Discovery of a selective 6-hydroxy-1,4-diazepan-2-one containing butyrylcholinesterase inhibitor by virtual screening and MM-GBSA rescoring

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Table S1. The inhibitory activities against AChE and BChE of the hits from virtual screening

| Compound | BChE | AChE |
|----------|------|------|
|          | IR² (%) | IC₅₀ (μM) | IR² (%) | IC₅₀ (μM) |
| 5        | 66.0 ± 1.4 | 1.4 ± 0.006 | 21.6 ± 4.8 | nd.² |
| 6        | 27.8 ± 3.8 | nd. | 16.8 ± 3.9 | nd. |
| 7        | 37.8 ±3.8 | nd. | 24.5 ± 3.8 | nd. |
| 8        | 23.9 ± 8.0 | nd. | 15.1 ± 3.0 | nd. |
| 9        | 35.4 ± 1.3 | nd. | 21.0 ± 6.9 | nd. |
| 10       | 2.9 ± 5.7 | nd. | 2.8 ± 7.1 | nd. |
| 11       | 35.7 ± 6.9 | nd. | 7.6 ± 5.6 | nd. |
All data are shown as mean ± SD of three experiments. SD = standard deviation.  

\(^{a}\) Inhibition ratio (IR) against BChE at 10 μM.  

\(^{b}\) IC\textsubscript{50} values represent the concentration of inhibitor required to decrease enzyme activity by 50%.  

\(^{c}\) Inhibition ratio (IR) against AChE at 10 μM.  

\(^{d}\) nd = not determined.

**Figure S1.** The dose-dependent inhibition of compound 5 against BChE.

**Table S2.** The apparent \(V_{\text{max}}\) and \(K_{\text{m}}\) values for compound 5 in kinetic studies.

| Concentration (µM) | \(V_{\text{max}}\) (µM min\(^{-1}\)) | \(K_{\text{m}}\) (µM) |
|-------------------|---------------------------------|-----------------|
| 0                 | 0.38 ± 0.02                     | 217.6 ± 24.8    |
| 0.25              | 0.35 ± 0.01                     | 287.6 ± 24.9    |
| 0.5               | 0.34 ± 0.02                     | 422.7 ± 42.1    |
| 1.0               | 0.28 ± 0.03                     | 443.2 ± 90.2    |
| 1.5               | 0.24 ± 0.02                     | 490.7 ± 89.6    |

Data are shown as the mean ± SD of three experiments.
**Figure S2.** The primary AChE and BChE IR(%) screening of test compounds under 50 μM (A and B).