Abstract: Introduction: Carbonic anhydrase (CA) is a zinc-enzyme widely spread in the animal, bacterial, vegetal and human which catalyzes one of the simplest physiological reactions: the reversible inter conversion between CO2 and HCO3⁻ by a proton transfer (PT). Proton transport is an important event in many biological processes that influenced by environmental electrostatic.

Method: All calculations were performed using the Gaussian software. The geometries of carbonic anhydrase enzyme active site (CA), activator and its protonated form. The complex between activators and CA were fully optimized using DFT method with B3LYP functional. The calculations were performed with the standard 6-31G* basis set. The harmonic vibrational frequencies were computed to confirm that an optimized geometry correctly corresponds to a local minimum that has only real frequencies. Also the thermodynamic properties of all compounds were obtaine from frequency calculations at 298.15 K and 1.0 atmosphere pressure. The solvent effects on the conformational equilibrium and contribution to the total enthalpies were investigated with the PCM method at the B3LYP/6-31G* level.

Results: The results of our calculation indicate that the histamine is a potent activator for CA enzyme. Histamine binds within the CA active site without interacting with the metal center directly.

Conclusion: This research can help for design Alzheimer’s drugs and other conditions in need of achieving spatial learning and memory therapy. Also to design the new potent activators.

Carbonic anhydrase, Activator, Histamine, QM calculation.