An Insilico Approach to Confront Monoamine Oxidase by Synthetic and Herbal Antidepressant Drug

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ABSTRACT

Monoamine oxidase (MAO) is an enzyme that metabolizes monoamines, and are also vital to the inactivation of monoaminergic neurotransmitters, such as serotonin, norepinephrine, dopamine for which they display different specificities. Lower level of such neurotransmitters leads to depression which is considered to be a menace in current scenario and there is need for a treatment. Hence it is necessary to confront Monoamine oxidase (MAO).Antidepressant drugs are formulated to handle a sensitive issue called depression where Venlafaxin a synthetic drug is a highly configured drug for depression .This is referred with Lithium carbonate a chemical which generally has the capacity to tackle depression. The study alternatively compares the compounds essential as anti depressant in *Clitoria ternatea* which is said to be a brain tonic and *Hypericum perforatum* whose capsules are standardized as antidepressant drugs. The phytocompounds along with Venlafaxine and lithium carbonate is contested to evaluate their efficiency to combat the protein Monoamine oxidase thereby conflicting depression.

Keywords

Antidepressant, *Clitoria ternatea*, *Hypericum perforatum*

1. INTRODUCTION

Recent work in behavioural genetics has stressed the importance of inter- actions between genetic predispositions and environmental contingencies [1]. The MAO gene codes for the enzyme monoamine oxidase that plays a key role in the catabolism of neurotransmitters, including dopamine, norepinphrine, and serotonin [2],[3]. Among humans, a functional polymorphism in the MAO gene can mediate the impact of traumatic early life events on the propensity to engage in aggression as they grow up. In particular, young children with maltreatment and who had the low activity form of MAO were much more likely to develop antisocial problems as they mature later in their life. [4],[5]. Inadequate quantities of MAO, in combination with distressing incidents in lifes, direct either the normal individual or the affected persons to antagonistic behavior. [6].

An antidepressant is a psychiatric medication used to alleviate mood disorders, such as major depression leading to dysthymia and anxiety disorders such as social anxiety disorder. Venlafaxine (also called Effexor or Efexor) is an antidepressant of the serotonin-norepinephrine reuptake inhibitor (SNRI) class [7]. *Clitoria ternatea* is reported as a brain energizer, nervine stimulant and laxative. Literatures as per Ayurvedic texts refer *Clitoria ternatea* as a "Medhya-Rasayana" and used as d drug for its action on the CNS (Central Nervous System), especially to enhance reminiscence and intelligence [8]. The major phytoconstituents found in *Clitoriaternatea* are the pentacyclictriterpenoids such as taraxerol and taraxerone[9], [10]. A prior study revealed that Kaempferol a phytochemical from *Clitoria ternatea* seems to have a potential role as an antidepressant [11]. St John's wort (*hypericum perforatum)* has active ingredients of hypericin

and hyperforin that help depression by preventing nerve cells in the brain from reabsorbing the chemical messenger serotonin. This report presents an insilico approach to counteract monoamine oxidase with the synthetic antidepressant drug and the phyto constituents from *Clitoria ternatea*. Structure-based virtual screening and post-screening analysis are emergent tasks in computer-based drug discovery. Combination of these methods effectively reduces the false positives from large compounds. Databases are considered as a key step for finding the lead compounds.

2. METHODOLOGY

2.1 Target Identification

The three dimensional structure of the target Monoamine Oxidase B was retrieved from PDB. The bioactive co crystallized ligand FLAVIN-ADENINE DINUCLEOTIDE N-[(E)-METHYL](PHENYL)-N-[(E)-2-PROPENYLIDENE]METHANAMINIUM was found to interact with the target.

2.2 Preparation of compounds

The data set of compounds were taken from the literature and downloaded from Pubchem in SDF format and converted to PDB format using the online tool smile translator (*cactus.nci.nih.gov/translate*). The compound structures were energy minimized and considered for docking studies.

2.3 Anti –Depressant drugs

Anti depressant drug Venlafaxine and the chemical compound Lithium Carbonate was also downloaded from pubchem and converted to PDB format and used for docking for the comparative analysis.

2.4 Molecular Docking

Graphical-Automatic Drug Design System for Docking, Screening and Post-Analysis program iGEMDOCK was used to gain the docking results of the listed compounds with the target. The binding site of the target was prepared and the energy minimized compounds were imported. The docking protocol consisted of 25 generations per ligand and the population size of 100 random individuals. All the docking conformations were performed twice using genetic evolutionary algorithm and the fitness of the docked structures were calculated. The hydrophobic preference and electrostatic preference were set to 1.00. The binding site of the target was identified at a distance 8Å. The empirical scoring function of iGEMDOCK was estimated as:

$$Fitness = vdW + H\ bond + Elec.$$

Here, the vdW term is van der Waal energy. H bond and Elect terms are hydrogen bonding energy and electro statistic energy, respectively.

3. RESULTS AND DISCUSSION

Docking studies

The targeted protein Monoamine Oxidase was assayed with that of the phytocompounds of *Clitoria ternatea* and *Hypericin perfortum,* synthetic drug Venlafaxine and Lithium Carbonate .Docking simulations with the target monoamine oxidase protein was performed with other phytocompounds and antidepressant drugs. The Interactions of all the test compounds are depicted in the Fig. 1 -5 with the ligand (pink) within the active site residues of the target.

3.1 Interactions of Velafaxine with target

Docking simulations of Venlafaxine (Fig 1) with the monoamine oxidase resulted in energy of -86.5 Kcal/mol and showed the Hydrogen bond interactions with the residues Gly12, Arg42, Alg263.03.

3.2 Interactions of Kaempferol with target

Docking simulations of Kaempferol (Fig 2)with the target monoamine oxidase resulted in energy of -98.8 Kcal/mol and showed the Hydrogen bond interactions with the Tyr 398, Ile 14, Cys397, Met 436, Gly41, Gly58, and Gly434.

3.3 Interactions of Hypericin with target

Docking simulations of Hypericin(Fig 3) with the target monoamine oxidase resulted in energy of -90.6Kcal/mol and showed the Hydrogen bond interactions with the residues Val39, Ser214, Gly40.

3.4 Interactions of Hyperforin with target

Docking simulations of Hyperforin(Fig 4) with the target monoamine oxidase resulted in energy of -33.8 Kcal/mol and showed the Hydrogen bond interactions with the residues Thr339, Ser433, Thr1882, and Leu291.

3. 5 Interactions of Lithium Carbonate with target

Docking simulations of Lithium Carbonate(Fig 5) with the target Monoamine Oxidase resulted in energy of -35.7 Kcal/mol and showed the Hydrogen bond interactions with the residues Tyr388, Tyr398, Cys397
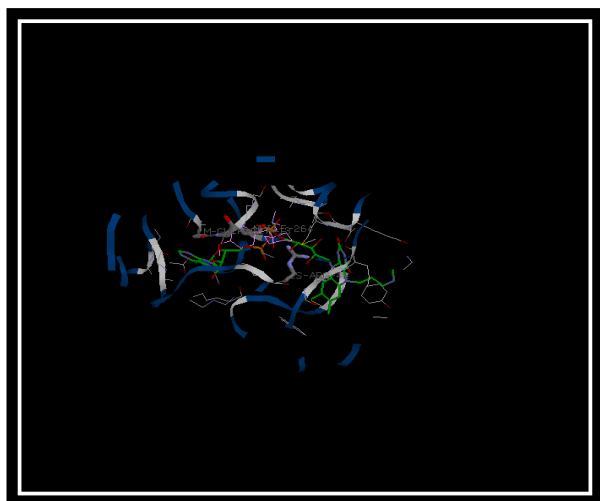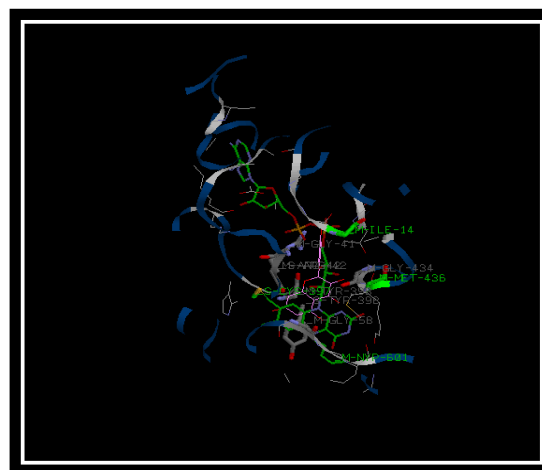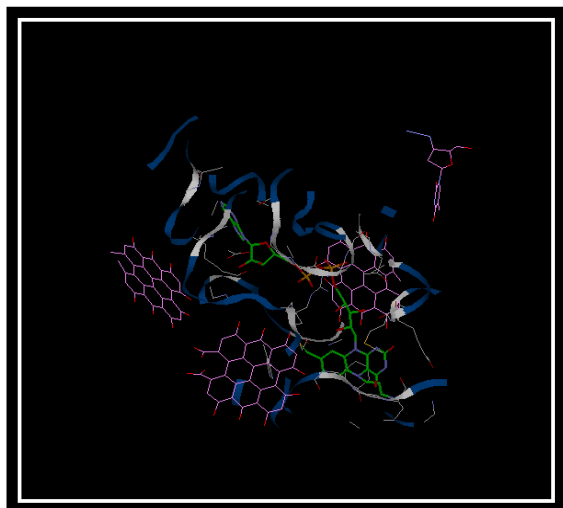

Fig 1: Venlafaxin

Fig 2: Kampeferol
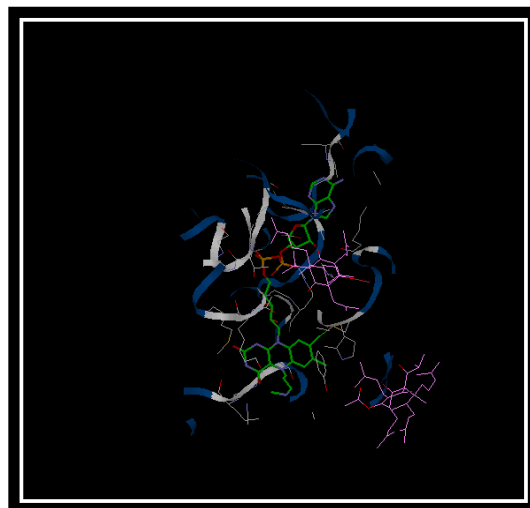
Fig 3: Hypericin
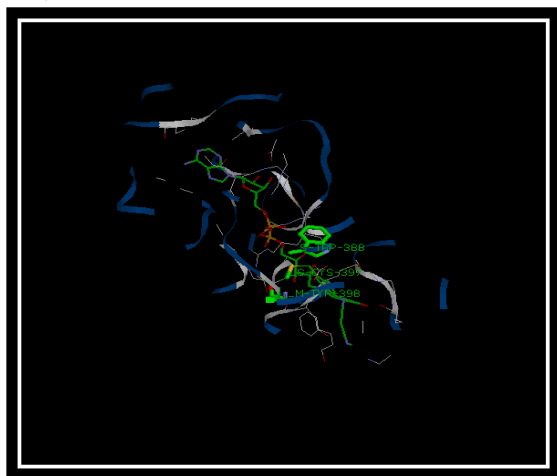

Fig 4: Hyperforin

Fig 5: Lithium Carbonate

From the results of docking, the compounds Kaempferol, Hypericin are found to dock well and exhibit minimum energy values. These compounds also inhibit the target efficiently on comparing with the drug Venlafaxine.

4. CONCLUSION

Depression has been a chief problem in the current scenario and its essential to produce a solution. This work evaluates the binding efficiency and the counteraction with the protein Monoamine Oxidase. Both synthetic antidepressant drug and natural phytocompounds from Clitoria ternatea and Hypericin perfortum were analysed .Inferring the In-Silico studies, the compound Kaempferol resulted in energy of - Kcal/mol and showed the Hydrogen bond interactions with the Tyr 303, Tyr 306, Ser725, Ser 975, Phe332, Phe724,Phe974 of the target. This is better than the standard synthetic drug and is efficient enough to inhibit the target Monoamine Oxidase.

Hence it is concluded that the compound kaempferol can inhibit Monoamine Oxidase effectively and can act as an inhibitor against depression. Hence future studies can be extended to know the pharmacological action of kaempferol on depression. The performed study has identified the ideal compound as antidepressant. This would lead to vital in vitro and invivo studies with clinical trials to fetch an elucidation against depression.

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