Association of indomethacin with phospholipids increases their potential application against colorectal cancer

Autorzy

Anna Palko-Łabuz

Olga Wesołowska

Anna Gliszczyńska

Vaikunthavasan Thiruchenthooran

Magdalena Skonieczna

Kamil Wojtkowiak

Aneta Jezierska

Anna Uryga

Kamila Środa-Pomianek

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Kolekcja

Naukowa

Streszczenie

Colon cancer is currently the leading cause of cancer death in men and the second in women under 50. Standard therapy includes surgical resection and - in the case of non-resectable CRC -radiotherapy, chemotherapy and immunotherapy. One of the therapeutic approaches is also a combinational regimen. Numerous experimental, epidemiological and clinical studies suggest that non-steroidal anti-inflammatory drugs (NSAIDs) may exert anticancer effects against colon cancer. In our work, we studied the effect of pure indomethacin (IND) and two lipid hybrids containing IND on HT29 and HT29/Dx cells. We analyzed the cytotoxicity and anti-inflammatory potential of the compounds but also their ability to induce apoptosis and produce reactive oxygen species. Experimental investigations were complemented by theoretical studies on the based on Density Functional Theory (DFT), molecular docking and classical molecular dynamics. These studies enabled a detailed description of the ligands and host-guest complexes. Based on the molecular docking study a general picture of the binding affinity to ABCB1 and COX-2 proteins was obtained. Moreover, we were able to detect amino acids involved in the protein-ligand complex formation. Classical molecular dynamics provided information on the thermodynamic properties and stability of the investigated complexes. We found that lysophosphatidylcholine containing IND represented a promising candidate for adjuvant therapy of colon cancer.

Słowa kluczowe

Adjuvant therapy, Colon cancer, Indomethacin (IND), Indomethacin-phospholipid conjugates, Density functional theory (DFT), Molecular docking, Molecular dynamics