of the catalytic pocket or Arg120 and Tyr355 in the bottom of the pocket. For instance, diclofenac binds to the first group residues (top) and flurbiprofen interacts to the latter group residues (bottom), mainly via electrostatic interactions that are made between polar heads of such residues and the carboxylate group in these NSAID structures. The NSAIDs hydrophobic groups also have a role in binding via making van der Waals interactions with the hydrophobic residues lining the active pocket.

Binding energies of the best docked pose of all six compounds are shown in Table 4.1, along with the flurbiprofen and celecoxib scoring as a reference. All compounds seem to fit well in the COX-1 as well as in the COX-2 active site (they have favorable binding energies). Interestingly, Am6 has shown a remarkable binding energy (-8.6 kcal/mol) in the COX-1 active site, which is very close to the diclofenac's binding energy (-8.7 kcal/mol). As shown in Figure4.2.A, Am6 also possesses a similar binding mode to diclofenac where the best pose seems to pleasantly fit in the COX-1 catalytic pocket and to make the same hydrogen bonding interactions that is made by diclofenac. These interactions are made by the ligand protonated amino group and the cyclic carbonyl group. Obviously, these interactions are assisted by the existence of the acetylenic group which acts as an anchor; via placing these two polar groups at the correct position for binding. In addition to these electrostatic interactions, extensive hydrophobic interactions are made between the ligand carbon atoms and the side chains of Tyr348, Val349, Le352, Phe381, Leu384, Trp387, and Leu534.