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Computational Modeling Approaches for the Identify of Potent Inhibitors as Anticancer Agents Phosphoinositide 3-Kinase Gamma (PI3Kγ)

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Abstract

Phosphoinositide 3-kinase gamma (PI3Kγ) is recognized as a promising target for inhibiting the activity of cancer cells, leading to increased efforts to develop PI3Kγ inhibitors as potential cancer therapies. In this study, Quantitative Structure-Activity Relationship (QSAR) modeling using Coral software was performed on a dataset comprising 243 PI3Kγ inhibitor compounds, and the promoters that enhance and reduce their biological activity were interpreted. Subsequently, virtual screening was conducted on 217,999,321 molecules employing structure-based pharmacophore modeling methods and molecular docking, ultimately identifying nine new PI3Kγ inhibitors. The molecular docking results confirmed the promoters identified in the QSAR modeling. Additionally, ADMET computational studies were carried out to evaluate the safety and pharmacokinetic properties of the selected compounds. The findings of this research indicate that the nine identified molecules can be utilized to design new PI3Kγ inhibitors with improved efficacy. Overall, this study highlights the potential of computational modeling techniques in accelerating the drug discovery process for anti-cancer therapies.

Keywords: Phosphoinositide 3-kinase gamma, inhibitor, QSAR, Virtual screening