Research Article

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Exploring in silico drug design and pharmacokinetics study for identification of potent antidepressant agents

Sabitu Babatunde Olasupo[a*], Adamu Uzairu[b], Gideon Shallangwa[b] and Sani Uba[b]

[a]*National Agency for Food and Drug Administration and Control (NAFDAC), Abuja, Nigeria*
[b]*Department of Chemistry, Ahmadu Bello University Zaria, Nigeria*

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ABSTRACT

In furtherance to our previous study, in silico drug design and pharmacokinetics study were employed on some arylpiperazine derivatives as inhibitors of serotonin transporter (SERT) for identification of potential antidepressant agents. A simulated molecular docking study carried out showed that the binding affinity between the receptor (PDB: 4m48) and the ligands range from -8.1 to -10.35kcal/mol with prominent hydrogen bonding and hydrophobic interactions. Some selected ligands displayed good binding affinity range from -9.55 to -10.35kcal/mol and remarkable biochemical interactions were revealed at the active site of the protein target compared to an FDA approved drug (Brexpiprazole) with a lower binding affinity (-9.5kcal/mol). More so, compound 15 shows an exceptional non-bonding interactions with five (5) hydrogen bonds to important amino acid residues (TYR124, ASP46, PHE319, SER421 and ASP475) at a shorter bond length (2.939Å) compared to Brexpiprazole with only one hydrogen bond to the amino acid residue (ASP401) at a longer bond length (3.754Å). Similarly, the predicted ADMET profiles revealed that all the selected compounds possessed good pharmacokinetics properties. Likewise, the computed drug-like properties of the selected compounds portends good pharmacological profiles/ bioavailability tendency as drug candidates. The BOILED-Egg graphics shows that all the selected compounds would be absorbed by the human gastrointestinal system and penetrate to the brain. Furthermore, the calculated physicochemical parameters of all the newly designed compounds having smaller molecular weights when compared with template compound with higher molecular weight satisfied the perquisites of drug-like compounds, an indication that the designed compounds would be orally bioavailable. Also, toxicity profiles of the designed compounds showed that none of the compounds portends carcinogenicity or skin sensitization toxicities. In consequence, all the selected and the designed compounds could be developed and optimized as potential antidepressant agents. However, further experimental studies and in vivo investigations are suggested to evaluate the mode of the actions and other pharmacological effects on these compounds.

1. Introduction

Depression is a multifarious and severe psychiatric disorder characterized by excessive and extensive anxiety, feelings of sadness, unruly emotions, hopeless altitude, insomnia and loss of interest that affects millions of people across the world with a considerable number of morbidity and mortality rates [1][2]. Apart from major implications of depression which include a remarkable reduction in quality of life, loss of job and expensive cost of treatments, a great occurrence of suicidal attempts in depressed patients suggested that mental disorder associated with depression would be the second leading cause of death globally in the nearest future [3][2]. Serotonin transporter (SERT) is the major target of therapeutic for antidepressant agents/drugs in which inhibitors of the serotonin transporter (SERT) are considered as the standard treatment/medication for

∗ Corresponding author. e-mail: olasabit@yahoo.com