Identification Of 11- Hydroxytephrosin And Torosaflavone A as Potential Inhibitors Of 3- Phosphoinositide-Dependent Protein Kinase 1 (PDPK1): Toward Anticancer Drug Discovery	
Authors	**Akhtar Atiya 1, Fahad A Alhumaydhi 2, Sharaf E Sharaf 3 4, Waleed Al Abdulmonem 5, Abdelbaset Mohamed Elasbali 6, Maher M Al Enazi 7, Anas Shamsi 8 9, Talha Jawaid 10, Badrah S Alghamdi 11 12, Anwar M Hashem 13 14, Ghulam Md Ashraf 12 15, Moyad Shahwan**
Publication Year	2022
Grant Number	
DOI link	https://doi.org/10.3390/biology11081230

The 3-phosphoinositide-dependent protein kinase 1 (PDPK1) has a significant role in cancer progression and metastasis as well as other inflammatory disorders, and has been proposed as a promising therapeutic target for several malignancies. In this work, we conducted a systematic virtual screening of natural compounds from the IMPPAT database to identify possible PDPK1 inhibitors. Primarily, the Lipinski rules, ADMET, and PAINS filter were applied and then the binding affinities, docking scores, and selectivity were carried out to find effective hits against PDPK1. Finally, we identified two natural compounds, 11-Hydroxytephrosin and Torosaflavone A, bearing substantial affinity with PDPK1. Both compounds showed drug-likeness as predicted by the ADMET analysis and their physicochemical parameters. These compounds preferentially bind to the ATP-binding pocket of PDPK1 and interact with functionally significant residues. The conformational dynamics and complex stability of PDPK1 with the selected compounds were then studied using interaction analysis and molecular dynamics (MD) simulations for 100 ns. The simulation results revealed that PDPK1 forms stable docked complexes with the elucidated compounds. The findings show that the newly discovered 11-Hydroxytephrosin and Torosaflavone A bind to PDPK1 in an ATP-competitive manner, suggesting that they could one day be used as therapeutic scaffolds against PDPK1-associated diseases including cancer.