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Corrigendum

Corrigendum to "Epibatidine structure–activity relationships" [Bioorg. Med. Chem. Lett. 14 (2004) 1889]

F. Ivy Carroll*

Organic and Medicinal Chemistry, Research Triangle Institute, Research Triangle Park, NC 27709, USA

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A correction to Ref. 25 in this review article was published in June 2004 *J. Chem. Soc., Perkin Trans.* Issue. The correction showed that the data reviewed in Table 9 (page 1893) for structures **12** and **15** should be transposed and the discussion on page 1894 updated. The revised table and discussion follow.

The 5- and 6-(2′-chloro-5′-pyridinyl)heptanes **12–15** can be viewed as epibatidine analogs where the 7-position nitrogen of epibatidine (**1**) has been moved to the 5- or 6-position of the 7-azabicyclo[2.2.1] ring. Cox et al. have synthesized all four analogs and evaluated their α4β2 and α7 nAChR potency for inhibition of [^{3}H]nicotine binding to rat cortical membranes and [^{125}I]BTX binding in rat hippocampal membranes, respectively.[25] These authors found that **14** and **15** with K_i values of 0.045 nM and 0.056 nM for α4β2 nAChRs were almost as potent as epibatidine (**1**), which showed a K_i value of 0.02 nM in their studies (Table 9). Compounds **12** and **14** showed K_i values of 1600 and 3.9 nM for α7 nAChR (Table 9). Compounds **12** and **13** possessed low affinity for both α4β2 as well as α7 nAChRs. Dart and coworkers also synthesized analogs **12–14** and evaluated their α4β2 nAChR potency using whole rat brain tissue and [^{3}H]cytisine as the radioligand. These authors also found **14** to be the more potent compound. Under these conditions, compound **14** with a K_i value of 0.032 nM was equipotent to epibatidine with a K_i value of 0.04 nM. Similar to Cox and Malpass et al.,[25] Dart et al. found analog **12** to have relatively low affinity (K_i 6.6 nM compared to >38 nM) for α4β2 nAChRs.

Table 9. Radioligand binding and antinociceptive potency of 7-azabicyclo[2.2.1]heptane ring modified analogs of epibatidine

Compd	[^{3}H]Ligand (K_i, nM)	[^{125}I] α-BTX[b]	Tail-Flick EC_{50} (mg/g)
Epibatidine (**1**)	0.090,[a] 0.02,[b] 0.04,[c] 0.26[d]		0.01[a]
10	0.47[a]		0.04[a]
11	0.34[a]		1.4[a]
12	>38,[b] 6.6[c]	1600	
13	>38,[b] 30[c]	3300	
14	0.045,[b] 0.032[c]	3.9	
15	0.056[b]	6.3	
(+)-**16**	0.13[d]		
(−)-**16**	0.35[d]		
17	1.25[d]		
18	1.6[e]		
19	3.9[f]		
20	5.0[f]		

[a] Taken from Ref. 32; [^{3}H]cytisine.
[b] Taken from Ref. 25; [^{3}H]nicotine.
[c] Taken from Ref. 11; [^{3}H]cytisine.
[d] Taken from Ref. 33; [^{3}H]nicotine.
[e] Taken from Ref. 34; [^{3}H]epibatidine.
[f] Taken from Ref. 35; [^{3}H]cytisine.

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* Tel.: +1 919 541 6679; fax: +1 919 541 8868; e-mail: fic@rti.org

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