UNIVERSITI TEKNOLOGI MARA

SERUM METABOLIC PROFILING FOR DETECTION OF ALZHEIMER'S DISEASE

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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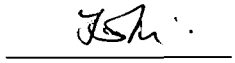
Signature of Student	: 
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ABSTRACT

Alzheimer's disease (AD) is characterised by loss of memory and deterioration of cognitive function. To date, AD treatment remains a great challenge as pathogenesis of this disease is still poorly understood. Reliable AD biomarkers would therefore be of high relevance, not only to assist early detection but also to uncover potential drug targets that can be manipulated to slow down disease progression. This study compared metabolomic profiles of blood serum from AD patients to those of the non-demented controls. Qualitative metabolomic profiles of blood serum were acquired using the liquid chromatography/mass spectrometry quadrupole time-of-flight (LC-MSQTOF) and Nuclear Magnetic Resonance (NMR). The most important finding that emerged from this study is that lipids and amino acids are responsible for the metabolic changes linked to AD. The present study has revealed four LC-MS-derived metabolites [(N-(2-hydroxyethyl)palmitamide, N-(2-hydroxyethyl)icosanamide, dihydroceramide, phytosphingosine] and four NMR-derived metabolites (isoleucine, creatinine, VLDL, lipid) that might be implicated in AD pathogenesis. These metabolites panel may serve as potential biomarkers which are associated with neuronal β amyloid release, apoptosis, dysregulated energy metabolism and brain oxidative impairment that will lead to neuronal cell death. In terms of pathways, sphingolipid metabolism and biosynthesis of valine, leucine and isoleucine were found to be perturbed in AD. Comparison of metabolomic profiles obtained through LC-MS and NMR indicated high complementarity between these two platforms. The present findings demonstrated the complementary nature of NMR and LC/MS, implying that combination use of NMR and LC/MS facilitated a more comprehensive profiling of metabolite.

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TABLE OF CONTENTS