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Usnic acid as potential inhibitors of BCL2 and PI3K protein through network pharmacology-based analysis, molecular docking and molecular dynamic simulation

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Abstract

Usnic acid (UA) lately piqued the interest of researchers for its extraordinary biological characteristics, including anticancer activity. Here, the mechanism was clarified through network pharmacology, molecular docking and molecular dynamic simulation. Sixteen proteins were selected through network pharmacology study as they are probable to interact with UA. Out of these proteins, 13 were filtered from PPI network analysis based on their significance of interactions ($p < 0.05$). KEGG pathway analysis has also aided us in determining the three most significant protein targets for UA, which are BCL2, PI3KCA and PI3KCG. Therefore molecular docking and molecular dynamic (MD) simulations throughout 100 ns were performed for usnic acid onto the three proteins mentioned. However, UA's docking score in all proteins is lower than their co-crystallised ligand, especially for BCL2 (-36.5158 kcal/mol) and PI3KCA (-44.5995 kcal/mol) proteins. The only exception is PI3KCG which has comparable results with the co-crystallised ligand with (-41.9351 kcal/mol). Furthermore, MD simulation has also revealed that usnic acid does not stay fit in the protein throughout the simulation trajectory for PI3KCA protein evident from RMSF and RMSD plots. Nevertheless, it still poses good ability in inhibiting BCL2 and PI3KCG protein in MD simulation. In the end, usnic acid has exhibited good potential in the inhibition of PI3KCG proteins, rather than the other proteins mentioned. Thus further study on structural modification of usnic acid could enhance the ability of usnic acid in the inhibition of PI3KCG as anti-colorectal and anti-small cell lung cancer drug candidate. Communicated by Ramaswamy H. Sarma. © 2023 Informa UK Limited, trading as Taylor & Francis Group.

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MD simulation; molecular docking; network pharmacology; PPI; usnic acid

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