

## ORIGINAL RESEARCH ARTICLES

### EXPLORING THE BINDING MODES OF PIPERAZINE COMPOUNDS ON MAO-A FOR A STEP TOWARDS DEPRESSION THERAPY

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#### ABSTRACT

Sadness, often referred to as “depression,” is a normal emotion. The World Health Organization (WHO) claims that depression is a prevalent psychological condition that affects 264 million people worldwide, involving complex interactions between social and psychological behaviors. Piperazine, a heterocyclic scaffold, has been extensively used in various research studies due to its remarkable pharmacological effects in pharmaceutical chemistry. It has been modified to discover a new reversible neuroactive compound, along with pyrazoline. Early investigations have demonstrated significant inhibition of MAO-A by both compounds. The docking of molecules was performed by employing Autodock Vina programme, an *in silico* approach. Using the docking software AutoDockTools 1.5.6, the molecular docking studies on MAO-A enzyme targeting depression [Protein Data Bank (PDB) ID: 2BXR] was conducted. Compound **C17**, demonstrated significant interactions with specific residues, including Gly25, Arg51, Ser24, Thr435, Lys305, Gly66, Tyr407, Cys406, Gly67, Gly443, Ile23, Thr52, Gly22 and Ala448. This finding suggests that compound **17** could potentially serve as a promising and innovative candidate for the treatment of depression. This study focuses on designing a hybrid molecule combining piperazine and pyrazoline as MAO-A inhibitors. The results of the study indicate that **C17** and **C20** exhibit the greatest affinity, having interaction values of  $-10.9 \text{ kcal mol}^{-1}$  and  $-10.8 \text{ kcal mol}^{-1}$ , respectively. All the chemicals demonstrated similar behavior within the binding pocket of MAO-A. In this study, the *in silico* tool Swiss ADME were used to predict the drug-likeness of all designed compounds. The analysis indicated that all the compounds, except one, comply with Lipinski’s rule of five, which defines the drug-like compounds. Further, synthesis and biological evaluations need to be conducted in the future.