

Figure 1. The native position of the nicotine molecule at the interface between two identical subunits of AChBP (1UW6) (**A**) and the best theoretical binding positions of (S)-nicotine (**B**), (S)-cotinine (**C**) and (S)-6-Hydroxynicotine (**D**). The ligands are displayed as ball and sticks, the NIC binding site-residues are shown as sticks – the residues with side chain colored in magenta belong to the principal side (+) while the residues with side chain in dark blue belongs to the complementary side (-), the hydrogen bonds are represented as green dashed lines and the rest of the receptor as surface.

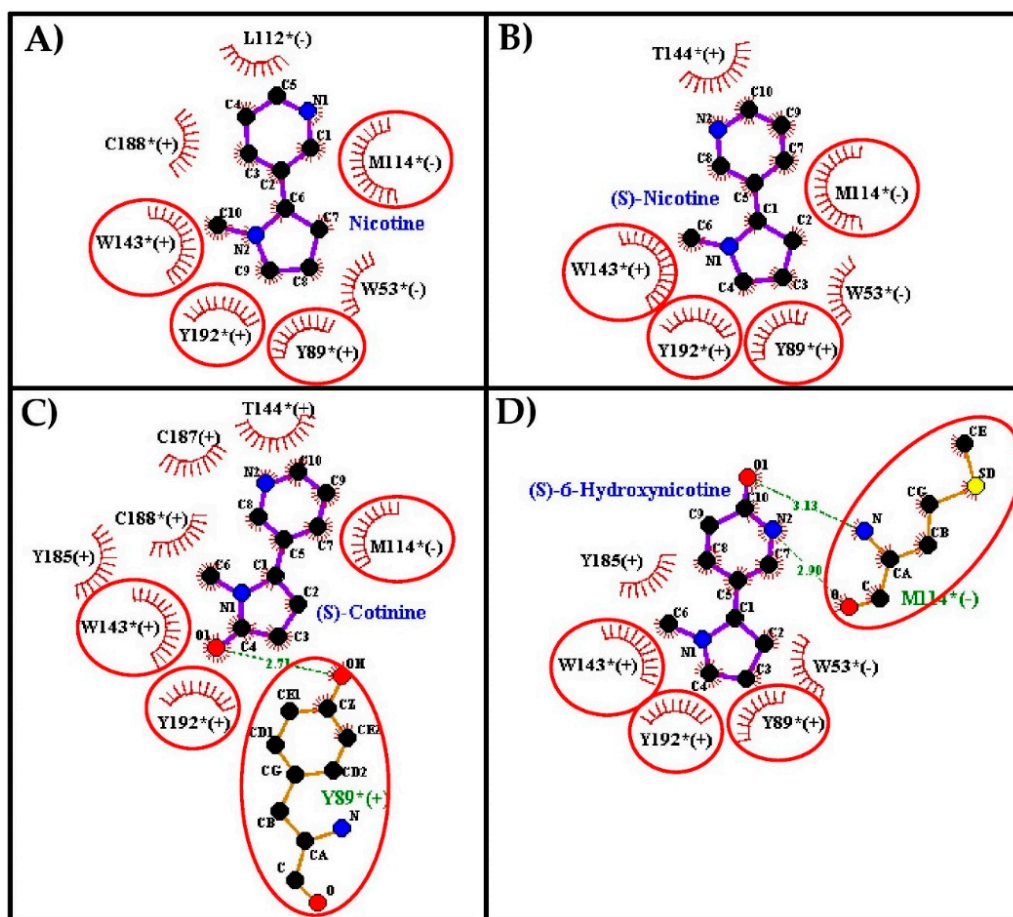


Figure 2. Schematic diagram of the interactions between the residues of the nicotine-binding interface of AChBP and nicotine (A), (S)-nicotine (B), (S)-cotinine (C) and (S)-6-hydroxynicotine (D). The residues that are marked with * are common with those from literature and the encircled residues are common for all the selected ligands. The hydrophobic contact(s) between the residues and the corresponding atoms of the ligands as well as the hydrogen bonds are illustrated according to the Ligplot+ software.

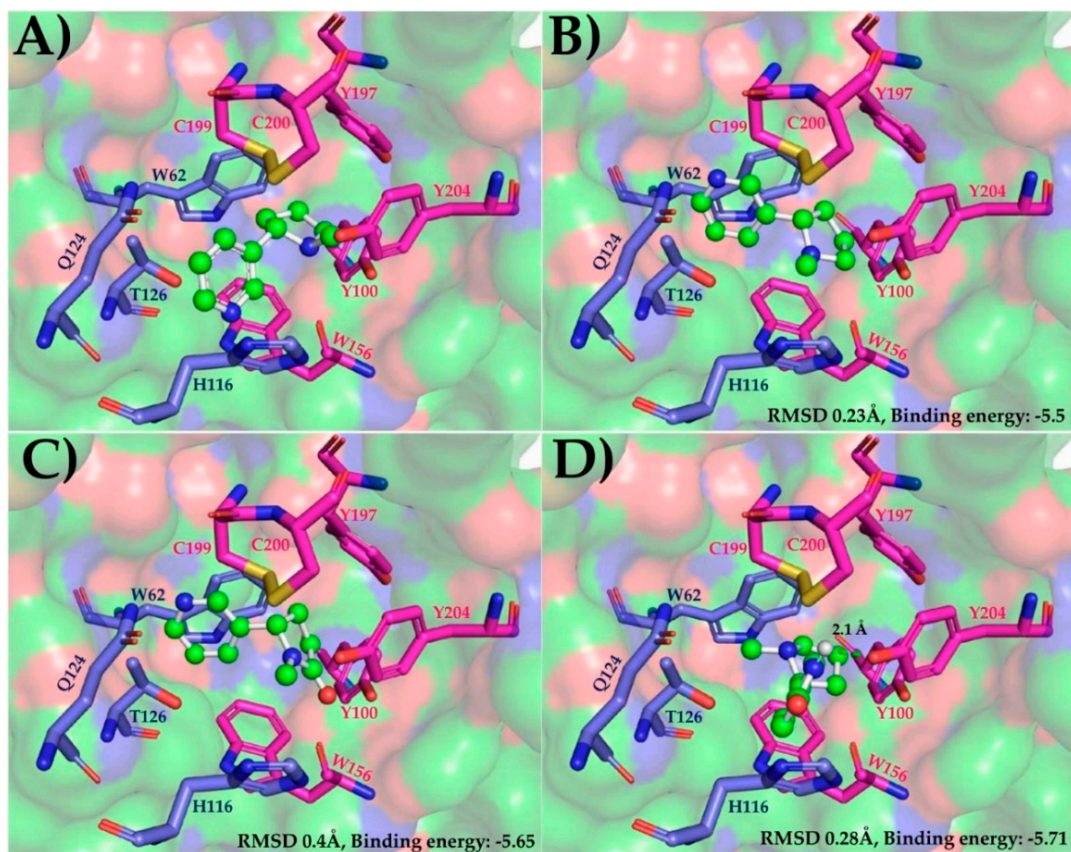


Figure 3. The native position of the nicotine molecule in the $\alpha 4$ - $\alpha 4$ site of $\alpha 4\beta 2$ nAChRs (3 α :2 β , 6CNK) (A) and the best theoretical binding positions of (S)-nicotine (B), (S)-cotinine (C) and (S)-6-Hydroxynicotine (D). The ligands are displayed as ball and sticks, the NIC binding site-residues are shown as sticks, the residues with side chain colored in magenta belong to the principal side $\alpha 4+$ while the residues with side chain in dark blue belongs to the complementary side $\alpha 4-$, the hydrogen bonds are represented as green dashed lines and the rest of the receptor as surface.

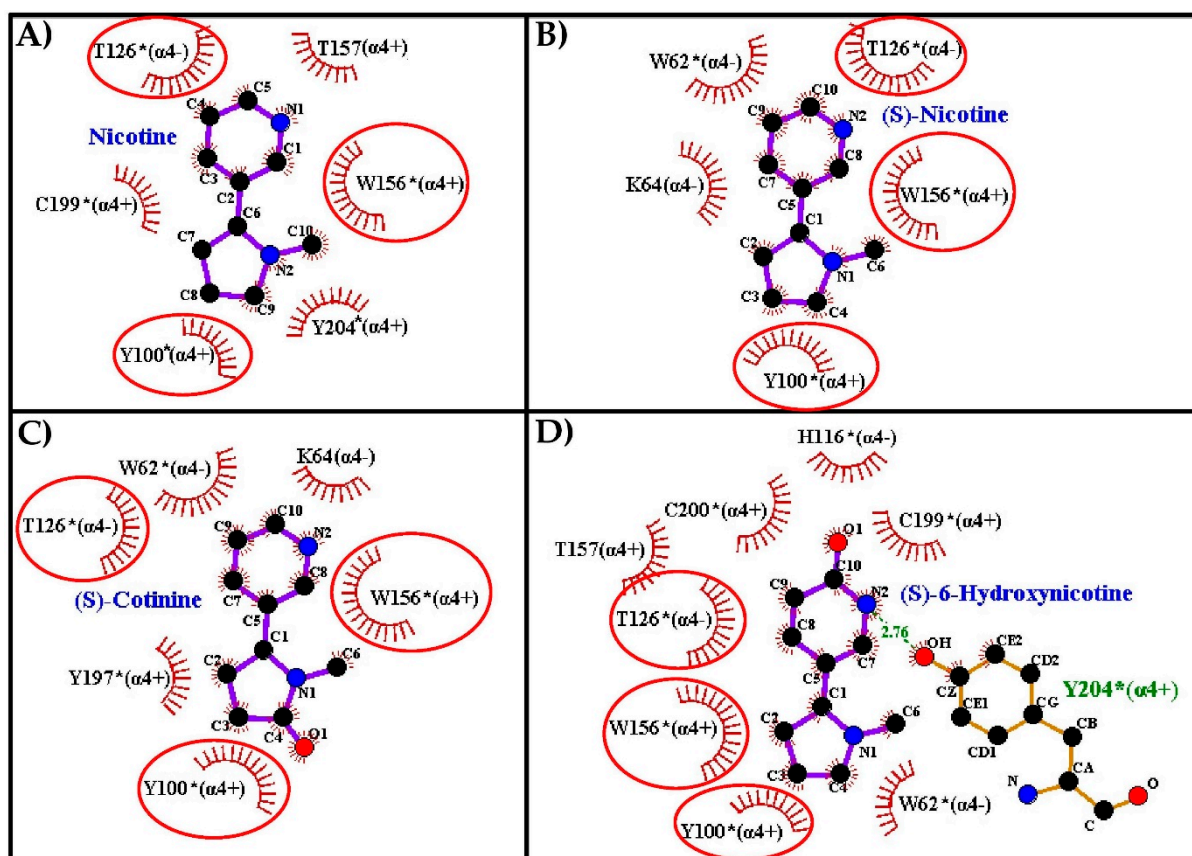


Figure 4. Schematic diagram of the interactions between the residues of $\alpha 4$ - $\alpha 4$ nicotine-binding interface of $\alpha 4\beta 2$ nAChRs and nicotine (A), (S)-nicotine (B), (S)-cotinine (C) and (S)-6-hydroxynicotine (D). The residues that are marked with * are common with those from literature and the encircled residues are common for all the selected ligands. The hydrophobic contact(s) between the residues and the corresponding atoms of the ligands as well as the hydrogen bonds are illustrated according to the Ligplot* software.

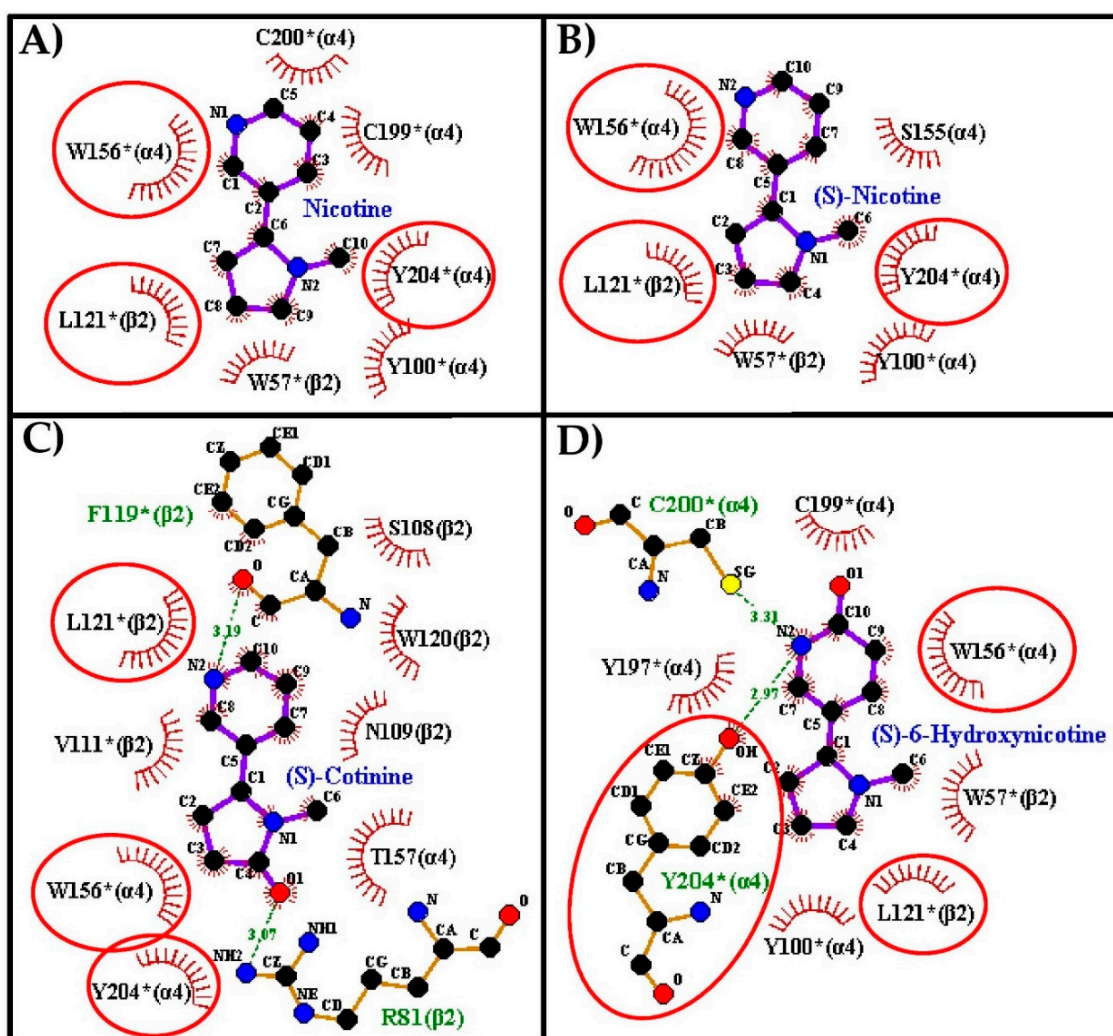


Figure 5. Schematic diagram of the interactions between the residues of $\alpha 4$ - $\beta 2$ nicotine-binding interface of $\alpha 4\beta 2$ nAChRs and nicotine (A), (S)-nicotine (B), (S)-cotinine (C) and (S)-6-hydroxynicotine (D). The residues that are marked with * are common with those from literature and the encircled residues are common for all the selected ligands. The hydrophobic contact(s) between the residues and the corresponding atoms of the ligands as well as the hydrogen bonds are illustrated according to the Ligplot⁺ software.