REPORT ON MOLECULAR DOCKING OF AMYLOID BETA (5HOX) AND TRORILUZOLE

Introduction to Protein and Ligand

- **Protein**: Proteins are complex macromolecules essential for numerous biological processes. They serve various roles, including enzymatic catalysis, structural support, cellular signaling, and immune response. The amyloid beta protein (Aβ) is associated with Alzheimer's disease and forms plaques in the brain, disrupting neural function. Specifically, **5HOX** is the crystal structure of the amyloid beta fibrils, providing insights into the aggregation of Aβ peptides.

  PDB Link: **RCSB PDB - 5HOX: X-ray crystallographic structure of an A-beta 17_36 beta-hairpin. Synchrotron data set. (LVFFAEDCGSNKCAII(SAR)LMV).**

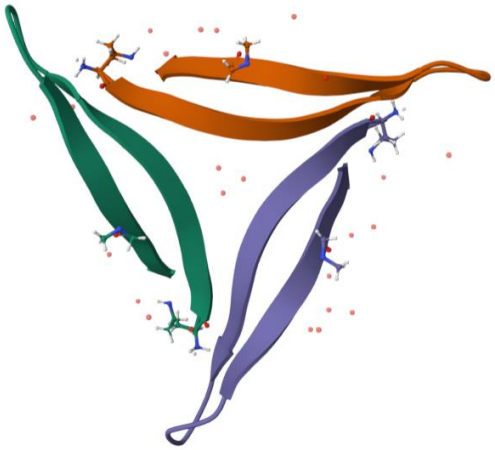

Fig: 3D Structure of the 5HOX protein

- **Ligand**: A ligand is a small molecule that binds to a specific site on a protein, potentially altering its function. Ligands are crucial in drug discovery, as they can modulate protein activity. **Troriluzole** is a derivative of Riluzole, designed to modulate glutamatergic activity in the central nervous system. It has potential therapeutic implications for neurodegenerative disorders.

  Pubchem Link: Troriluzole | C15H16F3N5O4S | CID 121488186 - PubChem

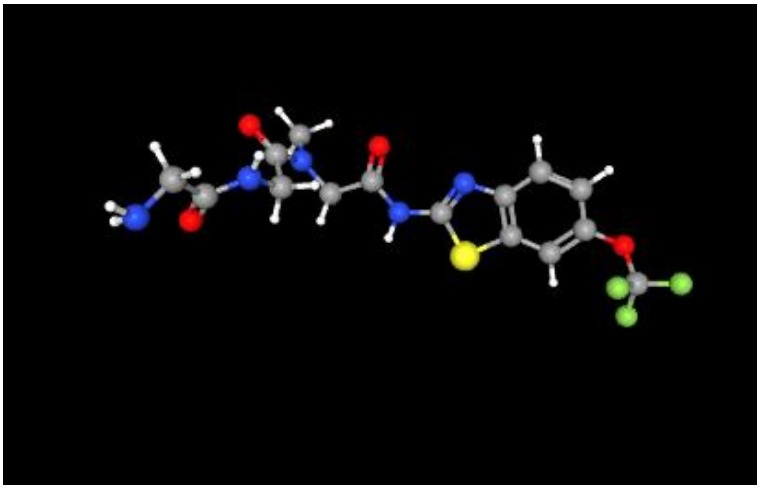

Fig: 3D Structure of Ligand Troriluzole

Molecular Docking

Molecular docking is a computational technique used to predict the interaction between a protein and a ligand. It helps visualize how the ligand binds to the protein's active or binding site, providing insights into the binding affinity and interaction strength.

Amyloid Beta (5HOX) and Troriluzole Interaction

1. **Protein Structure (5HOX)**:
    - **Description**: 5HOX is the resolved structure of amyloid beta fibrils derived from Alzheimer's disease. It offers insights into the arrangement of Aβ peptides into plaques, essential for understanding aggregation mechanisms.
    - **Key Features**:
        - Composed of β-sheet structures.
        - Contains hydrophobic regions critical for fibril formation.
    - **Significance**: Targeting amyloid beta can disrupt plaque formation, a key therapeutic strategy.
2. **Ligand Properties (Troriluzole)**:
    - **Chemical Formula**: $C_{15}H_{16}F_3N_5O_4S$
    - **Mechanism of Action**: Modulates glutamate signaling by inhibiting excitotoxicity, potentially reducing neuroinflammation and oxidative stress.

- **Therapeutic Goal**: Improve cognitive function and slow neurodegeneration.

Docking Process

1. **Preparation**:
   - Retrieve 3D structure of 5HOX from **RCSB Protein Data Bank**.
   - Obtain Troriluzole's structure from chemical databases (e.g., PubChem).
   - Perform energy minimization to optimize the geometry of both structures.
2. **Tools and Methods**:
   - Use molecular docking software like **AutoDock** and **PyMOL**
   - Define the binding site using the active region identified in 5HOX.
3. **Docking Simulation**:
   - Simulate the interaction between 5HOX and Troriluzole.
   - Analyze binding affinities, docking scores, and interaction residues.
4. **Key Observations**:
   - Troriluzole binds to hydrophobic pockets within the amyloid beta structure.
   - Hydrogen bonds, hydrophobic interactions, and π-π stacking contribute to binding stability.

Docking Results

- **Binding Affinity**: Quantified using scoring functions (e.g., Gibbs free energy, ΔG).

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-6.6	0.000	0.000
2	-6.5	7.368	10.408
3	-6.3	8.010	10.684
4	-6.2	3.296	6.110
5	-6.2	18.387	20.148
6	-6.1	18.616	21.830
7	-6.1	14.588	17.618
8	-6.0	2.645	3.908
9	-6.0	7.506	9.835

Fig: Docking Analysis

- **Key Interactions**:
    - Hydrogen bonding with amino acid residues.
    - Stabilization via hydrophobic contacts in the fibril core.
- **Biological Implications**: Suggests Troriluzole may interfere with amyloid aggregation, reducing plaque formation.
- **Docked Molecule Image**:

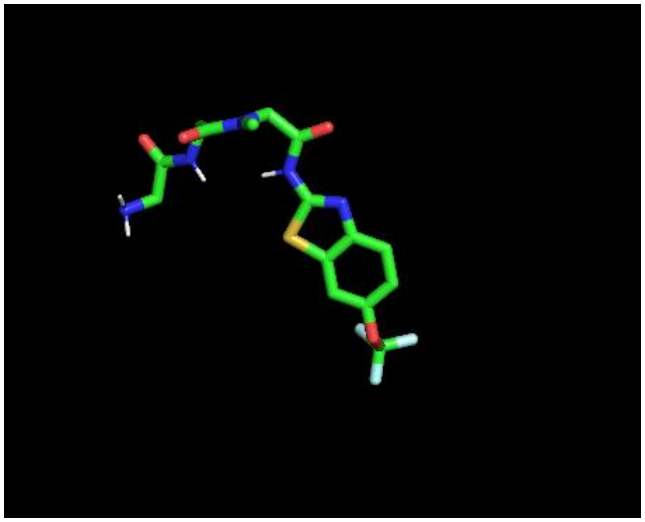

Fig: Docked Molecule

Conclusion

The molecular docking of amyloid beta (5HOX) and Troriluzole provides a detailed view of their interaction. By targeting amyloid beta fibrils, Troriluzole exhibits potential as a therapeutic candidate for mitigating Alzheimer's disease progression. Further experimental validation is essential to confirm its efficacy.