Docking studies of selective serotonin reuptake inhibitor (citalopram) and selective serotonin reuptake enhancer as potential target of serotonin transporter

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Serotonergic antidepressants preferably selective serotonin reuptake inhibitors (SSRIs) are considered to be the most prescribed antidepressants owing to their pharmacokinetic characteristics. The present study aims to elucidate the docking studies of 5-hydroxytryptamine (5HT), selective serotonin reuptake inhibitors (SSRI, citalopram) and selective serotonin reuptake enhancer (SSRE, tianeptine) with serotonin transporter (PDB ID; 6w2c) with the help of simultaneous multiple ligand docking by AutoDock Vina. In addition to pharmacokinetic studies of drugs, the present study also determined the serum tryptophan and corticosterone levels (hypothalamic pituitary adrenal axis; HPA axis activity) following chronic administration (4weeks) of citalopram (20mg/kg/ml) and tianeptine (10mg/kg/ml) to Albino Wistar rats Results were analyzed and the amino acid conformation of the active site of protein (6w2c) was identified using discovery studio visualization. Further, two-dimensional graphical depiction of best complexes was assessed and the detailed analysis on the physicochemical properties of the docked complexes were obtained by using PLIP (protein ligand interaction profile) fully automated protein-ligand interaction tool and Ligplot plus. Serum tryptophan and serum corticosterone levels were measured spectrophotometrically using standard laboratory procedures. Results showed reduction in serum tryptophan concentration by both citalopram ($p<0.05$) and tianeptine ($p<0.01$) compared to controls while marked increase ($p < 0.5$) in corticosterone levels were found by both drugs. The binding affinity of the compounds were determined by the length of hydrogen bond, binding energy, amino acid residues, clusters and RMSD values. We found that citalopram showed higher binding affinity (-9.0 kcal/mol) compared to tianeptine and its substrate (serotonin) that suggests its mechanism of reuptake inhibition at serotonin transporter. Further, reduction in free serum tryptophan levels and the increased corticosterone levels shows contribution of drugs to increase free tryptophan uptake by the brain to augment serotonin levels in the brain.

Biography

Dr. Iffat Ara has completed her PhD in 2013 from University of Karachi and serving as an Assistant Professor in the School of Biochemistry, Minhaj University, Lahore. She has published more than 10 publications in reputed Journals and serving as editorial Board member in "Open access Journal of Pharmaceutical Research". She is also a member of reviewing committee of "Pakistan Science Foundation" and "Board of advance studies and research" in University of Karachi and Dow International University of Health sciences, Pakistan. She is also a member of Pakistan Society for Biochemistry and Molecular Biology and working in collaboration on national and international projects.