Screening of potential PI3K inhibitors from food compound database (FooDB)

Cancer is the second-most common cause of death in the United States and a significant global public health issue. As one of the most often activated pathogenic signaling pathways in human malignancies, the phosphatidylinositol-3 kinase (PI3K) pathway is a relevant and significant target for developing novel anticancer therapy. Phosphatidylinositol 3-kinases (PI3Ks) consist of a family of three distinct classes of lipid kinases. The most explored of these classes is Class I PI3K, which has a clear role in oncogenic transformation and tumor growth. Our goal in this study was the screening of detected and quantified compounds from the food database (FooDB) first by using computational screening followed by Invitro assays to find potential dietary compounds that inhibit PI3K activity and prevent cancer risk. Lipinski's rule with molecular weight cutoff of 600 Da was used as a filter to minimize the compounds. The binding affinity of the selected compounds at the substrate binding site of the PI3Kα,γ,δ was assessed using a molecular docking approach, and top-hit compounds were selected based on binding energy (Kcal) and hydrogen bonding with catalytic lysine (K802), (K833) and (K779) respectively. Equol, Nepetin, Tricin, Cyclocurcumin, and Sakuranetin were identified as the top hit compounds for PI3Kα. In case of PI3Kγ Theaflavine, citracridone-I, delta-viniferin and coumestrol were identified as the top hit compounds. While for PI3Kδ the best compounds were Estrone, Xanthyletin, Tricin, Coumestrol and so on. Molecular dynamics studies will be performed to check the stability of the binding complexes. Further in vitro enzymatic assays and cell culture studies will be warranted in the future to find out potential PI3K inhibitors.