Supporting information

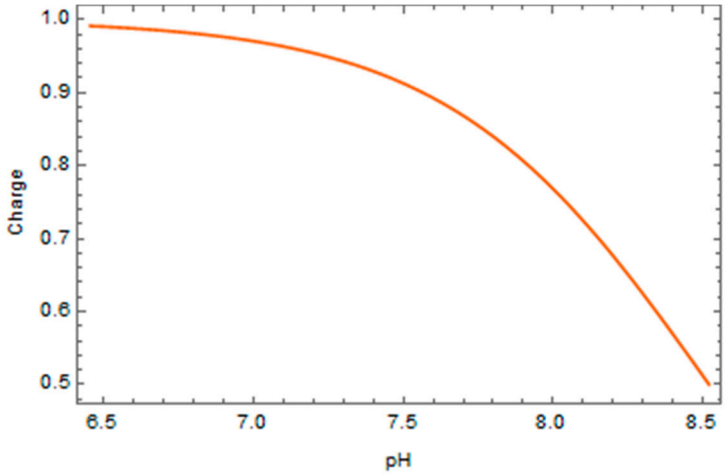
Supplementary Material 2: Figures S3,S4

Figure S3. Mathematica script to determine net charge distribution for open-ring (OR) and closed-ring (CR) forms of midazolam and benzodiazepines according to Henderson-Hasselbalch equation.

```
y = ((-1. / ((10 ^ (8.52 - x)) + 1)) + 1)
```

$$1 - \frac{1.}{1 + 10^{8.52-x}}$$

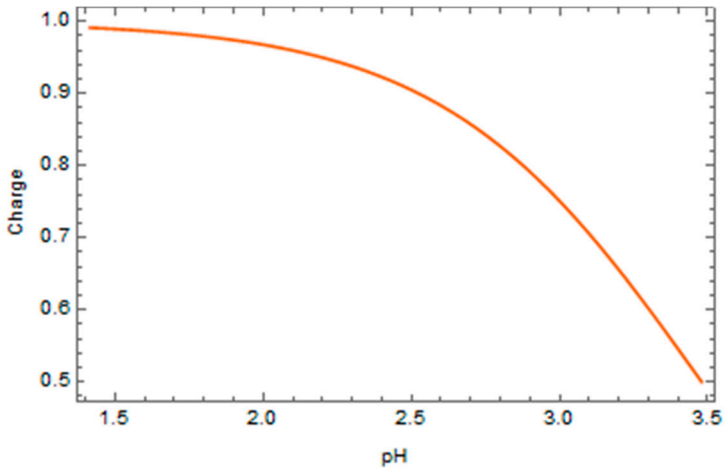
Show[%3, AxesLabel → {None, Nine}, FrameLabel → {{HoldForm[Charge], None}, {HoldForm[pH], None}}, PlotLabel → None, LabelStyle → {GrayLevel[0]}]




```
y = ((-1. / ((10 ^ (3.48 - x)) + 1)) + 1)
```

$$1 - \frac{1.}{1 + 10^{3.48-x}}$$

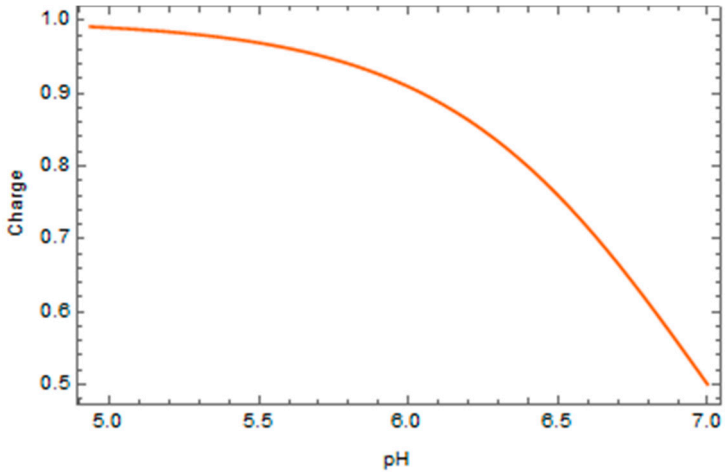
Show[%13, AxesLabel → {None, Nine}, FrameLabel → {{HoldForm[Charge], None}, {HoldForm[pH], None}}, PlotLabel → None, LabelStyle → {GrayLevel[0]}]




```
y = ((-1. / ((10 ^ (7.0 - x)) + 1)) + 1)
```

$$1 - \frac{1.}{1 + 10^{7.-x}}$$

Show[%18, AxesLabel → {None, Nine}, FrameLabel → {{HoldForm[Charge], None}, {HoldForm[pH], None}}, PlotLabel → None, LabelStyle → {GrayLevel[0]}]




```
y = ((-1. / ((10 ^ (2.4 - x)) + 1)) + 1)
```

$$1 - \frac{1.}{1 + 10^{2.4-x}}$$

Show[%25, AxesLabel → {None, Nine}, FrameLabel → {{HoldForm[Charge], None}, {HoldForm[pH], None}}, PlotLabel → None, LabelStyle → {GrayLevel[0]}]

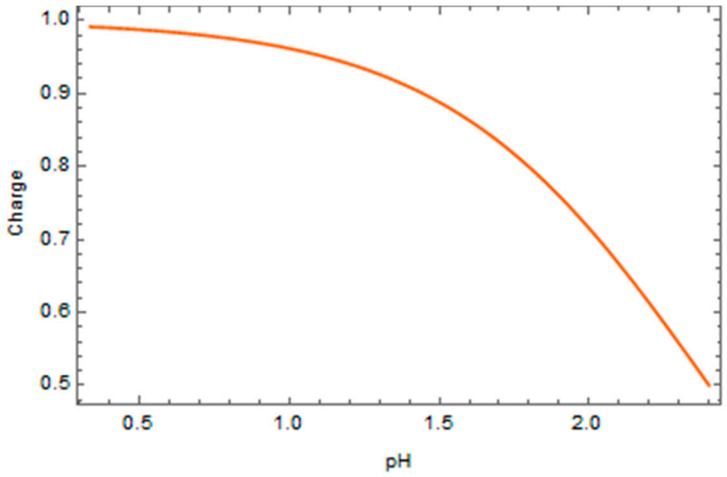


Figure S4. Mathematica script to determine net charge for open-ring (OR) and closed-ring (CR) forms of midazolam and benzodiazepines according to Henderson-Hasselbalch equation at physiological pH.

```
y = ((-1. / ((10^(8.52 - 7.36)) + 1)) + 1)
0.935293
y = ((-1. / ((10^(3.48 - 7.36)) + 1)) + 1)
0.000131808
 y = ((-1. / ((10^(7.0 - 7.36)) + 1)) + 1)
0.303871
 y = ((-1. / ((10^(2.4 - 7.36)) + 1)) + 1)
0.0000109647
```