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Computation analysis of histone deacetylases with curcumin

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Abstract

The assessment of histone deacetylases in conjunction with curcumin, conducted through the Mcule Database employing the Autodock Vina algorithm, involves an examination of molecular interactions. This analysis includes the calculation of binding energies, revealing the strength and stability of the interactions between curcumin and various histone deacetylase targets. The comparison encompasses diverse aspects such as binding energies, specific binding sites, interactions across different targets, structural details, and potential implications for biological activity. The results imply that curcumin shows heightened affinity for histone deacetylase 4 in comparison to other investigated histone deacetylases.

Keywords: *HDACs, Curcumin, Molecular docking*

1. Introduction

Histone deacetylases (HDACs) are a group of enzymes that play a crucial role in the regulation of gene expression. They are involved in the modification of histones, which are proteins that help package DNA into a compact structure called chromatin. The acetylation and deacetylation of histones are dynamic processes that influence the accessibility of DNA to transcriptional machinery, thereby affecting gene expression (Marks *et al.*, 2003; Gray and Ekström, 2001; Barneda-Zahonero and Parra, 2012). HDACs or EC 3.5.1.98 comprise a category of enzymes responsible for eliminating acetyl groups (O = C-CH_3) from the ε-N-acetyl lysine amino acid found on both histone and non-histone proteins (Cress and Seto, 2000). Inhibitors of histone deacetylase represent a novel category of cytostatic agents designed to impede the proliferation of tumor cells (Marks *et al.*, 2004; Glozak and Seto, 2007; Dokmanovic *et al.*, 2007).

This brief theoretical study seeks to explore the potential role of curcumin, a natural substance recognized for its anti-tumor properties (Aggarwal *et al.*, 2003; Vallianou *et al.*, 2015), through an in silico approach employing Molecular Docking (Meng *et al.*, 2011). The objective is to ascertain whether curcumin demonstrates effective binding to histone deacetylases, evaluating the binding affinity and identifying the specific types of bonds involved in the interaction.To accomplish this objective, we utilized the Mcule Database (Odhar *et al.*, 2019), leveraging the Autodock Vina algorithm for an automated exploration of the role of curcumin in binding interactions.

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2. Material and methods

Several histone deacetylases are performed in this work:

- Histone deacetylase 8 (PDB Code 3mz6): Binding site center (ångström) x(0,1808), y(42,7338), z(2,1861).
- Histone deacetylase 6 (PDB Code 3gv4): Binding site center (ångström) x(-7,3659), y(4,9697), z(0,9734).
- Histone deacetylase-like amidohydrolase (PDB Code 1zz1): Binding site center (ångström) x(-28,5197), y(16,2263), z(-16,5053).
- Histone deacetylase 4 (PDB Code 2vqq) Binding site center (ångström) x(-17,5922), y(7,3406), z(-11,4742).
- Histone deacetylase 2 (PDB Code 3max) Binding site center (ångström) x(48,9732), y(15,6496), z(-43,4309).

3. Results and discussion

This study specifically delves into the potential interaction of curcumin with histone deacetylases using Molecular Docking via the Mcule Database. Molecular docking is a computational technique that simulates the interaction between molecules (Meng *et al.*, 2011), such as a ligand (e.g., curcumin) and a protein (e.g., histone deacetylase). Binding energy is a critical parameter in these studies, reflecting the strength and stability of the interaction between the ligand and the protein's binding site.

In general, a lower binding energy indicates a more favorable and stable binding interaction. Therefore, when comparing binding energies across different histone deacetylase targets, researchers can identify which one has the strongest binding affinity for curcumin. This information is valuable in understanding the potential effectiveness of curcumin as a ligand for different protein targets and can guide further exploration of its therapeutic applications. Notably, the results reveal a notably elevated binding energy of -9.7 kcal/mol within the Ligand Binding Site of histone deacetylase 4 (see below Figure 1). In Table 1 was shown the comparison binding energies of histone deacetylases targets with curcumin.

Histone Deacetylase 4 (HDAC4) is a gene that encodes a protein involved in regulating gene expression through the deacetylation of histones. The deacetylation of histones by HDAC4 is part of the larger process of epigenetic regulation, influencing how genes are turned on or off.

HDAC4, as a histone deacetylase, is involved in the regulation of gene expression through transcriptional processes. Transcription is the synthesis of RNA from a DNA template, a key step in gene expression.

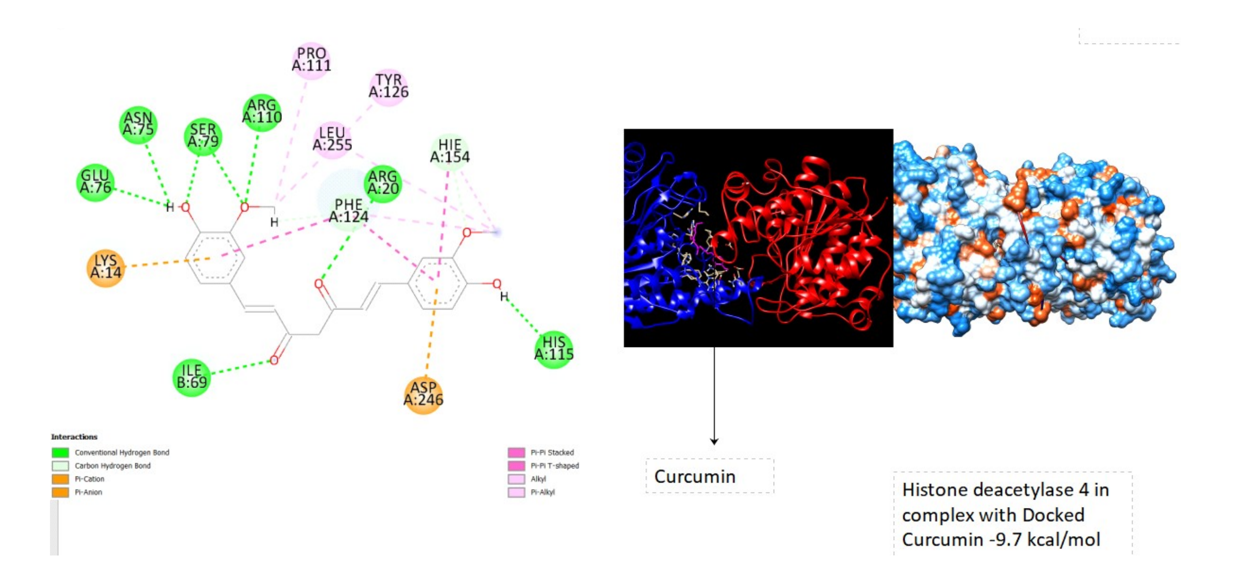

Figure 1: Displays the docking outcomes of Histone deacetylase 4 in conjunction with Curcumin within the Ligand Binding Site, as analyzed by Autodock Vina through the Mcule Database. On the left side, 2D diagrams illustrate the residue interactions between the protein and Curcumin. Meanwhile, the right side exhibits the Ligand Binding Site of the protein, highlighting the specific location of Curcumin

Table 1: Comparison of Histone deacetylases with Curcumin evaluated by Mcule Database with Autodock Vina

Histone deacetylases	Binding energies (kcal/mol)
Histone deacetylase 8	-6.4
Histone deacetylase 6	-6.5
Histone deacetylase 2	-8.4
Histone deacetylase 4	-9.7
Histone deacetylase-like amidohydrolas	-5.8

Understanding the role of HDAC4 in these pathways and its association with specific disorders provides insights into the broader impact of epigenetic regulation on human health and development. Additionally, these findings contribute to the exploration of potential therapeutic targets for conditions linked to HDAC4 dysfunction (Wang *et al.*, 2000; Vega *et al.*, 2004; Grozinger and Schreiber, 2000).

The binding energies (in kcal/mol) for curcumin with different histone deacetylases are as follows:

Histone deacetylase 8: -6.4

Histone deacetylase 6: -6.5

Histone deacetylase 2: -8.4

Histone deacetylase 4: -9.7

Histone deacetylase-like amidohydrolase: -5.8

The results indicate that curcumin exhibits a higher affinity for histone deacetylase 4 compared to other tested histone deacetylases. The more negative the binding energy, the stronger and more stable the interaction, suggesting that histone deacetylase 4 has a more favorable binding with curcumin in comparison to the other histone deacetylases tested.

4. Conclusion

This work is valuable for understanding the specificity of curcumin towards different histone deacetylases (HDAC) targets, which can have implications for potential therapeutic applications, especially in the context of diseases associated with HDAC dysregulation.

The findings suggest that curcumin demonstrates greater affinity for histone deacetylase 4 compared to other examined histone deacetylases. A more negative binding energy signifies a stronger and more stable interaction, indicating that the binding between curcumin and histone deacetylase 4 is more favorable when contrasted with other histone deacetylases that were tested.

Conflict of interest

Authors declare that they do not have any conflict of interest.

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