

# Influence of protonation on substrate and inhibitor interactions at the active site of human monoamine oxidase-A

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Although substrate conversion mediated by human monoaminooxidase (hMAO) has been associated with the deprotonated state of their amine moiety, data regarding the influence of protonation on substrate binding at the active site are scarce. Thus, in order to assess protonation influence, steered molecular dynamics (SMD) runs were carried out. These simulations revealed that the protonated form of the substrate serotonin (5-HT) exhibited stronger interactions at the protein surface compared to the neutral form. The latter displayed stronger interactions in the active site cavity. These observations support the possible role of the deprotonated form in substrate conversion. Multigrid docking studies carried out to rationalize the role of 5-HT protonation in other sites besides the active site indicated two energetically favored docking sites for the protonated form of 5-HT on the enzyme surface. These sites seem to be interconnected with the substrate/inhibitor cavity, as revealed by the t