Identification of α-glucosidase inhibitorsfrom Clinacanthus nutans leaf extract using liquid chromatography-mass spectrometry-based metabolomics and protein-ligand interaction with molecular docking

ABSTRACT

The present study used in vitro and in silico techniques, as well as the metabolomics approach to characterise α-glucosidase inhibitors from different fractions of Clinacanthus nutans. C. nutans is a medicinal plant belonging to the Acanthaceae family, and is traditionally used to treat diabetes in Malaysia. n-Hexane, n-hexane: ethyl acetate (1:1, v/v), ethyl acetate, ethyl acetate: methanol (1:1, v/v), and methanol fractions were obtained via partitioning of the 80% methanolic crude extract. The in vitro α-glucosidase inhibitory activity was analyzed using all the fractions collected, followed by profiling of the metabolites using liquid chromatography combined with mass spectrometry. The partial least square (PLS) statistical model was developed using the SIMCA P+14.0 software and the following four inhibitors were obtained: (1) 4,6,8-Megastigmatrien-3-one; (2) N-Isobutyl-2-nonen-6,8-diynamide; (3) 1′,2′-bis(acetyloxy)-3′,4′-didehydro-2′-hydro-β, ψ-carotene; and (4) 22-acetate-3-hydroxy-21-(6-methyl-2,4-octadienoate)-olean-12-en-28-oic acid. The in silico study performed via molecular docking with the crystal structure of yeast isomaltase (PDB code: 3A4A) involved a hydrogen bond and some hydrophobic interactions between the inhibitors and protein. The residues that interacted include ASN259, HID295, LYS156, ARG335, and GLY209 with a hydrogen bond, while TRP15, TYR158, VAL232, HIE280, ALA292, PRO312, LEU313, VAL313, PHE314, ARG315, TYR316, VAL319, and TRP343 with other forms of bonding.

Keyword: Clinacanthus nutans; LC-MS-QTOF; Metabolomics; α-Glucosidase inhibitors; Diabetes; Molecular docking