58.7 ± 23.9 (8) |
| **7.4** | 4.4 ± 3.0 (8) | 88.8 ± 38.7 (8) |
| Membranes from rat brain | | |
| **5.5** | 3.3 ± 0.5 (6) | 9.6 ± 0.9 (6) |
| **6.5** | 6.0 ± 0.9 (6) | 19.6 ± 2.8 (6) # |
| **7.4** | 7.7 ± 0.9 (6) | 60.9 ± 5.9 (6) # |

\*These IC50 values were the basis for the Ki value calculation published in [32].

Data are expressed as means ± SEM. The number of independent experiments is stated in brackets. # *P* < 0.05 vs Fen at the corresponding pH, Friedman one-way ANOVA and Dunn’s tests.