

In Silico Identification of Plant-Derived Dual-Target Inhibitors of BAX and ROCK1 for Triple-Negative Breast Cancer: A Structure-Based Virtual Screening and ADMET Profiling Study

Zubishah Rais

Delhi Technological University, New Delhi, India

Dr. Prakash Chandra

Delhi Technological University, New Delhi, India

Abstract

Triple negative breast cancer does not have any receptors such as those targeted by hormones or HER2; thus, chemotherapy remains the only known systematic treatment approach that results in poor outcomes, fast relapse rate, and high risk of metastasis. Discovery of novel drug targets and promising drug-like molecules should remain a top clinical goal. The current research analyzed 40 plant-derived bioactive compounds targeting two proteins of TNBC treatment, BCL-2 Associated X Protein (BAX) and Rho-associated Coiled-Coil Kinase 1 (ROCK1), using AutoDock Vina v1.2.7 docking simulation tool. BAX is a major mediator of cell apoptosis via intrinsic mitochondrial pathways, whereas ROCK1 mediates cell invasiveness and metastasis through the epithelial to mesenchymal transition. Dual-target inhibitors were further characterized for their physicochemical and pharmacokinetic properties using SwissADME. The best-scoring dual-target drug candidate was chosen based on total dual target score, with Luteolin scoring at -14.478 Kcal/mol indicating high affinity to both target proteins ADMET profiling confirmed Lipinski compliance with zero violations, high predicted gastrointestinal absorption, and a satisfactory bioavailability score of 0.55 The SwissADME BOILED-Egg results additionally proved that there is a great absorption in intestines without blood-brain barrier permeability, which is an ideal characteristic for peripheral anti-cancer drugs. In summary, Luteolin, a natural flavonoid present in different vegetables and fruits, was discovered as a possible two-target drug against TNBC because it has the ability to stimulate BAX and inhibit ROCK1 at the same time. The aforementioned facts provide the basis for future experimentation regarding Luteolin's cytotoxic effects on TNBC cells, apoptosis induction, and inhibition of cell invasion and migration.

Keywords

Triple-negative breast cancer, BAX, ROCK1, molecular docking, flavonoids, luteolin.