Molecular docking study of selected natural compounds for cancer stem cells targeted anti-cancer activity

Karthika M[1], Samarakoon SR[1], Tennekoon KH[1], Siriwardana A[2]

[1]Institute of Biochemistry, Molecular Biology and Biotechnology, University of Colombo

[2] Sri Lanka Institute of Nano Technology, Sri Lanka

Cancer stem cells (CSCs) play significant roles in tumor initiation, relapse, angiogenesis, metastasis and therapy. Collectively Wnt, notch and hedgehog are major pathways that have been linked to the resistance of CSCs to conventional therapy. Most conventional therapies are directed at the rapidly growing tumor mass but not at the slow dividing CSCs. Eliminating CSCs has been suggested as a promising approach to cure cancer. *In-silico* molecular docking simulations were carried out for the binding of 35 selected natural compounds with receptor proteins which are involved in the main signaling pathways of CSCs, such as β-catenin chain A and Smo receptor from the Wnt and hedgehog pathways respectively, using Hex 8.0.0, DOCK6 and AutoDockVina software. Additionally docking interaction residue analysis, score functions such as Drug score, X score, Per Contact Score (PCS) and Average affinity PCS and drug-likeness study were carried out for the selected compounds. Overall, 11 compounds were identified with good binding energy, interaction, binding affinity and better drug likeness for β-catenin chain A involved in Wnt inhibition. There was no considerable overall binding ability for Smo inhibition. Energy values for Wnt inhibition obtained using AutoDockVina were as follows. Gedunin (-7.3 kcal/mol), Kaempferol (-6.1

kcal/mol), Methylripariochromene A (-5.3 kcal/mol), Myrigalone G (-5.1 kcal/mol), Catechin (-6.5 kcal/mol), Myricetin (-6.5 kcal/mol), Discretine (-5.6 kcal/mol), Laurolitsine (-5.9 kcal/mol), Myricitrin (-6.3 kcal/mol), Nordicentrine (-6.0 kcal/mol) and Phloretin (-5.4 kcal/mol). These novel Wnt inhibitors need further attention to assess their potential application in CSC targeted therapy.