DEVELOPMENT OF AN ANTIRETROVIRAL AGENTS TARGETING REVERSE TRANSCRIPTASE

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Introduction

AIDS has been considered a death sentence, but because of the development of the treatment, many people can live normal lives. We are still far away from the 90/90/90 goal set by UNAIDS. In this project, we took another step in this program by trying to obtain a compound that would possibly be a supportive treatment for those with AIDS.

Impact of (ART)

Antiretroviral therapy reduces viral load and restores functioning of immune system. This raises possibility of using ART to not only to treat people but also to prevent new infections. (1) By doing this we can prevent pandemics of retroviruses that already exist and react faster in case of new pandemics. Impact of development of ART is invaluable because it does not only influence medical aspects of people's life but also social and economical ones possibly preventing futures lockdowns.

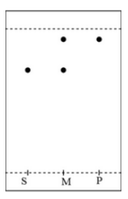
AIM

Develop potential reverse transcriptase inhibitor that will be part or ART and collect more data about this compound

Methodology

To 100 ml of acetonitrile, 500mg of 4-(2-cyclopropyl-4,5-dihydro-1,3-oxazol-5-yl) benzene-1-sulfonyl chloride, 26mg of DMAP, 2.7g of Hunnigs base polymer and 0.425g of 5-amino-2-chlorobenzotrifluoride has been added. Mixture was stirred and heated to 100C

TLC 1:4
(ethyl acetate:petroleum ether)



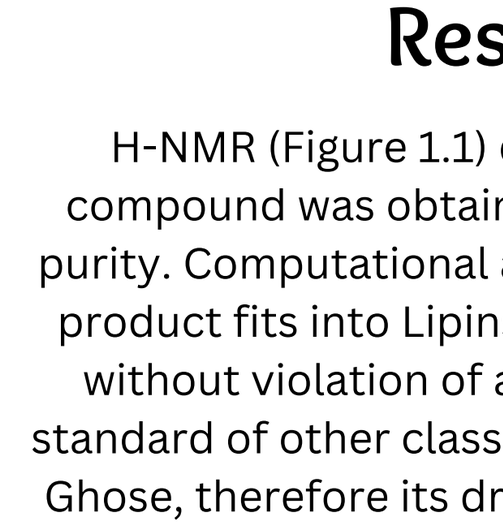
Suspension was vacuum filtered and solvent was removed under vacuum

10ml of ethyl acetate were added and stirred for 30 min

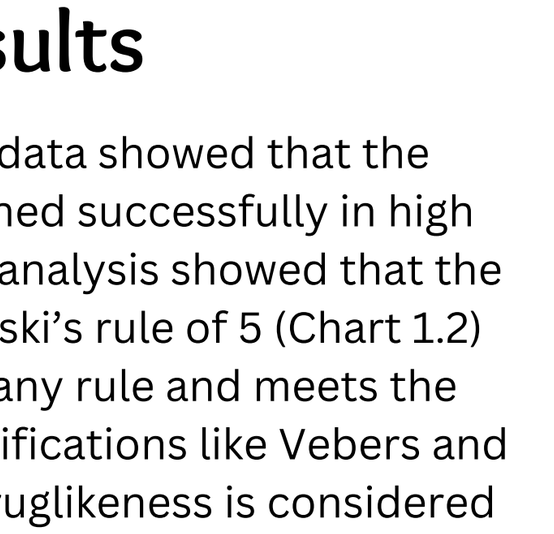
Suspension was vacuum filtered and 50mg of product were obtained

Results

H-NMR (Figure 1.1) data showed that the compound was obtained successfully in high purity. Computational analysis showed that the product fits into Lipinski's rule of 5 (Chart 1.2) without violation of any rule and meets the standard of other classifications like Vebers and Ghose, therefore its druglikeness is considered high. Its physicochemical properties indicate that the compound should be viable orally, should be absorbed in the gastrointestinal tract passively, and should not cross the blood-brain barrier.



1.1 Image shows HNMR results of the obtained compound, Peaks correspond to the Hydrogen atoms of the obtained compound (structure in the background of box 2)



1.2 Chart shows the most important physicochemical properties considered while designing the drug. The red zone shows the most suitable range and the red line shows the results of the obtained compound

Conclusions

The method used to synthesise this compound has let us obtain it in high purity and good yield. The physicochemical properties of the compound provide high bioavailability. It should also be absorbed in the gastrointestinal tract which creates the possibility to manufacture it in tablet form. That would be beneficial and make this drug more accessible. The obtained molecule is part of the group of compounds that are known inhibitors of reverse transcriptase

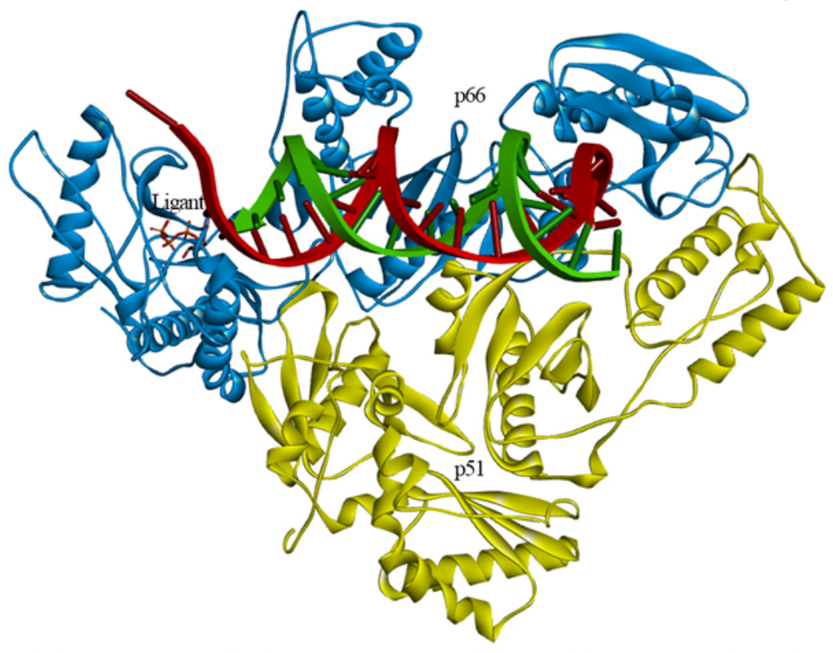


Figure 2.1 Crystal structure of a p66/p51 trimer-template complex (PDB code: 1 RTD) generated using Discovery Studio. For the part of RT, p66 is blue; p51 is yellow; In the two chains, DNA template strand is red and the primer strand is green.

References

1. Williams BG, Lima V, Gouws E. Modelling the impact of antiretroviral therapy on the epidemic of HIV. Curr HIV Res. 2011 Sep;9(6):367-82.

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