Abstract No: STEM 26 Science, Technology, Engineering and Mathematics

In silico study of physicochemical, pharmacokinetic, toxicity, metabolism and molecular docking of aristolactam E, a constituent of *Aristolochia elegans* Mast

Wadanambi P. M.[1]*, Seneviratne K. N.[1], Jayathilaka N.[1]

Aristolochia elegans Mast, also known as Calico flower, is an ornamental plant found around the world including Asia. In traditional medicine, the plant has been used to treat a variety of disorders by employing its broad spectrum of pharmacological properties such as antibacterial, antitumoral, antidiarrheal, anti-snake venom, and anti-scorpion venom. It is also rich in aristolactam alkaloids, which have a variety of biological effects including anti-inflammatory, antibacterial, and anticancer activities. Aristolactam E (AE) is one of the less studied aristolactam alkaloids found in *Aristolochia elegans* Mast. Therefore, this computational study was designed to investigate (a) physicochemical properties and drug likeness, (b) pharmacokinetic and toxicity, (c) mode of antibacterial, anticancer and antiinflammatory action, (d) sites of metabolism mediated by cytochrome P450 (CYP) 3A4 isoform and (e) probable metabolites of AE compound. The physicochemical attributes and drug likeness were assessed using molinspiration server. SwissADME, LASAR, and Pred-hERG 4.2 servers were used to estimate pharmacokinetic and toxicological characteristics. Molecular docking was performed using AutoDock 4.2 software to determine the binding affinity and molecular interactions of AE with protein targets namely, dihydropteroate synthase (DHPS), dihydroneopterin aldolase (DHNA), phospholipase A2 (PLA2) and tankyrase 2 (TNK2). SOMP, SMARTcyp, and RS-WebPredictor webservers were used to predict the sites of AE metabolism mediated by the CYP 3A4 isoform. Furthermore, the BioTransformer and GLORYx online tools were used to forecast the potential AE metabolites. AE demonstrated favorable physicochemical qualities and met the requirements for oral bioavailability and druggability by following both Lipinski's rule of five and the Veber rule. It also showed a high rate of human intestinal absorption and no blood-brain barrier permeability. Furthermore, the toxicity predictions revealed that AE was a mutagenic chemical, but it was not carcinogenic or cardiotoxic in the mouse model. The AE showed binding affinity of -5.45 kcal/mol, -8.79 kcal/mol, -7.32 kcal/mol, -8.30 kcal/mol and -8.41 kcal/mol with DHPS, DHNA, PLA2, TNK2 (nicotinamide binding site) and TNK2 (adenosine binding site) respectively. The AE exhibited a stronger binding affinity than the control compounds of DHNA and PLA2 while showing close binding affinity to the control of TNK2 (nicotinamide binding site). The overall evaluation identified two sites of metabolism of AE based on a consensus of different metabolism site predictions by CYP3A4 using SOMP, SMARTcyp and RS-WebPredictor webservers. Two probable metabolites of AE were proposed based on the consensus of the results of BioTransformer and GLORYx web tools. This computational analysis can aid in the development of AE derivatives with improved pharmacokinetic and toxicological profiles, hence accelerating drug discovery against microbial infections and inflammation.

Keywords: *Aristolochia elegans* Mast, Aristolactam E, Molecular docking, Metabolism, Toxicity

[1] Department of Chemistry, Faculty of Science, University of Kelaniya, Sri Lanka
∗ pwadanambi@gmail.com