In-silico investigation to predict the potential of HDAC inhibitors to inhibit the HDLP enzyme: A molecular dynamics study

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Histone deacetylase (HDACs) enzyme plays an important role in regulating gene expression, thus could be considered as an effective target for cancer treatment. HDAC inhibitors are the new and promising class of drugs that restrict tumor cells from growing. In this study, the inhibitory efficacy of some HDAC inhibitors such as SAHA, LBH589, ITF2357, and PXD101 was studied using molecular dynamics simulation. The inhibitory efficacy was examined in terms of stability of the enzyme, potential energy of the system, the number of hydrogen bonds, and interaction energies between HDLP enzyme and inhibitor. It is hoped that this research will help to get a better understanding of the atomic-level nature of the inhibitor binding site and how HDAC inhibitors modify the active site of the HDLP enzyme. The RMSD and potential energy have revealed that the stability of HDLP enzyme with SAHA, LBH589, and ITF2357 is higher than the wild-type HDLP (apo form). According to the calculated values for interaction energies, the stability of the HDLP enzyme varies as LBH589 > SAHA > ITF2357 > PXD101, and the distance analysis also shows the same trend. The findings revealed that the LBH589 is a potential lead compound similar to the reference inhibitor SAHA. Therefore, it is possible to suggest this molecule to further clinical researches and clinical tests. Also, the outcomes of this study could be utilized to discover new potent inhibitors for clinical research.

Keywords: HDAC inhibitors, PRODRG online server, SAHA

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