Communication

Exploring the Potential Role of Hypericin in Targeting PIM1 for Cancer Research

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Abstract: PIM1is involved in critical cellular processes, playing a key role in the regulation of the cell cycle, apoptosis, transcriptional activation, and broader signal transduction pathways . The exploration of PIM1inhibitors, such as small molecules or antibodies, represents a promising avenue in cancer research for developing novel treatment strategiess. Its significance in oncogenic signaling has led to extensive research on PIM1 as a target in cancer studies. Docking studies have revealed a robust interaction between hypericin and PIM1, suggesting a strong binding affinity (-12.5 kcal/mol). This research aims to explore the molecular dynamics of the hypericin-PIM1 interaction, identifying potential binding sites and elucidating the impact on PIM1-mediated cellular processes, such as cell cycle regulation and apoptosis. The findings may contribute valuable insights into developing hypericin-based therapies targeting PIM1, paving the way for novel and effective strategies in cancer research.

Keywords: PIM1 protein kinase ; hypericin ; docking analysis; cancer

1. Introduction

Pim-1 protein kinase is an enzyme encoded by the PIM1 gene in humans[1–3]. Originally identified as a proto-oncogene in murine T-cell lymphomas, it has been frequently activated by Moloney murine leukemia virus[4]. Subsequently, it has been associated with various human cancers, including prostate cancer, acute myeloid leukemia, and other hematopoietic malignancies. Pim-1 is expressed in several tissues, including spleen, thymus, bone marrow, prostate, oral epithelium, hippocampus, and fetal liver, and is particularly elevated in cell cultures isolated from human tumors[1–4].

Its main participation occurs in the regulation of cell cycle progression, apoptosis and transcriptional activation, as well as being involved in more general signal transduction pathways. Given its implications in oncogenic signaling, Pim-1 has become a significant target in cancer research. Numerous drug candidates that aim to inhibit this protein are currently being studied, indicating its potential as a therapeutic target in the treatment of tumors[1–4]. Due to its association with cancer and its involvement in oncogenic signaling pathways, Pim-1 has become a subject of intense investigation for potential therapeutic interventions.

The primary objective of this brief theoretical study is to simulate the interaction between the natural substance Hypericin with   the enzyme Pim-1. The focus is on comprehending the extent of their interaction, identifying the types of chemical bonds formed during this process, and assessing the energetic affinity between Hypericin and the Pim-1 enzyme. This simulation aims to provide insights into the molecular dynamics of their association, shedding light on potential mechanisms of action and contributing to a deeper understanding of the biochemical processes involved.

Hypericin is a natural compound that belongs to a class of organic compounds known as polycyclic polyprenylated acylphloroglucinols (PPAPs). It is found in the genus Hypericum, commonly known as St. John's wort. Hypericin is known for its pharmacological properties, and it has been studied for various potential medical applications.

There have been several studies suggesting potential anticancer properties of hypericin, the natural compound found in St. John's wort. The anticancer effects of hypericin have been explored in various in vitro and in vivo experiments[5,6].

2. Material and Methods

Proto-oncogene serine/threonine-protein kinase pim-1 target was taken from Protein Data Bank (PDB Code: 3bgz) and was prepared from Mcule Database [7], before to perform docking analysis with Autodock Vina[8]. Molecular Docking investigation was evaluated in the Binding site center of this target with the following coordinated: X(-19,2277), Y(37,3128) Z(-1,4445).

3. Results and Discussion

Detailed understanding of Pim-1 and its regulatory mechanisms may provide crucial information for the development of new therapeutic strategies in the treatment of pathological conditions, particularly those related to cancer [1–4]. The protein kinase Pim-1 is a crucial enzyme in the regulation of cellular processes such as growth, survival and differentiation. Deriving from the PIM1 gene, it is a proto-oncogene involved in the transformation of normal cells into cancerous cells. Initially associated with murine T-cell lymphomas, it is frequently activated by Moloney murine leukemia virus[1–4]. Expressed in different tissues and in human tumor cultures, Pim-1 regulates the cell cycle, apoptosis and transcriptional activation, also participating in cellular signaling pathways. Involved in several neoplasms, such as prostate cancer and acute myeloid leukemia, Pim-1 is the subject of intense oncological research[1–4].Considered a potential therapeutic target, studies are underway on drugs that aim to inhibit Pim-1, suggesting new prospects for cancer treatment. From docking results Hypericin showed a high score of binding energy of about -12.5 kcal/mol   with this target, indicating a relatively high binding affinity, suggesting that hypericin may form stable interactions with the Pim-1 enzyme (See below Figure 1). Lower scores, in this context, are generally associated with stronger interactions.This strong binding could have implications for potential therapeutic applications or further research exploring the interaction's biological significance.
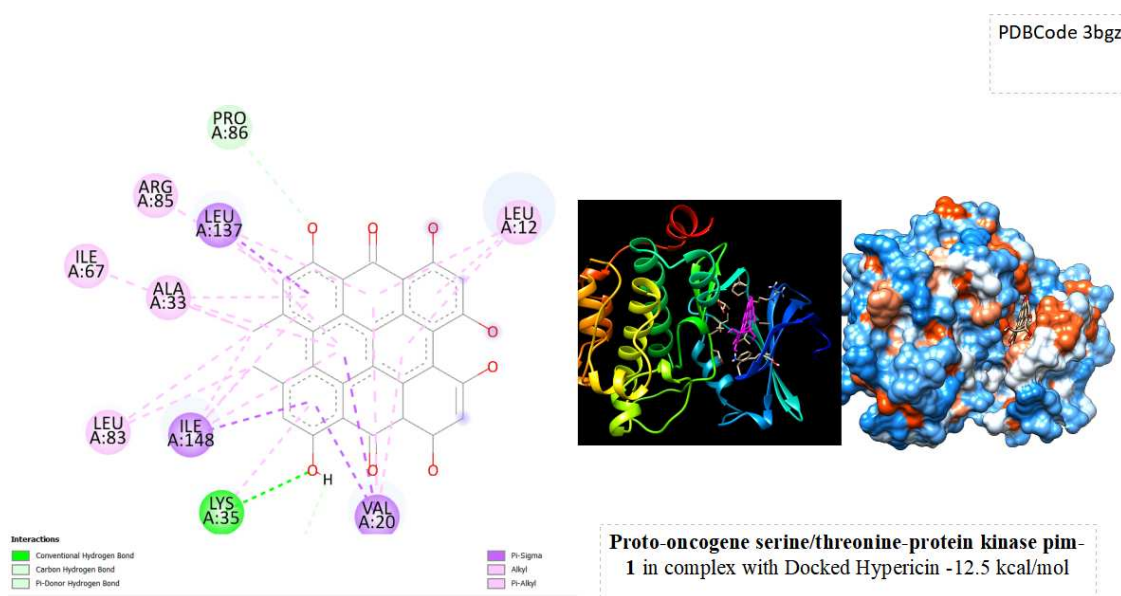

Figure 1. Displays the docking outcomes of Proto-oncogene serine/threonine-protein kinase pim-1 in conjunction with Hypericinwithin the Ligand Binding Site, as analyzed by Autodock Vina through the Mcule Database. On the left side, 2D diagrams illustrate the residue interactions between the protein and Hypericin. Meanwhile, the right side exhibits the Ligand Binding Site of the protein, highlighting the specific location of Hypericin.

4. Conclusion

From docking simulations Hypericin with   Pim-1 enzyme in the Ligand Binding Site obtained a Vina score of -12.5 kcal/mol , indicating a robust binding affinity.   The negative docking score suggests that hypericin is energetically favorable in its interaction with the Pim-1 enzyme. This could be indicative of a potential for hypericin to modulate the activity of Pim-1.

While docking studies provide valuable insights into potential interactions, experimental validation is crucial to confirm these predictions. Further studies, such as molecular dynamics simulations or binding assays, would help validate and characterize the nature of the Pim-1 and hypericin interaction.

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