

## SUPPLEMENTARY MATERIAL

### Pharmacophore Mapping Combined with dbCICA Reveal New Structural Features for the Development of Novel Ligands Targeting $\alpha 4\beta 2$ and $\alpha 7$ Nicotinic Acetylcholine Receptors

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Euclidian distance is based on a calculus involving the number of hydrogen acceptor and donor atoms and heavy atoms of each molecule, the resulting value of each molecule is compared to that of all the others.

**Mathematical formula S1.** - Mathematical formula to calculate Euclidean distance between the studied ligands.

$$D(i, j) = \sqrt{(HBDi - HBDj)^2 + (HBAi - HBDj)^2 + (NPi - NPj)^2}$$

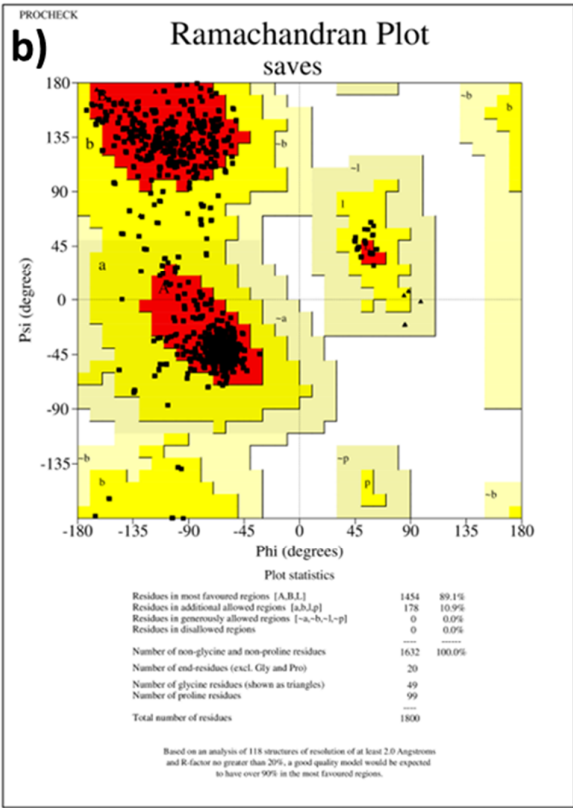
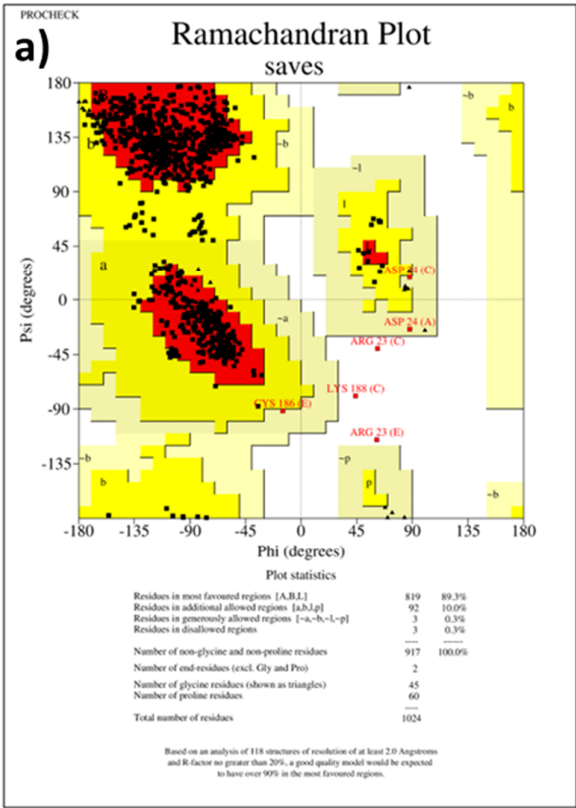
HBD = Hydrogen bond donor atoms

HBA = Hydrogen bond acceptor atoms

NP = Non-polar heavy atoms

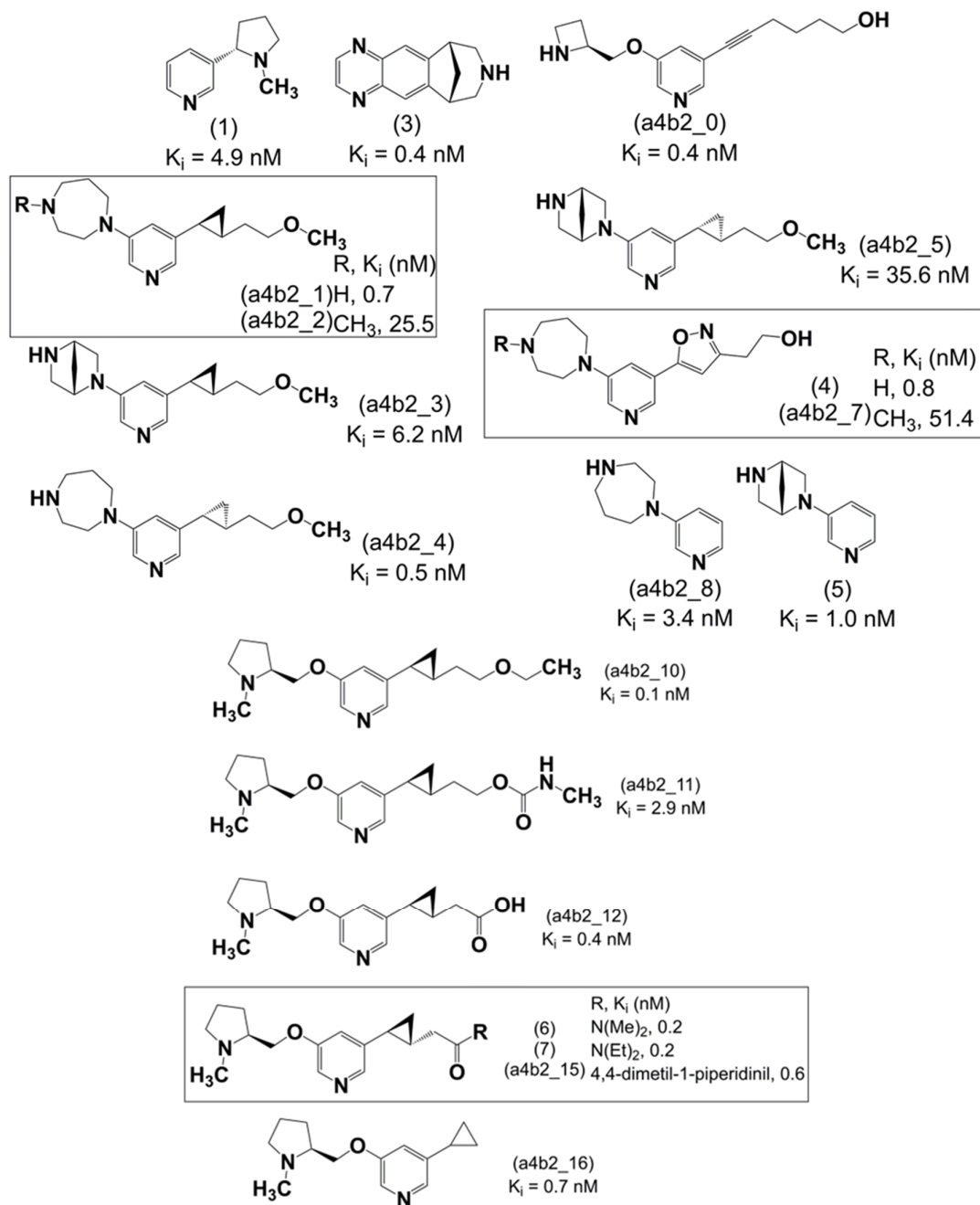
According to Ramachandran plot both nAChRs structures ( $\alpha 4\beta 2$  - PDB 5KXI and  $\alpha 7$  - PDB 5AFH) have at least 89% of their residues in favored regions and 10% in allowed regions. None of the amino acid residues used in the study are in generously allowed or disallowed regions.

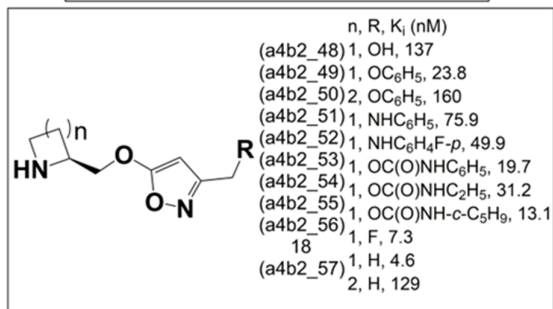
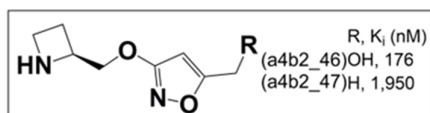
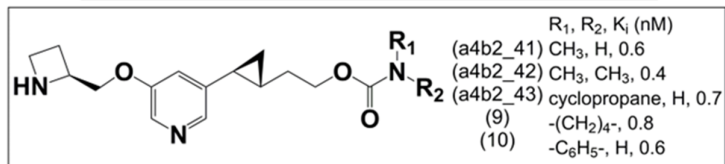
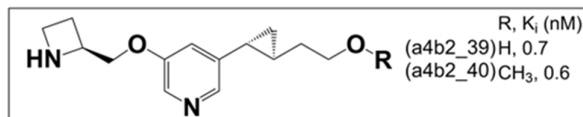
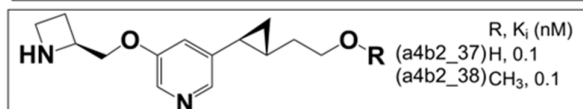
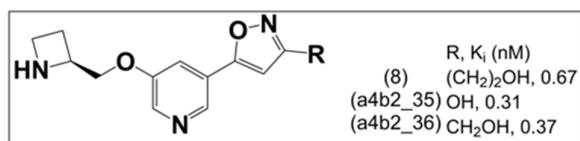
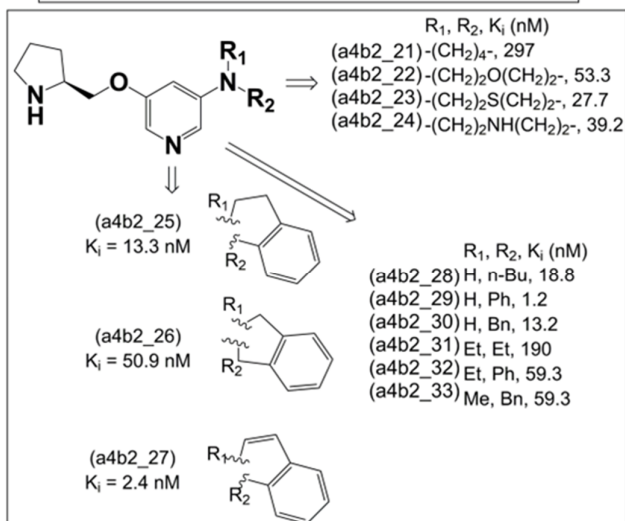
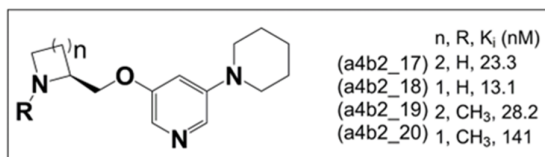
**Figure S1.** – Ramachandran plot of  $(\alpha 4)_2(\beta 2)_3$  (PDB 5KXI) (a) and  $\alpha 7$  nAChRs (PDB 5AFH) (b) structures.

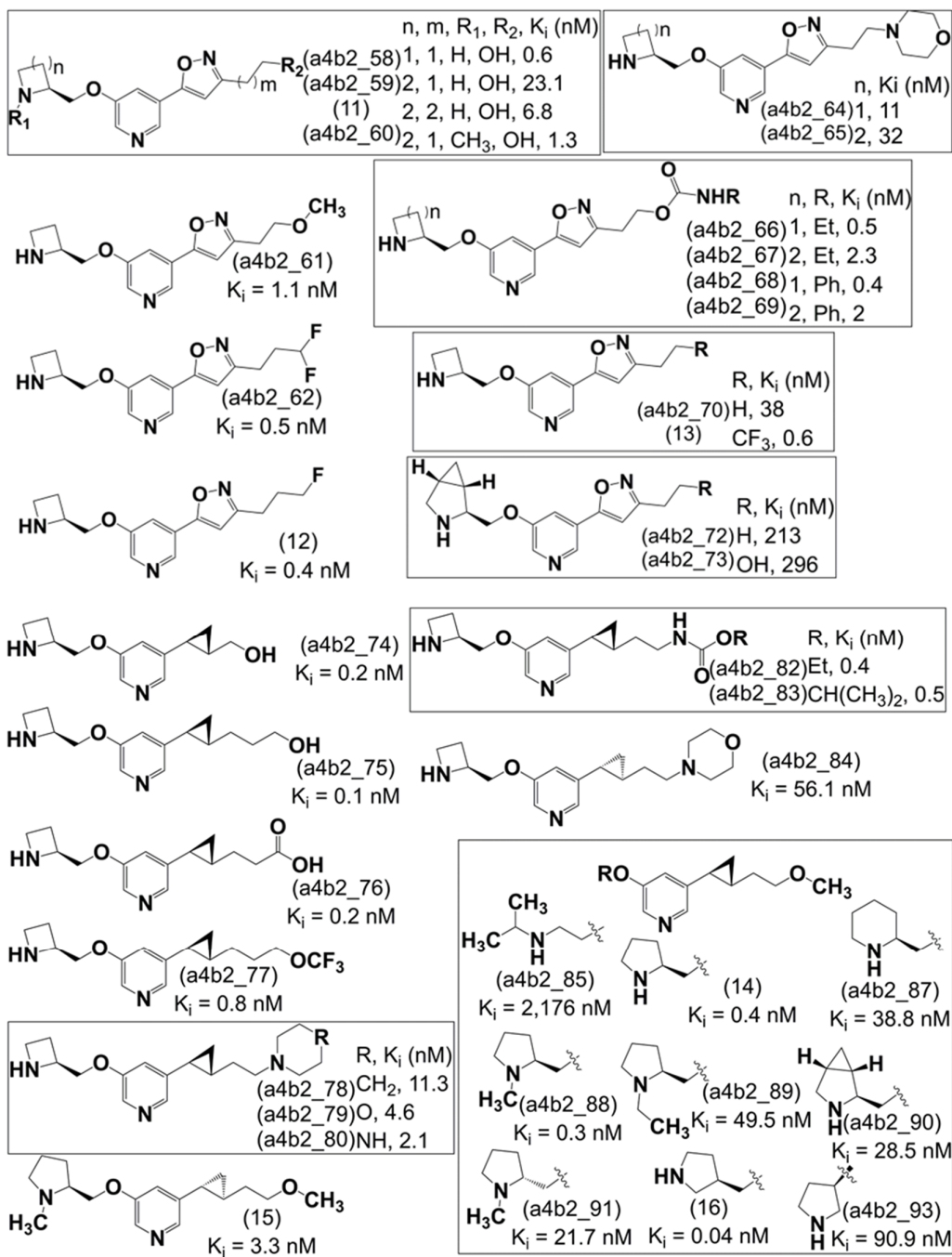


All 98 ligands structures and their  $K_i$  used for dbCICA analysis of  $(\alpha 4)_2(\beta 2)_3$  are shown in Supplementary figure 2.

**Figure S2.** – Chemical structures of the 98 ligands used to construct the dbCICA models for the  $(\alpha 4)_2(\beta 2)_3$  subtype nAChRs.

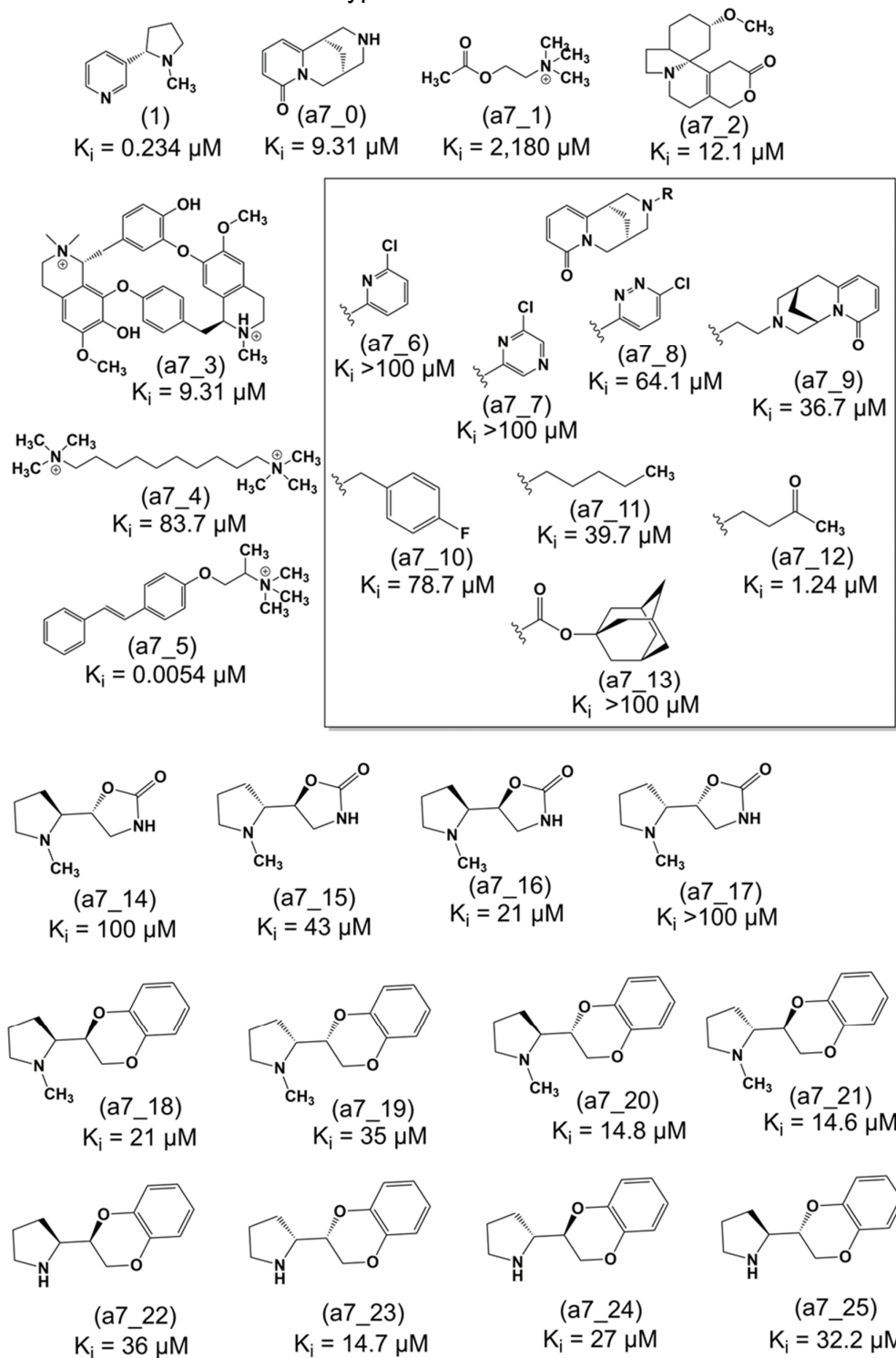


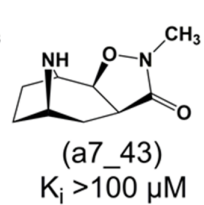
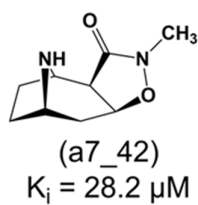
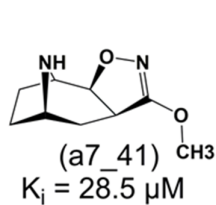
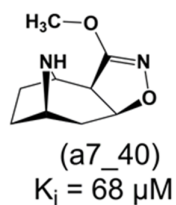
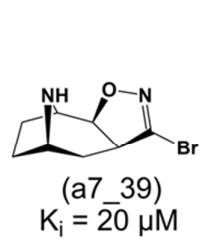
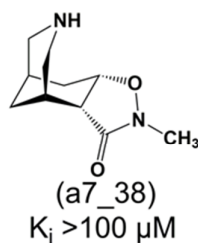
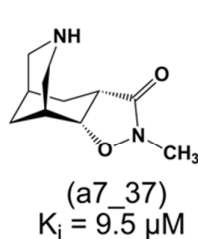
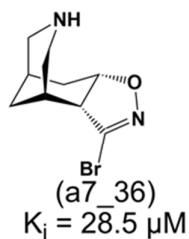
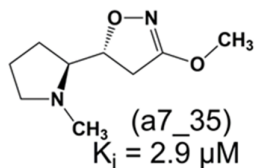
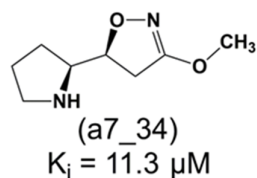
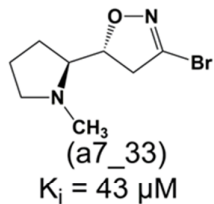
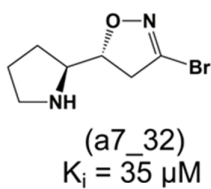
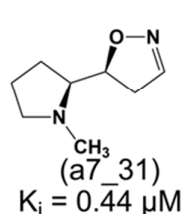
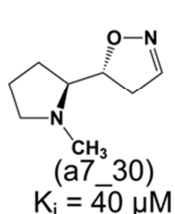
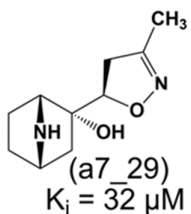
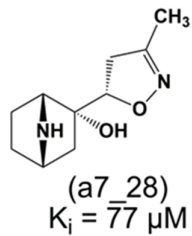
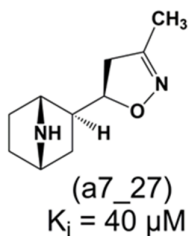
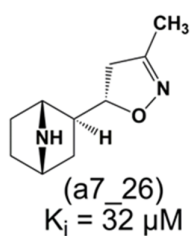




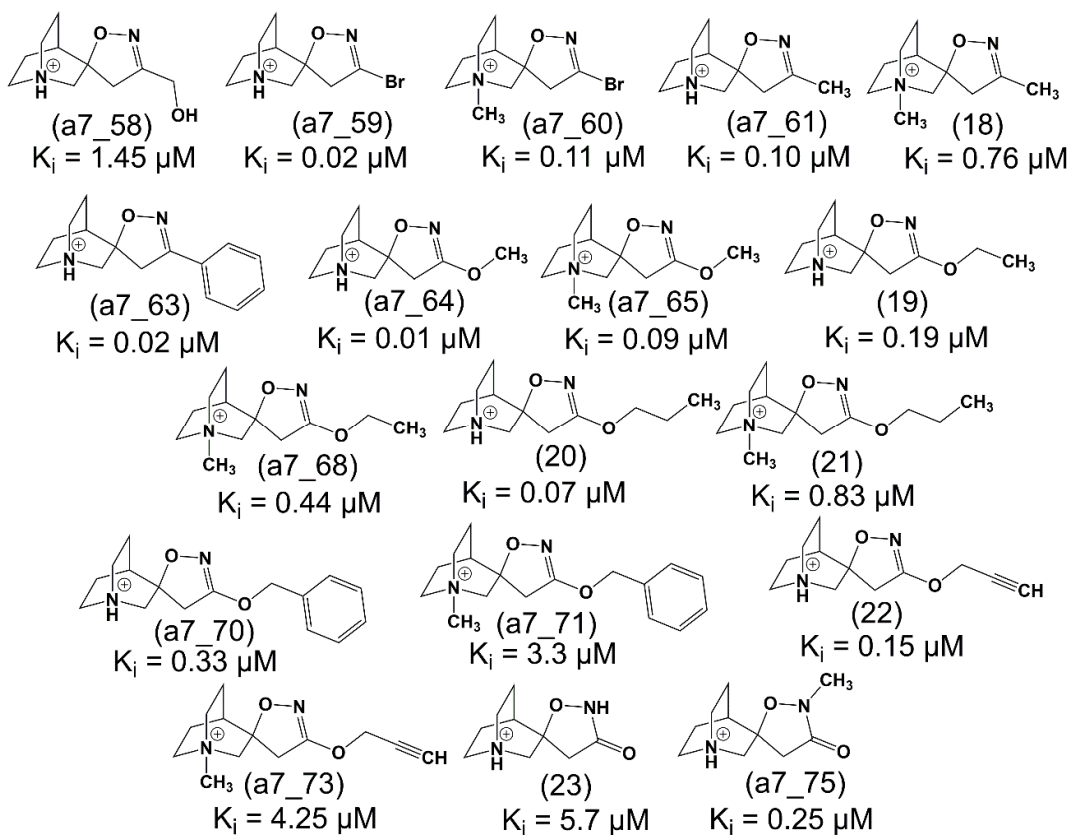
All 93 ligands structures and their  $K_i$  used for dbCICA analysis of  $\alpha 7$  are shown in Supplementary figure 3.

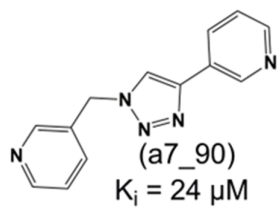
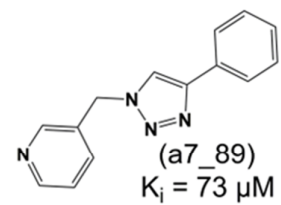
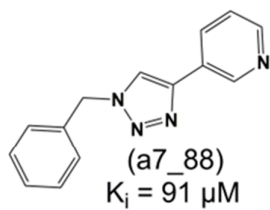
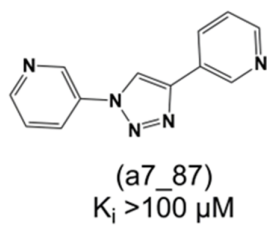
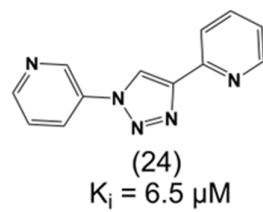
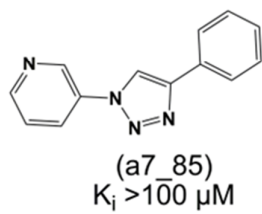
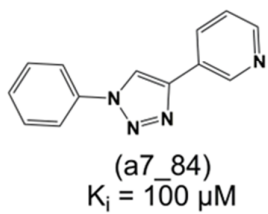
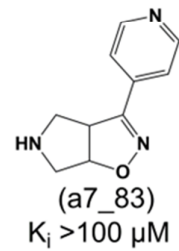
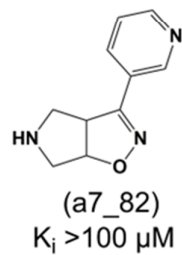
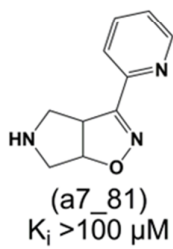
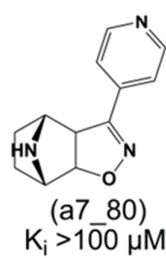
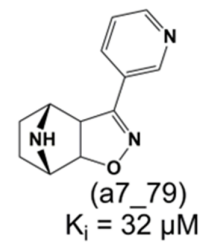
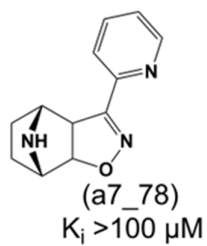
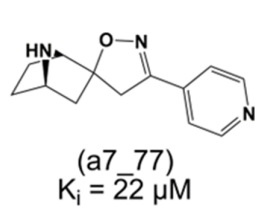
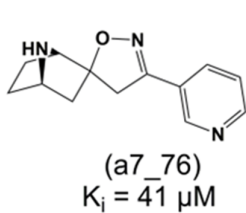
**Figure S3.** - Chemical structures of the 93 ligands used to construct the dbCICA models for the  $\alpha 7$  subtype nAChRs.











ROC curves for studied nAChRs are shown in supplementary figure 4. The ROC curve values are AUC of 0.78 and 0.86, AAC of 0.83 and 0.83, and YA of 0.25 and 0.13 for nAChRs\_α7\_1 and nAChRs\_α4β2\_1 dbCICA, respectively.

**Figure S4.** – ROC curves of (α4)<sub>2</sub>(β2)<sub>3</sub> (a) and α7 (b) nAChRs pharmacophore maps validation.

