



## Original Article

Identification of  $\alpha$ -glucosidase inhibitors from *Clinacanthus nutans* leaf extract using liquid chromatography-mass spectrometry-based metabolomics and protein-ligand interaction with molecular dockingSuganya Murugesu<sup>a</sup>, Zalikha Ibrahim<sup>a</sup>, Qamar Uddin Ahmed<sup>a</sup>, Bisha Fathamah Uzir<sup>a</sup>,  
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## ARTICLE INFO

## Article history:

Received 28 February 2018

Received in revised form

13 November 2018

Accepted 14 November 2018

Available online 15 November 2018

## Keywords:

*Clinacanthus nutans*

LC-MS-QTOF

Metabolomics

 $\alpha$ -Glucosidase inhibitors

Diabetes

Molecular docking

## ABSTRACT

The present study used *in vitro* and *in silico* techniques, as well as the metabolomics approach to characterise  $\alpha$ -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*  $\alpha$ -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<sup>+</sup> 14.0 software and the following four inhibitors were obtained: (1) 4,6,8-Megastigmatrien-3-one; (2) N-Isobutyl-2-nonen-6,8-dynamide; (3) 1',2'-bis(acetyloxy)-3',4'-didehydro-2'-hydro- $\beta$ ,  $\psi$ -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.

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## 1. Introduction

Regulating hyperglycemic conditions with modern medicine or herbal remedies is a therapeutic method that can be used to manage type-2 diabetes mellitus (DM). Many natural resources have been investigated for their ability to suppress the glucose production from carbohydrates in the gut, or absorption of glucose from the intestines [1]. Typically, type-2 DM is described as a metabolic disorder associated with hyperglycaemia and an increased blood glucose level, which results in damages to the human body. Presently, type-2 DM is regarded as the major leading

cause of mortality, and is referred to as an epidemic as the number of cases continues to increase epidemically [2]. Medicinal plants have been used traditionally in diabetes management. Nowadays, many researches performed are focused on the use of medicinal plants as an alternative form of type-2 DM management. Medicinal plants consist of a complex mixture of phytoconstituents that enables them to exhibit their medicinal properties through synergistic actions [3].

*Clinacanthus nutans* (*C. nutans*) (Burm. F) Lindau, a medicinal shrub commonly known as Sabah snake grass, belongs to the diverse family of Acanthaceae. This group of flowering plants can easily grow in many different habitats such as bushes, forests, swamps and mangrove areas. *C. nutans* is native to Malaysia, China, Indonesia, as well as Thailand, and is widely distributed in the locality of these countries. Many scientific studies have demonstrated the therapeutic potential of *C. nutans* including its antiviral, anti-inflammatory, antioxidant, neuromodulatory and

Peer review under responsibility of Xi'an Jiaotong University.

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