Machine learning-based virtual screening, molecular docking and drug-likeness to discover new inhibitors of the glycoprotein spike (S1) of SARS-CoV-2

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INTRODUCTION

Despite great advancements in COVID-19 immunization, the development of therapeutic interventions is urgent to control the ongoing pandemic, especially in infected patients. The spike protein (S1) of SARS-Cov-2 virus plays a major role in attachment to the host and further series of events **(Figure 1)**. We aimed to identify natural bioactive compounds (NBC) as potential inhibitors of S1 by means of *in silico* assays.

METHODS

170,906 NBCs with previous proved biological in vitro activity were obtained from the ZINC database and analyzed using several in silico methods **(Figure 2)** to identify those with higher affinity to the S1. Main results are presented in **Figures 3 and 4.**

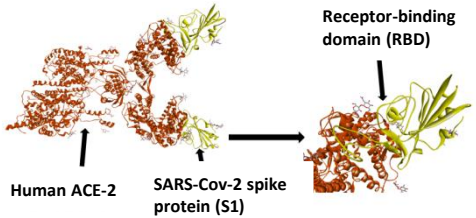

Figure 1. SARS-Cov-2 spike protein complexed with human ACE-2

1. • Ligand-based Virtual Screening (LBVS)
   • Software: PyRx
2. • Molecular Docking
   • Software: AutoDock tools and AutoDock Vina
3. • Machine learning (PCA, ANN, DT, KNN, LDA, PLS-DA, SIMCA)
   • Software: MATLAB
4. • Drug-likeness analysis (Lipinsk and Veber Rules)
   • Software: Swiss-ADME
5. • ADMET prediction
   • Software: ADMETLAB, PROTOX II and SOMP

Figure 2. In silico testing flowchart

RESULTS

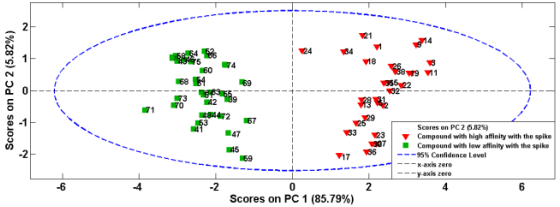

Figure 3. Principal component analysis-PCA model

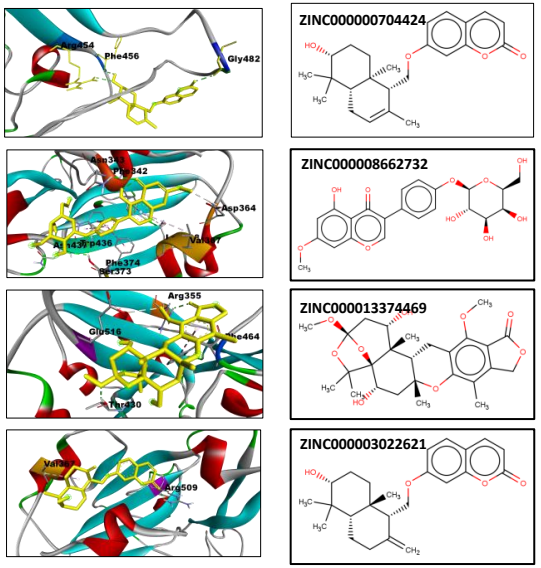

Figure 4. NBC with higher affinity to S1 and better ADMET results

CONCLUSIONS

Phaselol (ZINC000000704424) and others three NBC were the most promising candidates for treating COVID-19

REFERENCES

1.Yan, R et al. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2, Science, 2020, 367.