INHIBITION OF HISTONE DEACETYLASES BY A NOVEL SYNTHETIC HYDROMIC ACID COMPOUND

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Introduction: Cancer is one of the leading causes of death by disease and has become detrimental to our species. To decrease the amount of cancer growth, histone deacetylase inhibitors (HDACi) are used to impede one of many factors responsible for continued cancer expression. Although current inhibitors demonstrate promising results in the inhibition of HDACs, they suffer from limitation, such as, selectivity for a particular HDAC enzyme, leading to unforeseen and potentially adverse side effects in patients being treated for cancer.

Methods: The proposed inhibitor was synthesized to be an analog to SAHA. First, Autodock Vina and Pymol were used for an *in silico* analysis to generate docking results between the potential inhibitor and HDAC. When the results demonstrated the proposed inhibitor bound favorably, the analog was synthesized, and its molecular structure was confirmed using TLC, HNMR, and IR. Lastly, an inhibition study was conducted to both determine the IC50 value of the potential inhibitor and measure the analog's ability to inhibit HDAC.

Results: Autodocking results revealed the molecule's strong potential to bind with HDAC's active-site zinc ion. Following this docking simulation, an inhibition assay tested the analog's ability to inhibit HDAC1, where N-[6-(hydroxyamino)-6-oxyhexyl]benzamide showed an IC_{50} of 6.3 μM, indicating effective inhibitory properties. A subsequent assay in HeLa cell lysates against multiple HDACs demonstrated an IC_{50} of 12.0 μM.

Conclusion: Through experimentation, it has been determined that N-[6-(hydroxyamino) – 6 – oxyhexyl]benzamide has a high affinity for the zinc ion present in an HDAC active site. However, nothing is known about how the compound might behave on a physiological level, so future studies must be conducted to obtain more accurate results and determine its effectiveness as a drug.