Integrated in silico approach for the development of a new antipsychotic drug candidate to treat schizophrenia

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Schizophrenia

- A very complex mental disorder affecting many people worldwide and causing a lot of suffering. About 5-13% commit suicide1.
- Medicines are still far from the ideal profile and have limitations either in efficacy or in secondary effects2.
- It was found a molecule whose mixture of its two isomers has a potent antagonist activity at the 5-HT1A receptor.
- This receptor is a pharmacological target of interest related to schizophrenia and other psychiatric disorders2,3.
- One of the isomers may be responsible for the activity.
- An in silico approach was developed to study the case, to identify the isomer.

In silico approach

- Molecular docking, a computational tool to predict the preferred binding pose of a ligand in a specific protein target.
- Search algorithm, calculate and generate the poses.
- Scoring function (SF), analyze the poses and attribute a rank of affinity values, scores, for each solution.

In silico optimization of the affinity and ADMET properties of the molecule

- Most drug candidates fail in clinical trials and one of the main causes is poor ADMET properties, alongside with lack of efficacy3.
- In silico optimization of the affinity (for 5-HT1A and other targets) with the docking procedure, and of the ADMET properties with free predict tools and rules-of-thumb.

Conclusion

- These methodologies represent an economical, fast, environmentally friendly strategy for drug design and development, essential for the initial stages of the process as an attempt to optimize money, time and resources, and to increase the probability of success to get the market.