Computational study of linamarin and its synthetic analogues as substrates for alpha and beta human glucosidase enzymes

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Cancer is a potentially lethal non communicable disease. The objective of this study was to follow an *in-silico* approach to propose and verify synthetic organic analogues of the natural glucoside linamarin as targeted anti-cancer drugs. Being a β-glucoside, linamarin acts as a substrate for β-glucosidase enzymes. In *Cassava* plant, a β-glucosidase known as linamarase occurs. It hydrolyzes linamarin to form hydrogen cyanide. A hypothesis can be drawn out that if necessary conditions are available, this reaction could occur in a living human cell with the aid of any cytosolic β-glucosidase enzyme present. If the selected cell was a mutated cancer cell, this activity can kill the cell by cyanide toxicity. By conducting a BLAST search using natural linamarase enzyme (PDB entry; 1CBG) as the reference query sequence, two similar beta and alpha human glucosidase enzymes (PDB entries; 2E9L and 2QLY respectively) were found. The linamarin analogues and reference ligands were drawn in Spartan'14 as 3D builds. The geometry of each was optimized by HF/6-31G*. The initial crystal structures of proteins were docked separately with the set of ligands by using GOLD 5.3.0. All the docking results were visualized using BIOVIA Discovery Studio 2016 Client and interaction diagrams were obtained. The virtual screening study shows that furanoses have better affinity than pyranoses, as the substrate, regardless of the nature of the glucosidase enzyme.

Keywords: linamarin, analogues, docking, interactions